OMB Number: 4040-0001
Expiration Date: 10/31/2019

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier**

1. TYPE OF SUBMISSION*

❍ Pre-application ● Application ❍ Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

c. Previous Grants.gov Tracking Number

2. DATE SUBMITTED

Application Identifier
Cosme 27370

5. APPLICANT INFORMATION

Organizational DUNS*: 0792896260000

Legal Name*: UNIVERSITY OF OREGON
Department:
Division:
Street1*: c/o Sponsored Projects Services
Street2: 5219 UNIVERSITY OF OREGON
City*: EUGENE
County:
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 974035219

Person to be contacted on matters involving this application

Prefix: First Name*: Stephanie Middle Name: Last Name*: Gray Suffix:
Position/Title: Sponsored Projects Administrator, Pre-Award
Street1*: 5219 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-5219
Phone Number*: 541-346-5131 Fax Number: 541-346-5138 Email: sponsoredprojects@uoregon.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1464727800A1

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).

❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
A multi-method translational neuroscience approach to cancer prevention via health behavior change

12. PROPOSED PROJECT

Start Date* Ending Date*
09/01/2019 08/31/2025

13. CONGRESSIONAL DISTRICTS OF APPLICANT
OR-004

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: Danielle Middle Name: Last Name*: Cosme Suffix:
Position/Title:
Organization Name*: University of Oregon
Department: Psychology
Division: Ctr for Translational Neurosci
Street1*: 1227 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-1227
Phone Number*: [redacted] Fax Number: Email*: dcosme@uoregon.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$515,706.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$515,706.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Dr. First Name*: David Middle Name: O. Last Name*: Conover Suffix: Ph.D
Position/Title*: Vice President for Research and Innovation
Organization Name*: University of Oregon
Department: Research and Innovation
Division: Sponsored Projects Services
Street1*: 5219 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 97403-5219
Phone Number*: 541-346-5131 Fax Number: 541-346-5138 Email*: sponsoredprojects@uoregon.edu

Signature of Authorized Representative*
Completed on submission to Grants.gov

Date Signed*
02/12/2019

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:CoverLetter.pdf

424 R&R and PHS-398 Specific
Table Of Contents

OMB Number: 4040-0010
Expiration Date: 10/31/2019

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	UNIVERSITY OF OREGON
Duns Number:	0792896260000
Street1*:	5219 UNIVERSITY OF OREGON
Street2:	
City*:	EUGENE
County:	
State*:	OR: Oregon
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	974035219
Project/Performance Site Congressional District*:	OR-004

Additional Location(s) File Name:

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ○ **Yes** ● **No**

IRB Approval Date: 07-06-2018

Human Subject Assurance Number 00005914

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	ProjectSummaryAbstract.pdf
8. Project Narrative*	ProjectNarrative.pdf
9. Bibliography & References Cited	BibliographyReferencesCited.pdf
10.Facilities & Other Resources	FacilitiesOtherResources.pdf
11.Equipment	Equipment.pdf
12. Other Attachments	Letter_of_Institutional_Support.pdf

PROJECT SUMMARY / ABSTRACT

Health behaviors, such as poor diet, lack of physical activity, and tobacco and alcohol consumption, increase risk for developing various forms of cancer. These behaviors are modifiable and effective interventions have been developed to promote health behavior change. Critically, however, behavior change interventions do not work equally well for all people. To understand why an intervention works for some individuals and not for others requires *clearly defined neurobiological mechanisms of change* and *sensitive and specific tools to evaluate individual differences* in intervention targets. This proposal seeks to develop a coherent research framework to produce reliable neurobiological indices that can effectively index change in cancer-relevant intervention targets and individual differences in treatment responsivity. Maximizing sensitivity and generalizability requires a multi-method approach that applies advanced neuroimaging and statistical techniques to task-based and task-free fMRI data. I will receive training that will enable me to achieve this objective, including translational neuroscience and advanced longitudinal modeling during the F99 phase, and resting state fMRI and network analytic methods during the K00 phase. My dissertation evaluates the efficacy of an RCT to promote healthy eating and estimates the degree to which cancer-relevant intervention outcomes are moderated by change in a neurobiological index (i.e., “neural signature”) of the intervention target, craving reappraisal. I used machine learning with task-based fMRI to develop a whole-brain signature that is specific to craving reappraisal and has up to 95% out of sample prediction accuracy. This result is significant because it is the first objective measure of craving reappraisal that generalizes across people, thereby increasing sensitivity to detect individual differences in reappraisal ability. In the F99 phase of this proposal, I will assess the degree to which the reappraisal intervention is associated with change in this neural signature, and whether individual differences in neural signature change predict intervention outcomes. In the K00 phase, I will extend this research program to develop neural signatures using task-free resting state fMRI, which may reflect more enduring patterns of health behaviors. To characterize changes in brain networks related to cancer-relevant health behavior change interventions, I will identify reliable network connectivity profiles associated with treatment success and individual differences in treatment responsivity, and directly compare the predictive utility of neural signatures derived from task-based and task-free fMRI. This research program has the potential to substantially improve our ability to detect intervention-related change and individual differences and enable researchers to more effectively evaluate whether, how, and for whom health behavior change intervention is working. Additionally, by developing this framework for creating and validating neural signatures, and openly sharing materials and analytic code, this research program will facilitate the development of neurobiological indices for any number of cancer-relevant intervention targets at any point along the cancer continuum.

PROJECT NARRATIVE

Health behavior change interventions can reduce modifiable cancer risk factors such as unhealthy eating, lack of physical activity, and substance use, but interventions are not equally effective for all individuals. This project will leverage novel multivariate neuroimaging techniques to develop reliable neurobiological indices of target psychological processes in order to improve detection of intervention-related change and individual differences. The knowledge gained from this proposal will enable researchers to more effectively evaluate whether, how, and for whom interventions targeting cancer-relevant health behaviors are working.

BIBLIOGRAPHY & REFERENCES CITED

1. Colditz GA, Emmons KM. Accelerating the Pace of Cancer Prevention- Right Now. Cancer Prevention Research. 2018;11(4):171–184.
2. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, McCullough ML, Patel AV, Ma J, Soerjomataram I, Flanders WD, Brawley OW, Gapstur SM, Jemal A. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(1):31–54. PMID: 29160902
3. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults. New England Journal of Medicine. 2003 Apr 24;348(17):1625–1638. PMID: 12711737
4. Dougan MM, Hankinson SE, Vivo ID, Tworoger SS, Glynn RJ, Michels KB. Prospective study of body size throughout the life-course and the incidence of endometrial cancer among premenopausal and postmenopausal women. Int J Cancer. 2015 Aug 1;137(3):625–637. PMCID: PMC5241095
5. Hoyo C, Cook MB, Kamangar F, Freedman ND, Whiteman DC, Bernstein L, Brown LM, Risch HA, Ye W, Sharp L, Wu AH, Ward MH, Casson AG, Murray LJ, Corley DA, Nyrén O, Pandeya N, Vaughan TL, Chow W-H, Gammon MD. Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium. Int J Epidemiol. 2012 Dec;41(6):1706–1718. PMCID: PMC3535758
6. Wang F, Xu Y. Body mass index and risk of renal cell cancer: a dose-response meta-analysis of published cohort studies. Int J Cancer. 2014 Oct 1;135(7):1673–1686. PMID: 24615287
7. Vineis P, Alavanja M, Buffler P, Fontham E, Franceschi S, Gao YT, Gupta PC, Hackshaw A, Matos E, Samet J, Sitas F, Smith J, Stayner L, Straif K, Thun MJ, Wichmann HE, Wu AH, Zaridze D, Peto R, Doll R. Tobacco and Cancer: Recent Epidemiological Evidence. J Natl Cancer Inst. 2004 Jan 21;96(2):99–106.
8. World Health Organization. WHO report on the global tobacco epidemic 2015 [Internet]. WHO report on the global tobacco epidemic 2015. [cited 2019 Feb 18]. Available from: http://www.who.int/tobacco/global_report/2015/en/
9. Center for Disease Control. Health and Economic Costs of Chronic Disease [Internet]. 2019 [cited 2019 Feb 18]. Available from: https://www.cdc.gov/chronicdisease/about/costs/index.htm
10. Berkman ET, Hutcherson CA, Livingston JL, Kahn LE, Inzlicht M. Self-Control as Value-Based Choice. Curr Dir Psychol Sci. 2017 Oct 1;26(5):422–428.
11. Hare TA, Camerer CF, Rangel A. Self-Control in Decision-Making Involves Modulation of the vmPFC Valuation System. Science. 2009 May 1;324(5927):646–648. PMID: 19407204
12. Cooper N, Tompson S, O'Donnell MB, Vettel JM, Bassett DS, Falk EB. Associations between coherent neural activity in the brain's value system during antismoking messages and reductions in smoking. Health Psychology. 2018;37(4):375–384.
13. Cooper N, Bassett DS, Falk EB. Coherent activity between brain regions that code for value is linked to the malleability of human behavior. Scientific Reports. 2017 Feb 27;7:43250.
14. Doré BP, Tompson SH, O'Donnell MB, An LC, Strecher V, Falk EB. Neural Mechanisms of Emotion Regulation Moderate the Predictive Value of Affective and Value-Related Brain Responses to Persuasive Messages. J Neurosci. 2019 Feb 13;39(7):1293–1300. PMID: 30617213
15. Hutcherson CA, Plassmann H, Gross JJ, Rangel A. Cognitive Regulation during Decision Making Shifts Behavioral Control between Ventromedial and Dorsolateral Prefrontal Value Systems. J Neurosci. 2012 Sep 26;32(39):13543–13554. PMID: 23015444
16. Nook EC, Zaki J. Social Norms Shift Behavioral and Neural Responses to Foods. Journal of Cognitive Neuroscience. 2015 Feb 11;27(7):1412–1426.
17. Cosme D, Mobasser A, Zeithamova D, Berkman ET, Pfeifer JH. Choosing to regulate: does choice enhance craving regulation? Soc Cogn Affect Neurosci. 2018 Mar 1;13(3):300–309.
18. Giuliani NR, Mann T, Tomiyama AJ, Berkman ET. Neural Systems Underlying the Reappraisal of Personally Craved Foods. Journal of Cognitive Neuroscience. 2014 Jan 6;26(7):1390–1402.
19. Kober H, Mende-Siedlecki P, Kross EF, Weber J, Mischel W, Hart CL, Ochsner KN. Prefrontal–striatal pathway underlies cognitive regulation of craving. PNAS. 2010 Aug 17;107(33):14811–14816. PMID: 20679212
20. Siep N, Roefs A, Roebroeck A, Havermans R, Bonte M, Jansen A. Fighting food temptations: The modulating effects of short-term cognitive reappraisal, suppression and up-regulation on

mesocorticolimbic activity related to appetitive motivation. NeuroImage. 2012 Mar;60(1):213–220.
21. Yokum S, Stice E. Cognitive regulation of food craving: Effects of three cognitive reappraisal strategies on neural response to palatable foods. Int J Obes (Lond). 2013 Dec;37(12):1565–1570. PMCID: PMC3709002
22. Stice E, Yokum S, Veling H, Kemps E, Lawrence NS. Pilot test of a novel food response and attention training treatment for obesity: Brain imaging data suggest actions shape valuation. Behaviour Research and Therapy. 2017 Jul 1;94(Supplement C):60–70.
23. Stice E, Lawrence NS, Kemps E, Veling H. Training motor responses to food: A novel treatment for obesity targeting implicit processes. Clinical Psychology Review. 2016;49:16–27.
24. Cosme D, Ludwig RM, Berkman ET. Comparing two neurocognitive models of self-control during dietary decisions. Under review at Social Cognitive and Affective Neuroscience.
25. Berkman ET, Falk EB, Lieberman MD. In the Trenches of Real-World Self-Control: Neural Correlates of Breaking the Link Between Craving and Smoking. Psychological Science. 2011 Apr 1;22(4):498–506.
26. Demos KE, Heatherton TF, Kelley WM. Individual Differences in Nucleus Accumbens Activity to Food and Sexual Images Predict Weight Gain and Sexual Behavior. J Neurosci. 2012 Apr 18;32(16):5549–5552. PMID: 22514316
27. Dager AD, Anderson BM, Rosen R, Khadka S, Sawyer B, Jiantonio-Kelly RE, Austad CS, Raskin SA, Tennen H, Wood RM, Fallahi CR, Pearlson GD. fMRI Response to Alcohol Pictures Predicts Subsequent Transition to Heavy Drinking in College Students. Addiction. 2014 Apr;109(4):585–595. PMCID: PMC3951577
28. Doré BP, Weber J, Ochsner KN. Neural Predictors of Decisions to Cognitively Control Emotion. The Journal of Neuroscience. 2017 Mar 8;37(10):2580–2588.
29. Tooze JA, Subar AF, Thompson FE, Troiano R, Schatzkin A, Kipnis V. Psychosocial predictors of energy underreporting in a large doubly labeled water study. Am J Clin Nutr. 2004 May;79(5):795–804. PMID: 15113717
30. Nisbett RE, Wilson TD. Telling more than we can know: Verbal reports on mental processes. Psychological Review. 1977;84(3):231–259.
31. Miller EK. The prefontral cortex and cognitive control. Nat Rev Neurosci. 2000 Oct;1(1):59–65.
32. Norman KA, Polyn SM, Detre GJ, Haxby JV. Beyond mind-reading: multi-voxel pattern analysis of fMRI data. Trends in Cognitive Sciences. 2006 Sep;10(9):424–430.
33. Chang LJ, Gianaros PJ, Manuck SB, Krishnan A, Wager TD. A Sensitive and Specific Neural Signature for Picture-Induced Negative Affect. PLOS Biol. 2015 Jun 22;13(6):e1002180.
34. Richter FR, Chanales AJH, Kuhl BA. Predicting the integration of overlapping memories by decoding mnemonic processing states during learning. NeuroImage. 2016 Jan;124:323–335.
35. Wager TD, Atlas LY, Lindquist MA, Roy M, Woo C-W, Kross E. An fMRI-Based Neurologic Signature of Physical Pain. New England Journal of Medicine. 2013 Apr 11;368(15):1388–1397. PMID: 23574118
36. Shahane AD, Lopez RB, Denny BT. Implicit reappraisal as an emotional buffer: Reappraisal-related neural activity moderates the relationship between inattention and perceived stress during exposure to negative stimuli. Cogn Affect Behav Neurosci [Internet]. 2018 Nov 28 [cited 2019 Feb 18]; Available from: https://doi.org/10.3758/s13415-018-00676-x
37. Zeithamova D, Preston AR. Temporal Proximity Promotes Integration of Overlapping Events. Journal of Cognitive Neuroscience. 2017 Aug;29(8):1311–1323.
38. Gross JJ. Antecedent-and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. Journal of personality and social psychology. 1998;74(1):224.
39. Woo C-W, Chang LJ, Lindquist MA, Wager TD. Building better biomarkers: brain models in translational neuroimaging. Nature Neuroscience. 2017 Feb 23;20(3):365–377.
40. Giuliani NR, Pfeifer JH. Age-related changes in reappraisal of appetitive cravings during adolescence. Neuroimage. 2015 Mar;108:173–181. PMCID: PMC4817999
41. Esteban O, Markiewicz CJ, Blair RW, Moodie CA, Isik AI, Erramuzpe A, Kent JD, Goncalves M, DuPre E, Snyder M, Oya H, Ghosh SS, Wright J, Durnez J, Poldrack RA, Gorgolewski KJ. fMRIPrep: a robust preprocessing pipeline for functional MRI. Nature Methods. 2019 Jan;16(1):111.
42. Op de Beeck HP. Against hyperacuity in brain reading: Spatial smoothing does not hurt multivariate fMRI analyses? NeuroImage. 2010 Feb 1;49(3):1943–1948.
43. Friston KJ, Holmes AP, Worsley KJ, Poline J-P, Frith CD, Frackowiak RSJ. Statistical parametric maps in functional imaging: A general linear approach. Human Brain Mapping. 1994;2(4):189–210.
44. Rosseel Y. lavaan: An R Package for Structural Equation Modeling. Journal of Statistical Software.

2012;48(2):1–36.
45. R Core Team. R [Internet]. 2016. Available from: http://www.R-project.org
46. Cole MW, Bassett DS, Power JD, Braver TS, Petersen SE. Intrinsic and Task-Evoked Network Architectures of the Human Brain. Neuron. 2014;83(1):238–251.
47. Raichle ME. Two views of brain function. Trends in Cognitive Sciences. 2010 Apr;14(4):180–190.
48. Mueller S, Wang D, Fox MD, Yeo BTT, Sepulcre J, Mert R. Sabuncu, Rebecca Shafee, Jie Lu, Hesheng Liu. Individual Variability in Functional Connectivity Architecture of the Human Brain. Neuron. 2013;77(3):586–595.
49. Chen B, Xu T, Zhou C, Wang L, Yang N, Wang Z, Dong H-M, Yang Z, Zang Y-F, Zuo X-N, Weng X-C. Individual Variability and Test-Retest Reliability Revealed by Ten Repeated Resting-State Brain Scans over One Month. PLOS ONE. 2015 Dec 29;10(12):e0144963.
50. Liu W, Kohn N, Fernández G. Intersubject similarity of personality is associated with intersubject similarity of brain connectivity patterns. NeuroImage. 2019 Feb 1;186:56–69.
51. Tompson SH, Falk EB, Vettel JM, Bassett DS. Network Approaches to Understand Individual Differences in Brain Connectivity: Opportunities for Personality Neuroscience. Personality Neuroscience [Internet]. 2018;1. Available from: http://dx.doi.org/10.1017/pen.2018.4
52. Baldassarre A, Lewis CM, Committeri G, Snyder AZ, Romani GL, Corbetta M. Individual variability in functional connectivity predicts performance of a perceptual task. Proceedings of the National Academy of Sciences. 2012;109(9):3516–3521.
53. Reineberg AE, Gustavson DE, Benca C, Banich MT, Friedman NP. The Relationship Between Resting State Network Connectivity and Individual Differences in Executive Functions. Frontiers in Psychology. 2018;9:1600.
54. Bassett DS, Xia CH, Satterthwaite TD. Understanding the Emergence of Neuropsychiatric Disorders with Network Neuroscience. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2018;3(9):742–753.
55. Wang L, Hermens DF, Hickie IB, Lagopoulos J. A systematic review of resting-state functional-MRI studies in major depression. Journal of Affective Disorders. 2012;142(1–3):6–12.
56. Bassett DS, Nelson BG, Mueller BA, Camchong J, Lim KO. Altered resting state complexity in schizophrenia. NeuroImage. 2012 Feb 1;59(3):2196–2207.
57. Cao W, Cao X, Hou C, Li T, Cheng Y, Lijuan Jiang, Cheng Luo, Chunbo Li, Dezhong Yao. Effects of Cognitive Training on Resting-State Functional Connectivity of Default Mode, Salience, and Central Executive Networks. Frontiers in Aging Neuroscience. 2016;8:70.
58. Voss MW, Prakash RS, Erickson KI, Basak C, Chaddock L, Kim JS, Alves H, Heo S, Szabo AN, White SM, Wójcicki TR, Mailey EL, Gothe N, Olson EA, McAuley E, Kramer AF. Plasticity of Brain Networks in a Randomized Intervention Trial of Exercise Training in Older Adults. Front Aging Neurosci [Internet]. 2010 Aug 26 [cited 2019 Feb 19];2. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2947936/ PMCID: PMC2947936
59. Flodin P, Jonasson LS, Riklund K, Nyberg L, Boraxbekk CJ. Does Aerobic Exercise Influence Intrinsic Brain Activity? An Aerobic Exercise Intervention among Healthy Old Adults. Frontiers in Aging Neuroscience. 2017;9:267.
60. McGregor KM, Crosson B, Krishnamurthy LC, Krishnamurthy V, Hortman K, Kaundinya Gopinath, Kevin M. Mammino, Javier Omar, Joe R. Nocera. Effects of a 12-Week Aerobic Spin Intervention on Resting State Networks in Previously Sedentary Older Adults. Frontiers in Psychology. 2018;9:2376.
61. Tavor I, Jones OP, Mars RB, Smith SM, Behrens TE, Jbabdi S. Task-free MRI predicts individual differences in brain activity during task performance. Science. 2016 Apr 8;352(6282):216–220. PMID: 27124457
62. Dosenbach NUF, Nardos B, Cohen AL, Fair DA, Power JD, Church JA, Nelson SM, Wig GS, Vogel AC, Lessov-Schlaggar CN, Barnes KA, Dubis JW, Feczko E, Coalson RS, Pruett JR, Barch DM, Petersen SE, Schlaggar BL. Prediction of Individual Brain Maturity Using fMRI. Science. 2010;329(5997):1358–1361.
63. Xia CH, Ma Z, Ciric R, Gu S, Betzel RF, Kaczkurkin AN, Calkins ME, Cook PA, Garza AG de la, Vandekar SN, Cui Z, Moore TM, Roalf DR, Ruparel K, Wolf DH, Davatzikos C, Gur RC, Gur RE, Shinohara RT, Bassett DS, Satterthwaite TD. Linked dimensions of psychopathology and connectivity in functional brain networks. Nature Communications. 2018 Aug 1;9(1):3003.

FACILITIES AND OTHER RESOURCES

University of Oregon

The University of Oregon (UO) is classified as a Carnegie Doctoral/Research University–Extensive and has a history of substantial research, federal grant funding, and scientific inquiry. The College of Arts and Sciences (CAS), which includes the Department of, comprises 40 departments and programs, with 463 tenure-track faculty. The research activity of CAS faculty is the basis for the UO's status as a Carnegie Research I institution and its membership in the Association of American Universities. In the past 5 years, three faculty have been elected to the National Academy of Sciences, three named Sloan Research Fellows, five elected to the American Academy of Arts and Sciences, five named Guggenheim Fellows, seven elected as American Mathematical Society Fellows, and nine elected to the American Association for the Advancement of Science, with an additional faculty member elected as president of the AAAS.

UO provides comprehensive instructional, research, and public service programs that advance scientific and humanistic knowledge. Research programs serve the educational, cultural, and economic needs of the region and the nation. Administrative units provide direct oversight and support for graduate programs, grant proposal submission, research compliance, contracts and grant administration, and research initiatives. UO has collaborative research-based relationships with every school district in the state and in many other states in the United States. The facilities at UO will contribute substantially to the success of the proposed research.

Scientific Environment

The UO provides strong support for synergistic and multidisciplinary collaborations across departments, research centers, and institutes, and the Lewis Center for Neuroimaging. The UO Lewis Integrative Science Building also houses several UO strategic interdisciplinary research clusters focused on research across the spectrum of cellular processes to improving communities. The UO strategic research initiatives provide another collaborative forum for the investigators of this project to present and discuss their research. Access to an extensive research library at the University of Oregon campus are also available.

Center for Translational Neuroscience (CTN). The CTN, of which Dr. Berkman is Associate Director, is an interdisciplinary research center with the mission of translating discoveries in basic neuroscience, psychology, and related disciplines to improve well-being, promote resilience, and mitigate the effects of early adverse experiences on physical and emotional health. The CTN houses research projects, science communication initiatives, professional development, and intervention program development, implementation, and evaluation activities. The primary leadership of CTN are faculty in the Department of Psychology, where CTN is housed, and affiliated faculty work in departments across the university including biology, human physiology, and counseling psychology. In addition to faculty, CTN is home to numerous postdoctoral research associates, masters and doctoral graduate students, undergraduate research assistants, and University of Oregon employees. *Particularly relevant to the current proposal* are the training opportunities afforded by the CTN. The CTN offers a suite of professional development opportunities related to translational science, including science communication and knowledge dissemination workshops, grant writing seminars, a bi-weekly scientific discussion brownbag, a methods and data science discussion group, as well as a range of one-on-one and team mentorship programs to cross-train students with basic psychological science and neuroscience knowledge in clinical and intervention science, and vice versa.

Department of Psychology. The Department of Psychology supports a vibrant intellectual community that provides the research team with extensive opportunities to present their own research, receive feedback about ongoing projects, and learn of new and related research in the Pacific Northwest and beyond. There are departmental colloquium and bi-weekly brown bags attended by faculty and students for each of the social/personality, cognitive/neuroscience, clinical, and developmental areas. Lecture series are further supplemented by talks offered at off-campus research institutes that are affiliated with the Department of Psychology and relevant to the current proposal: Oregon Social Learning Center, Child and Family Center, Oregon Center for Applied Sciences, and Oregon Research Institute.

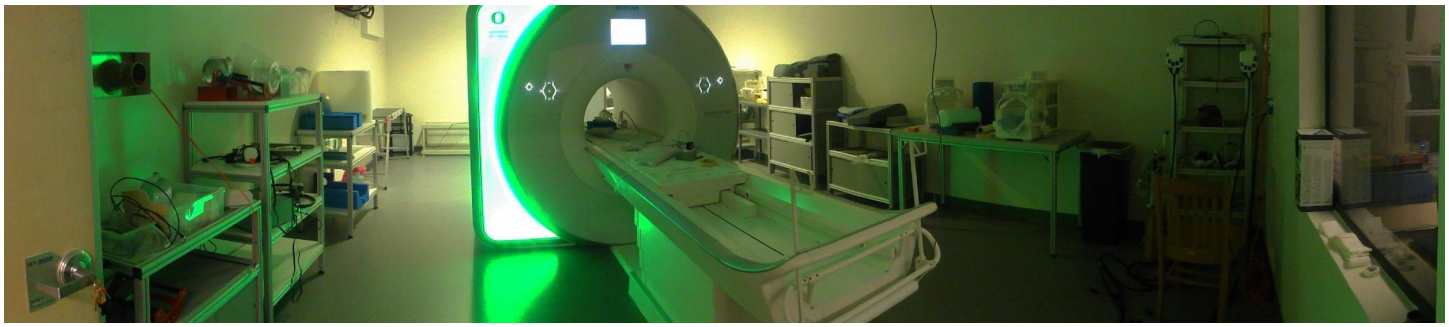
Health Promotion and Obesity Prevention Initiative. The UO is home to a unique cluster of faculty, including collaborator Dr. Nicole Giuliani, that were hired as part of the Health Promotion and Obesity Prevention (HPOP) initiative. Building on the strong tradition of prevention science at the UO, this initiative

seeks to bring together faculty from diverse fields to combat the obesity epidemic. The goal of this initiative is to leverage basic research in the biological and social sciences to understand the etiology and underlying mechanisms of obesity and develop effective interventions and outreach programs to prevent and mitigate associated negative health outcomes. This initiative provides expertise and opportunities, such as reading groups, colloquia, and graduate seminars, that are highly relevant to the current proposal.

Lewis Center for Neuroimaging (LCNI)

The LCNI is a core-research facility under the auspices of the office of the vice president of research and innovation. It is designed to enhance access to state-of-the-art MRI-related research by the UO faculty and surrounding research community. The center, with its own private entrance (see photo at right), is housed in the Lewis Integrative Science Building (LISB) and contains a Siemens Skyra 3-Tesla MRI machine dedicated to research (see photo below). A generous endowment by the Lewis family provides unparalleled infrastructure support for staff and equipment dedicated to center activity. The center is located just steps away from Dr. Berkman's Social and Affective Neuroscience (SAN) Lab, which is located on the 2nd floor of LISB, directly above the LCNI. Dr. Mills' lab space is directly below Dr. Berkman's lab and adjacent to the LCNI, on the 1st floor of LISB.

Laboratory. The centerpiece of the LCNI is the Siemens Skyra 3T MRI machine. This magnet is approximately 2 years old and was recently upgraded with multiband sequences. We have multiple coils, including a 32-channel head coil with optimized sequences based on the latest Human Connectome Project's published work. We support both Mac and PC presentation with both goggle and projector systems with 5-fingered response boxes for both hands. With a large magnet room and control room that are optimal for research training, our lab is ideal for the type of cross-disciplinary work proposed in this application. The LCNI has a large electronics laboratory for coil design and hardware construction and directly adjacent to the console room, a separate room contains an MR-simulator used to acclimate participants to the MR-environment, with moveable participant table, full visual/audio presentation and response measurement capabilities, and accurate auditory simulation of EPI sequences.



Clinical. The LCNI has space for private physical exams, pre-testing, and interviews that is situated across the hall from the magnet room and is equipped with interview table, chairs, and computer for pretesting.

Computing. The LCNI maintains a variety of computing equipment, including a grid-server for large neuroimaging analysis jobs and a dedicated image analysis room. The analysis room contains two workstations for smaller analyses and data manipulation and two other terminals for interaction with the grid-server. Data are stored on a separate file server.

Office. The LCNI has a dedicated and regularly staffed reception area with a separate entrance to facilitate participant access and comfort. This provides an exceptionally professional feel typically not seen in research settings, which can be especially helpful when scanning sensitive populations, including children and clinical populations who may be accompanied by family members or caregivers. Additional office space for center staff and related trainees is available down the hall from the magnet and other center space. This proximity enables

center staff to provide maximal interaction with investigators and to be accessible for troubleshooting or problem solving.

Computer Support
The UO operates a centralized data and authentication system (Red Hat Enterprise). All faculty and staff have accounts and have direct access on campus or via VPN from off campus. Internet access is provided at no cost. Data access and transfer capacity are excellent. Computer support is available from the university's Computing Center and from in-house staff in the Department of Psychology. The Computing Center also employs statistical and computer consultants to assist faculty and staff with other computer needs.

Dr. Berkman has ample research space in his lab as part of the Department of Psychology at UO. The Social and Affective Neuroscience (SAN) Laboratory, located in the recently built LISB directly above the LCNI, is equipped with 10 Apple workstations (see the Equipment section of this proposal) that have all necessary software for training stimulus presentation (MATLAB with Psychophysics Toolbox) and analytic software for fMRI analysis, including SPM12 and FSL. These computers have additional software for all other analyses described in the "Analytic Strategy" subsection of the Approach, including HLM, EQS, MPLUS, SAS, R, and SPSS. Dr. Mills has comparable computational resources available to her, and both Berkman and Mills have access to the University of Oregon's High Performance Computing Cluster, Talapas.

Talapas High Performance Computing Cluster
The Talapas supercomputer is a high performance computing cluster that will be used to process fMRI data. Talapas enables rapid processing of the massive quantity of fMRI data that will be collected in the proposed research, including preprocessing and multivariate pattern analyses. Talapas is maintained by the Research Advanced Computing Services, which has four full-time staff dedicated to administration and maintenance of Talapas and provide support for application software, training, and consulting services for the UO computational research community. Talapas has 96 general purpose computational nodes providing 2,688 physical cores, 24 compute nodes with quad Graphics Processor Units (GPUs), eight large memory nodes with up to 4TB of RAM for high memory applications, full EDR Infiniband interconnect for fast message passing in high-performance applications, and 1.5 petabytes of fast data storage.

EQUIPMENT

Lewis Center for Neuroimaging (LCNI) Equipment

Functional magnetic resonance imaging (fMRI) scans will be conducted at the Robert and Beverly Lewis Center for Neuroimaging (LCNI) located in the Lewis Integrative Sciences Building (LISB) at the University of Oregon (Fred Sabb, director), which also houses Dr. Berkman and Dr. Mills' lab and office spaces. Major resources in the neuroimaging center include the following:

- Three full-time staff, including an MRI radiology technologist, MR physicist, and administrative staff. The technologist has extensive experience scanning in clinical and research settings.
- Research-dedicated 3T MRI system (Siemens Skyra), MRI-compatible electrostatic headphones (Koss), digital projector, and MRI-compatible button boxes
- Multiple head coils, including a phased array coil
- MRI/RF coil development lab with Agilent network analyzer, RF signal generator, digital oscilloscope, computer interface of test gear to a lab PC, and resistance/inductance/capacitance meters
- Image analysis computer hardware
- Several fMRI data analysis programs, including locally developed programs (e.g., MRIConvert for converting DICOM files into SPM/Analyze format), MATLAB, and standard packages (AFNI, FSL, BrainVoyager, SPM, MarsBaR, Neuroelf)
- MRI simulator unit (with internal dimensions identical to those of the Siemens Skyra scanner) with moveable participant table, full visual/audio presentation and response measurement capabilities, and accurate auditory simulation of EPI sequences

Dr. Berkman's Social Affective Neuroscience Laboratory Equipment

- 10 Apple iMacs (3.2 GHz Intel Core i5 processors, 8 GB RAM, 4 TB hard drives)
- 2 MacPros (2 x 2.4 GHz QuadCore Intel Xeon processors, 16 GB RAM, 2 TB hard drives)
- 2 MacBook Pros (2.66 GHz Intel Core i7 processors, 8 GB RAM, 1 TB hard drives)
- 16 TB RAID 0 independent storage/backup server
- Laser printer
- Document scanner
- Clinical-quality scale, ruler, and tape measure to accurately assess height, weight, BMI, and waist-to-hip ratio

Talapas High Performance Computing Cluster

The Talapas supercomputer is a high performance computing cluster that will be used to process fMRI data. Talapas enables rapid processing of the massive quantity of fMRI data that will be collected in the proposed research, including preprocessing and multivariate pattern analyses. Talapas is maintained by the Research Advanced Computing Services, which has four full-time staff dedicated to administration and maintenance of Talapas and provide support for application software, training, and consulting services for the UO computational research community. Talapas has the following specifications:

- 96 standard nodes, each with: 28 cores, 128 GB RAM, 200 GB SSD local storage
- 24 GPU nodes, each with: 28 cores, 256 GB RAM, 200 GB SSD local storage
- 8 large memory nodes, each with: 56 cores, 1, 2, or 4 TB RAM, dual 480 GB SSD local storage
- 1.5 PB fast storage
- SLURM cluster management and job submission
- Relevant software installed: Singularity, Python, MATLAB, SPM, AFNI, FSL, Freesurfer, R

UNIVERSITY OF OREGON
College of Arts and Sciences
Department of Psychology

National Cancer Institute
9000 Rockville Pike
Bethesda, MD 20892

February 19, 2019

Dear colleagues,

I am delighted to confirm Dani Cosme's nomination as the University of Oregon applicant for the NCI Predoctoral to Postdoctoral Fellow Transition Award (F99/K00). Dani is a doctoral candidate in the Department of Psychology and is committed to becoming a successful independent cancer researcher. Under the guidance of her primary sponsor, Elliot Berkman, Dani has developed an innovative research proposal to evaluate health behavior change interventions targeting modifiable, cancer-relevant risk factors, such as diet, physical activity, and substance use, using advanced multivariate neuroimaging techniques.

The Department of Psychology and the University of Oregon are committed to supporting Dani's training and research career goals by providing access to physical infrastructure, such as the Talapas High Performance Computing Cluster and research-dedicated MRI scanner in the Lewis Center for Neuroimaging, as well as intellectual resources, including brownbags, journal clubs, and colloquia on relevant topics, such as translational neuroscience, advanced statistical methods, and resting state fMRI. I am confident that the proposed training plan will advance Dani's research career trajectory and provide her the opportunities and specific training to become a leading independent cancer researcher.

The University of Oregon solicited nominations for this program through outreach to graduate students and faculty at the department level, as well as university-wide communications through the Office of the Vice President for Research and Innovation. Interested applicants submitted a pre-proposal detailing their research and training plan, along with their NIH biographical sketch. A panel of faculty members with success in obtaining NIH research career development awards reviewed the pre-proposals. As per guidance from the Office of the Vice President for Research and Innovation, faculty reviewers evaluated the pre-proposals based on the following criteria:

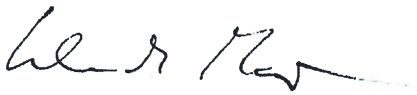
- Applicant's desire and potential to become an independent cancer researcher
- Strength of applicant, including prior grant funding, publication record, and academic performance
- Impact and intellectual merit of the proposed project
- Sponsor's training record and strength of the training plan

DEPARTMENT OF PSYCHOLOGY
1227 University of Oregon, Eugene OR 97403-1227 T (541) 346-4921
http://www.uoregon.edu

The committee's evaluations were shared with Dr. David Conover, Vice President for Research and Innovation, who selected Dani as the University of Oregon applicant. I can confirm Dani's eligibility for the program, as she is a United States citizen and is a fourth year student who is expected to graduate within two years.

Dani is no doubt on the path to becoming a successful independent cancer researcher. She is committed to gaining the technical skills and research expertise necessary to establish a strong, independent research program to contribute to the development of novel interventions to reduce engagement in health-risking behaviors such as, unhealthy eating, physical inactivity, and substance use, which represent significant risk factors for many types of cancers. I enthusiastically support Dani's nomination and am committed to providing the institutional support necessary for her to achieve her research career goals.

Sincerely,



Ulrich Mayr
Lewis Professor, Psychology
Chair, Department of Psychology

Stephanie Gray
Authorize Organizational Representative
Sponsored Projects Administrator

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: Danielle Middle Name Last Name*: Cosme Suffix:

Position/Title*:
Organization Name*: University of Oregon
Department: Psychology
Division: Ctr for Translational Neurosci
Street1*: 1227 University of Oregon
Street2:
City*: Eugene
County: Lane
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 97403-1227

Phone Number*: [redacted] Fax Number:

E-Mail*: dcosme@uoregon.edu

Credential, e.g., agency login: dcosme16

Project Role*: PD/PI Other Project Role Category:

Degree Type: PHD,MS,MS,BS Degree Year: 2021,2015,2016,2009

Attach Biographical Sketch*: File Name: Biosketch_Cosme.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Elliot Middle Name Todd Last Name*: Berkman Suffix:

Position/Title*: Assistant Professor
Organization Name*: University of Oregon
Department:
Division:
Street1*: Department of Psychology
Street2: 1227 University of Oregon
City*: Eugene
County:
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 97403-1227

Phone Number*: 541-346-4909 Fax Number: 541-346-4911

E-Mail*: berkman@uoregon.edu

Credential, e.g., agency login: BERKMANET1

Project Role*: Other (Specify) Other Project Role Category: Sponsor

Degree Type: PHD,MA,MA,BA,BS Degree Year: 2010,2004,2005,2002,2002

Attach Biographical Sketch*: File Name: Biosketch_Berkman.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Kathryn Middle Name L Last Name*: Mills Suffix:

Position/Title*: Assistant Professor
Organization Name*: University of Oregon
Department:
Division:
Street1*: 1227 University of Oregon
Street2: Department of Psychology
City*: Eugene
County:
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 97403-1227

Phone Number*: 5023772362 Fax Number:

E-Mail*: klmills@uoregon.edu

Credential, e.g., agency login: KLMILLS16

Project Role*: Other (Specify) Other Project Role Category: Co-Sponsor

Degree Type: PHD,BA Degree Year: 2015,2011

Attach Biographical Sketch*: File Name: Biosketch_Mills.pdf

Attach Current & Pending Support: File Name:

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: Danielle (Dani) Cosme

eRA COMMONS USER NAME (credential, e.g., agency login): DCOSME16

POSITION TITLE: Doctoral Candidate

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Chapman University	BS	08/2005	05/2009	Psychobiology, minor in chemistry
Stockholm University	MS	08/2012	01/2015	Psychology
University of Oregon	MS	09/2015	12/2016	Psychology
University of Oregon	PHD	09/2015	06/2021 (expected)	Psychology

A. Personal Statement

My long-term career goal is to become a leading independent cancer researcher in the field of translational neuroscience. The overarching objective of my research program is to leverage advanced multivariate neuroimaging techniques to build sensitive and specific neurobiological indices of target psychological processes, using task-based and task-free neuroimaging data, in order to more effectively evaluate whether, how, and for whom cancer-relevant health behavior change interventions are working. To achieve this goal, I have worked with my mentors to craft a training plan that builds on my present knowledge and skill set to develop expertise in translational neuroscience, and advanced neuroimaging and longitudinal modeling techniques. Through my academic training and research experience, I have developed a strong foundation in psychology and neuroscience. As an undergraduate, I excelled with rigorous scientific coursework, majoring in psychobiology and minoring in chemistry. To gain a broad overview of neuroscience and psychology, I worked as a research assistant in Dr. William Wright's marine neurobiology lab studying evolutionary mechanisms of learning and memory, as well as Dr. Connie Shears' cognitive psychology lab studying the effect of emotional language on inference processing. As a master's student at Stockholm University, I narrowed my research interests to human behavior and worked with Dr. Stefan Wiens, leading a study to investigate individual differences in emotional reactivity using various psychophysiological measures[1]. As a lab manager for Drs. Elliot Berkman and Jennifer Pfeifer, I gained substantial experience with functional neuroimaging (fMRI), including experimental design, task programming and optimization, data collection, and univariate analysis, as well as critical "soft skills", such as project management, troubleshooting, and on-the-fly problem solving. I also gained experience with longitudinal fMRI analysis, with which I have continued to develop expertise as a PhD student in Dr. Pfeifer's lab, presenting an innovative developmental analysis method as an invited speaker at a methodological workshop[2].

As a PhD student, my primary focus has been on appetitive self-regulation and its relationship to health-risking behaviors, including substance use and unhealthy eating. Ultimately, I seek to improve our ability to predict real-world behavior using neural and behavioral data in order to more effectively design and evaluate health behavior change interventions targeting modifiable risk factors for various cancers. Towards this goal, I have focused on improving the ecological validity of a task assessing appetitive self-regulation ability by incorporating choice into the paradigm[3]. I conducted a year-long longitudinal pilot study using this task to characterize its ability to predict changes in substance use and other health-risking behaviors across freshman year. I analyzed this data and, together with Dr. Pfeifer, wrote an R21 application funded by the National Institute on Drug Abuse. I have tested competing models of food-related decision making to better understand

the neural mechanisms underlying eating behavior[4]. Next, I plan to improve our ability to predict real-world behavior by improving the sensitivity and specificity of neural predictors. As part of my dissertation, I am developing a neurobiological index (i.e., neural signature) of craving reappraisal, which I will use in the F99 phase of this proposal to evaluate a craving reappraisal intervention to improve healthy eating in overweight and obese adults, and assess individual differences in cancer-relevant intervention outcomes using advanced longitudinal modeling techniques. Under the mentorship of Dr. Berkman, an expert in translational neuroscience for cancer control, and Dr. Kathryn Mills an expert in longitudinal modeling with neuroimaging data and resting state fMRI, I am confident I will acquire the skills necessary to launch the next phase of my research program as a postdoctoral scholar and achieve my career goal of becoming a leading translational neuroscientist.

1. **Cosme, D.**, & Wiens, S. (2015). Self-Reported Trait Mindfulness and Affective Reactivity: A Motivational Approach Using Multiple Psychophysiological Measures. *PLOS One*, 10(3), e0119466.
2. **Cosme, D**., Flournoy, J. C., Telzer, E., Pfeifer, J. H. (2017) Traditional modeling approaches. Presented at the Modeling Developmental Change workshop, September 15, Portland, Oregon.
3. **Cosme, D.**, Mobasser, A., Zeithamova, D., Berkman, E. T., & Pfeifer, J. H. (2018). Choosing to regulate: Does choice enhance craving regulation?. *Social Cognitive and Affective Neuroscience*, 13(3), 300-309.
4. **Cosme, D.**, Ludwig, R. M., & Berkman, E. T. Comparing two neurocognitive models of self-control during dietary decisions. Under review at *Social Cognitive and Affective Neuroscience*.

B. Positions and Honors

Positions and Employment

2007-2009	Undergraduate research assistant, Wright Lab, Chapman University, Orange, CA
2008-2009	Undergraduate research assistant, Shears Lab, Chapman University, Orange, CA
2012-2014	Masters student, Wiens Lab, Stockholm University, Stockholm, Sweden
2014-2015	Lab manager, Pfeifer and Berkman Labs, University of Oregon, Eugene, OR
2015-	Graduate research fellow, Pfeifer and Berkman Labs, University of Oregon, Eugene, OR
2016-2018	Facilitator, Data Science Club, University of Oregon, Eugene, OR
2017	Fellow, Neurohackweek, University of Washington, Seattle, WA

Other Experience and Professional Memberships

2015-	Member, Flux Society, Social and Affective Neuroscience Society
2016	Organizer, Brainhack Global Hackathon
2016-2017	Departmental Steward, Graduate Teaching Fellows Federation
2017-	Member, American Psychological Society
2017-2018	Vice President of Organizing, Graduate Teaching Fellows Federation
2018	Co-Chair, Brainhack Global Hackathon

Honors

2005	Norris Foundation Scholar for the Biological Sciences, Chapman University
2005-2009	Presidential Scholar, Chapman University
2009	Graduated Magna Cum Laude with Honors in Psychology, Chapman University
2009	Undergraduate Travel Grant, Chapman University
2014	Student Travel Award, International Symposium for Contemplative Sciences
2015	Jacobs Foundation Young Scholars Award, Society for Research in Child Development
2016	Clarence and Lucille Dunbar Scholarship, University of Oregon
2017	Miller Family Graduate Award in Technology and Science, University of Oregon
2017	General University Scholarship, University of Oregon
2017	Graduate School “Special Opps” Travel and Research Award, University of Oregon
2018	Beverly Fagot Dissertation Fellowship, University of Oregon
2019	Lokey Doctoral Science Fellowship, University of Oregon

C. Contributions to Science

1. **Individual differences in emotional reactivity.** Together with my master’s thesis advisor, Dr. Stefan Wiens, I developed a rigorous psychophysiological experiment to test whether emotional reactivity varies as a function of trait mindfulness. Prior research suggested that mindfulness meditation reduces emotional

reactivity by facilitating disengagement from emotional stimuli. However, the evidence was mixed as to whether individuals with higher trait mindfulness actually have decreased reactivity to emotional stimuli. We assessed emotional reactivity using a multi-method approach, collecting electrocortical brain activity (EEG), skin conductance, startle response, and self-reported responses to highly arousing positive and negative emotional pictures. Across all measures, we did not find any evidence for moderation by trait mindfulness. These findings are significant because they suggest that either self-reported trait mindfulness is not related to spontaneous reactivity or that the available questionnaires may not be valid measures of mindfulness[a].

a) **Cosme, D.**, & Wiens, S. (2015). Self-Reported Trait Mindfulness and Affective Reactivity: A Motivational Approach Using Multiple Psychophysiological Measures. *PLOS One*, 10(3), e0119466.

2. **Neurodevelopmental trajectories of self and social processing across adolescence.** Human adolescence is a formative period characterized by major shifts in self and social development. However, the specific neurodevelopmental trajectories of self and social evaluations are not well characterized. While a lab manager in Dr. Jennifer Pfeifer's lab, I began analyzing behavioral and fMRI data from a well-powered 6-year longitudinal neuroimaging study to assess how self and social processing develops during adolescence[a]. Further, these developmental effects are often subtle and not well-powered using traditional analytic methods. Because of this, I helped develop an innovative analysis technique to probe developmental effects across the whole brain while increasing power. We used a standardized parcellation atlas to divide the brain into 350 regions of interest (ROIs) rather than 70,000 voxels (volumetric pixels), extracted the mean signal within each ROI for each subject, time point, and condition, and used this data as inputs to a linear mixed effects model. This approach is significant because it substantially reduces the number of multiple comparisons and stabilizes estimates by averaging across ROIs. To facilitate the adoption of this method by others, I presented this approach and shared analysis code at the NSF-sponsored Modeling Developmental Change workshop[b]. Our results showed expected increases in activation for self and social processing in their respective neural networks, but also that self-evaluations in the academic domain become highly salient, affirming the importance of academic identity during adolescence. I have further investigated the neural correlates of self and social processing when late adolescents reflect on their own well-being using a novel, trial-by-trial modeling approach[c]. The results showed that mean activation in relevant cortical midline structures (e.g., pgACC, vmPFC) explain additional variance in and are associated with item-level well-being endorsements, but not individual differences in overall well-being. These results suggest that mean activation in ROIs improve prediction during evaluation of personal well-being in the moment but is not sensitive enough to differentiate people's trait well-being.

a) **Cosme, D.**, Flournoy, J. C., Livingston, J. L., Mazziotta, J., Dapretto, M., & Pfeifer, J. H. (2017) Neurodevelopmental trajectories of self and social evaluation across adolescence. Poster presented at the Flux Congress, September 16-18, Portland, Oregon.
b) **Cosme, D**., Flournoy, J. C., Telzer, E., & Pfeifer, J. H. (2017) Traditional modeling approaches. Talk presented at the Modeling Developmental Change workshop, September 15, Portland, Oregon.
c) **Cosme, D.**, Mobasser, A., Ross, G., & Pfeifer, J. H. If you're happy and you know it: Neural correlates of self-evaluated well-being. Submitted to *Frontiers in Human Neuroscience*.
d) Telzer, E. H., McCormick, E. M., Peters, S., **Cosme, D.**, Pfeifer, J. H., & van Duijvenvoorde, A. C. (2018). Methodological considerations for developmental longitudinal fMRI research. *Developmental cognitive neuroscience*.

3. **The effect of choice on appetitive self-regulation.** Although the ability to engage in regulation to avoid goal-incongruent temptations is critical for healthy development, individuals who are otherwise capable often *choose not* to regulate. In most self-regulation tasks, participants are explicitly told when to regulate, and thus these tasks are only able to assess participants' abilities to regulate when prompted to do so. However, this approach lacks fidelity to the regulatory process outside the lab. To improve ecological validity and assess whether and how self-regulation may differ when individuals choose to regulate, I designed a novel neuroimaging paradigm to test the hypothesis that choosing to regulate improves appetitive self-regulation for personally-craved foods[a]. Despite the strong theoretical prediction that choice should facilitate regulation, we observed the opposite effect; choice disrupted regulation. Collaborating with Dr. Dagmar Zeithamova, I used a multivariate neuroimaging technique, multivoxel pattern analysis (MVPA), to show that the disruption may be due to inefficient resource allocation on choice trials. This work is significant because it shows that standard task paradigms instructing individuals when to regulate may not generalize to behavior outside the lab, when they must first choose to regulate.

a) **Cosme, D.**, Mobasser, A., Zeithamova, D., Berkman, E. T., & Pfeifer, J. H. (2018). Choosing to regulate: Does choice enhance craving regulation?. *Soc. Cogn. Affect Neurosci.*, 13(3), 300-309.

4. **Autonomy, appetitive self-regulation, and health-risking behaviors during the transition to college.** Designing effective interventions to reduce collegiate substance use and other health-risking behaviors requires the identification of risk factors that are amenable to change, such as appetitive self-regulation. Further, because there is a sudden increase in autonomy and decrease in regulatory scaffolding during the transition to college, it is important to understand how autonomous motivation interacts with regulatory ability. Together with my PhD advisor, Dr. Jennifer Pfeifer, I designed and carried out a year-long pilot study assessing the ability of self-initiated, autonomous appetitive self-regulation to predict changes in substance use across freshman year. Our results indicated that autonomous appetitive self-regulation better predicted outcomes than either standard measures of appetitive self-regulation or other known predictors, such as gender, SES, or ethnicity. Dr. Pfeifer and I used this pilot data to write an R21 grant application to conduct this study in a large, well-powered sample, and it was funded by the National Institute on Drug Abuse[a]. We collected neuroimaging data and baseline assessments from 117 incoming college freshman during the summer of 2018 and are currently tracking their health and well-being via quarterly self-report assessments. I am also first author on a manuscript in the *Journal of Health Psychology* that extends this work beyond college freshman to discusses ways in which autonomy might facilitate the self-regulation of emotion across the lifespan, both in healthy adults as well as in adults with cancer[b].
   a) PI Pfeifer J. H. (2017) Choosing to Regulate: An fMRI Investigation of Autonomous Versus Controlled Self-Regulation and Substance Use in Late Adolescence. NIDA (R21DA043015).
   b) **Cosme, D.**, & Berkman, E. T. (2018). Autonomy can support affect regulation during illness and in health. *Journal of health psychology*, 1359105318787013.

5. **Eating behavior and reactivity, regulation, and valuation.** A strong understanding of the mechanisms underlying eating behavior is required to develop effective interventions to improve dietary habits and reduce the prevalence of overweight and obesity. My colleagues and I have put forth a neurocognitive model that focuses on the interplay between three key psychological processes–cue reactivity, self-regulation, and valuation[a] in food-related decision making. In contrast to predominant dual-process models of food choice, which emphasize the antagonistic relationship between reactivity and regulation, our model posits that subjective value plays a critical role in reactivity and regulation during decision making. I tested this model in the context of an ecologically valid food decision making paradigm in which participants placed monetary bids on healthy and unhealthy foods. I extracted estimates of neural activation from regions associated with reactivity, regulation, and valuation, and used multilevel modeling to directly test the predictions of these two models. The results supported our model emphasizing the importance of valuation and were not consistent with the dual-process model of regulation[b]. This research adds critical evidence that refines models of self-regulation and eating behavior.
   a) Giuliani, N. R., Merchant, J. S., **Cosme, D.**, & Berkman, E. T. (2018). Neural predictors of eating behavior and dietary change. *Annals of the New York Academy of Sciences*.
   b) **Cosme, D.**, Ludwig, R. M., & Berkman, E. T. Comparing two neurocognitive models of self-control during dietary decisions. Under review at *Social Cognitive and Affective Neuroscience*.

Complete list of published work in Google Scholar and full Curriculum Vita:
https://scholar.google.com/citations?user=fAkRXQoAAAAJ&hl=en
https://dcosme.github.io/cv_d.cosme.pdf

D. Additional Information: Research Support and/or Scholastic Performance

F31CA232357 (pending, scored 9th percentile) Cosme (PI) 04/01/2019 - 03/31/2021
Cognitive reappraisal can be used to reduce food craving and unhealthy eating (a key risk factor for several kinds of cancer), but interventions to train reappraisal ability are not equally effective for all individuals. This project aims to leverage multivariate neuroimaging and machine learning techniques to develop an objective, neurobiological index of craving reappraisal ability that can be used to assess individual differences in treatment responsivity.

YEAR	COURSE TITLE	GRADE	COURSE TITLE	GRADE
CHAPMAN UNIVERSITY (P = Equivalent to C or higher, AU = Audit, FW = Failure to withdraw, R = Repeated)				
2005	Writing about literature	A	Single variable calculus I	A
	Socrates trial: Reasoning and critical analysis	B	Introduction to American politics	B+
2006	General biology I	A	General chemistry and lab I	A
	Intro to film aesthetics	A	Volleyball – intermediate	A
	Single variable calculus II	A	College biology	A
	Introduction to ethics	A	Human nutrition	A
	Introduction to psychology	A	General physics for life science I	FW R*
	Ecology and evolution	A-	*Retaken in 2007 for an A (see below)	
2007	Eastern concepts of health and healing	A	Student faculty research	P
	Neuroanatomy and neurophysiology	A-	Organic chemistry and lab I	A
	General chemistry and lab II	A-	General physics for life science I	A
	Ultimate Frisbee	A	Introduction to statistics	A-
	Psychology of learning	A	Sensation and perception	A
	Physiological psychology	A		
2008	Photography	A	Cellular and molecular biology	B+
	Chemistry of the natural world	A	Biochemistry I, biomolecules and lab	A
	Physics	C	Leadership and experiential learning	P
	Study abroad science	A	Research methods behav. sciences	A
	Foundation course photography	AU	Individual research	A
	Student faculty research	P		
2009	Independent study: Cog. Psych. research	A	Elementary German I	AU
	Genetics	A-	Individual research	A
	Research in biology	A	Advanced American sign language I	B
	Advanced topics in environmental chemistry	A-		
STOCKHOLM UNIVERSITY (A = Excellent, B = Very good, TG = Transferred credit)				
2012	Psychology: history and science	A	Applied questionnaire methods	A
	Research methods I	B		
2013	Biological psychology	A	Biochemistry of the brain	B
	Statistics I	A	Memory	A
	Neuroscience	A	Applied study design	B
	Emotion psychology & affective neuro.	A	Higher cognitive functions	B
2014	Master's thesis in psychology	A	Statistical methods with R	TG
UNIVERSITY OF OREGON (P = Equivalent to B- or higher)				
2015	Seminar programming in R	P	Seminar developmental research	P
	Seminar adolescence	A+	Seminar first year research	P
	Seminar social personality group	P	Data analysis I	A+
	Research developmental social neuro.*	P	*Credits taken every quarter; passed each time	
2016	Seminar first year ethics	P	Advanced applications in MRI	P
	Social personality core	A	Data analysis III	A
	Data analysis II	A	Reading first year project	A+
	Seminar first year research	P	Seminar programming in R	P
	Advanced cognitive neuroscience	A+		
2017	Seminar brain decoding	A	Seminar statistical analyses in R	P
	Seminar grant writing	A	Developmental core	A
	Reading machine learning	A	Structural equation modeling	A
2018	Seminar data science	A-		

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Berkman, Elliot Todd

eRA COMMONS USER NAME (credential, e.g., agency login): BERKMANET1

POSITION TITLE: Associate Professor of Psychology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Stanford University	B.S.	06/2002	Mathematics
Stanford University	B.A.	06/2002	Psychology
Stanford University	M.A.	04/2004	Psychology
University of California, Los Angeles	M.A.	12/2005	Psychology
University of California, Los Angeles	NIH / NIDA T90 Training Grant	12/2008	UCLA Neuroimaging Training Program
University of California, Los Angeles	Ph.D.	06/2010	Social Psychology

A. Personal Statement

This proposal is to provide training to Dani Cosme in translational neuroscience, multivariate neuroimaging and machine learning, and open and reproducible neuroscience. Dani is an outstanding candidate for an F99/K00 fellowship because she is an exceptionally strong researcher on an excellent trajectory, and the F99 would provide the final additions that she needs in her graduate training to become an independent, federally-funded scholar in the emerging area of translational neuroscience. Only with F99 funding would Dani be able to immerse herself in the design and implementation of an R01-scale translational neuroscience intervention for cancer prevention *and* master the advanced statistical techniques that we plan to use to examine the mediators and moderators of that intervention. Dani has been involved in projects in my lab, but with F99 support, she could focus her time and energy on acquiring the skills laid out in the Training Plan.

I am the PI of the parent study that will provide support for Dani's F99 training, R01 CA211224. As her Primary Sponsor and PI of the parent grant, I will be responsible for overseeing all aspects of the training, especially training in translational neuroscience as it relates to the parent grant supporting the translational neuroscience intervention trial. I will also coordinate carefully with Co-Sponsor Mills, a close collaborator, to ensure that Dani completes the proposed training and is well poised to begin postdoctoral training in the K00 phase.

The research in my lab research focuses on the neurocognitive underpinnings of cancer-relevant health goals in adults, such as dietary change and smoking cessation. This research emphasizes the roles of valuation, motivation, and executive function, and integrates neurocognitive measures into prevention and intervention trials as indices of underlying targeted processes. I am PI on three NIH-funded grants that test theory-driven hypotheses about the mechanisms underlying health and wellbeing interventions using neuroimaging. I received training on a NIDA-funded F31 that investigated the longitudinal association between neural activations during inhibitory control and smoking cessation outcomes. I received training in advanced neuroimaging methods from a NIDA T90 comprehensive neuroimaging training grant at UCLA. All of my current neuroimaging projects focus on elucidating mediators and/or moderators of experimental and intervention effects by synthesizing cognitive neuroscience knowledge with psychological theory related to cognitive control, social processing, and reward or motivational states.

1. Cosme, D., Mobasser, A., Zeithamova, D., Berkman, E.T., & Pfeifer, J.H. (2018). Choosing to regulate: Does choice enhance craving regulation? *Social Cognitive and Affective Neuroscience*, *13*, 300-309.
2. Berkman, E. T., Hutcherson, C. A., Livingston, J. L., Kahn, L. E., & Inzlicht, M. (2017). Self-control as value-based choice. Current Directions in Psychological Science, 26(5), 422-428.
3. Berkman, E. T. (2017). Value-based choice: An integrative, neuroscience-informed model of health goals. Psychology and Health, in press.
4. Berkman, E. T., Graham, A. M., & Fisher, P. A. (2012). Training self-control: A domain-general translational neuroscience approach. Child Development Perspectives, 6(4), 374–384.

B. Positions and Honors

Positions and Employment

2007 Fellow, Summer Institute for Cognitive Neuroscience, University of California, Santa Barbara
2008 Fellow, Neuroimaging Training Program, University of California, Los Angeles
2010-2016 Assistant Professor, Department of Psychology, University of Oregon, Eugene, OR
2016- Associate Professor, Department of Psychology, University of Oregon, Eugene, OR
2016- Associate Director, Center for Translational Neuroscience, University of Oregon
2017- Co-Director, Center for Translational Neuroscience, University of Oregon

Other Experience and Professional Memberships

2004- Member, American Psychological Association
2005- Member, Association for Psychological Science
2006- Member, Society for Personality and Social Psychology
2007- Member, Cognitive Neuroscience Society
2008- Member, Social and Affective Neuroscience Society
2011-2014 Treasurer, Social and Affective Neuroscience Society
2012- Member, American Psychosomatic Society
2012- Member, Society for Research on Nicotine and Tobacco
2012-2013 Conference Co-Chair, Social and Affective Neuroscience Society
2014- Member, Society for Affective Science
2016- Editorial Board Member, *Social and Personality Psychology Science*
2017- Associate Editor, *Journal of Personality and Social Psychology*, Section I
2017- Associate Editor, *Social Cognitive and Affective Neuroscience*
2017- Standing member, Social Personality and Interpersonal Processes (SPIP) study section, NIH

Honors

2004 UC Regents Distinguished Achievement Fellowship, University of California, Los Angeles
2006 Graduate Research Mentorship Fellowship, University of California, Los Angeles
2007 Distinguished Student Teaching Award, University of California, Los Angeles
2008 Graduate Students Present Award, Cognitive Neuroscience Society
2008 J. Arthur Woodward Peer Mentoring Award, University of California, Los Angeles
2008 National Research Service Award, National Institute on Drug Abuse
2009 Travel Award, Society for Personality and Social Psychology
2010 Social Psychology Area Dissertation Award, University of California, Los Angeles
2010 Joseph A. Gengerelli Distinguished Dissertation Award, University of California, Los Angeles
2017 Social-Personality Health Network Early Career Award
2017 College of Arts and Sciences Dean's Fellow, University of Oregon
2018 APS Janet Taylor Spence Transformative Early Career Contributions Award
2018 Excellence in Graduate Mentorship Award, University of Oregon Graduate School

C. Contribution to Science

1. **Neural measures as predictors of real-world, cancer-relevant outcomes**. We have identified instances (e.g., in health behaviors and persuasion) where neural measures explain unique variance in subsequent outcomes, above and beyond task-based and self-report measures. This "brain-as-predictor" approach can suggest candidate hypotheses about the role of a particular mental process in a particular outcome. Often, these hypotheses are not obvious without insight from imaging.

a. Berkman, E. T., & Falk, E. B. (2013). Beyond brain mapping: Using neural measures to predict real-world outcomes. Current Directions in Psychological Science, 22(1), 45-50.
b. Berkman, E. T., Falk, E. B., & Lieberman, M. D. (2011). In the trenches of real-world self-control: Neural correlates of breaking the link between craving and smoking. Psychological Science, 22(4), 498-506.
c. Falk, E. B., Berkman, E. T., Mann, T., Harrison, B., & Lieberman, M. D. (2010). Predicting persuasion-induced behavior change from the brain. Journal of Neuroscience, 30(25), 8421-8424.
d. Falk, E. B., Berkman, E. T., Whalen, D., & Lieberman, M. D. (2011). Neural activity during health messaging predicts reductions in smoking above and beyond self-report. Health Psychology, 30(2), 177-185.

2. **Self-regulation of food craving as a model for appetitive craving regulation in general**. My lab has developed a laboratory task that yields behavioral and neural measures of self-regulation of food craving. The regulation of food craving is significant on its own given that food craving precipitates eating and relates to overweigh/obesity. Additionally, this paradigm provides a window into the neurocognitive processes involved in appetitive craving regulation more broadly, and has been deployed with children.
    a. Berkman, E.T. (2018). Value-based choice: An integrative, neuroscience-informed model of health goals. *Psychology & Health, 33*, 40-57.
    b. Giuliani, N. R., Tomiyama, A. J., Mann, T., & Berkman, E. T. (2015). Prediction of daily food intake as a function of measurement modality and restriction status. Psychosomatic Medicine, 77(5), 583–590.
    c. Giuliani, N. R., Mann, T., Tomiyama, A. J., & Berkman, E. T. (2014). Neural systems underlying the reappraisal of personally craved foods. Journal of Cognitive Neuroscience, 26(7), 1390–1402.
    d. Giuliani, N. R., Calcott, R. D., & Berkman, E. T. (2013). Piece of cake: Cognitive reappraisal of food craving. Appetite, 64, 56–61.

3. **Training-related improvement in executive functions such as inhibitory control**. There is much debate about this question in the literature, and our contribution to that debate is to show how a mechanistic understanding of how executive functions work at the level of neural function can provide insights into the questions of how those functions can be improved with training and why training so frequently fail to produce generalizable effects.
    a. Beauchamp, K. G., Kahn, L. E., & Berkman, E. T. (2016). Does inhibitory control training transfer? Behavioral and neural effects on an untrained emotion regulation task. Social Cognitive and Affective Neuroscience, 11, 1374-1382.
    b. Berkman, E. T. (2015). Self-regulation training. In Vohs, K. D., Baumeister, R. F. (eds.), Handbook of Self-Regulation (3rd edition, pp. 440-457). New York: Guilford Press.
    c. Berkman, E. T., Kahn, L. E., & Merchant, J. S. (2014). Training-induced changes in inhibitory control network activity. The Journal of Neuroscience, 34(1), 149-157.
    d. Berkman, E. T., Graham, A. M., & Fisher, P. A. (2012). Training self-control: A domain-general translational neuroscience approach. Child Development Perspectives, 6(4), 374-384.

4. **Ecological validity of executive function and emotion regulation tasks**. This work uses both neuroimaging and longitudinal experience sampling methodology, often together, to investigate whether and how well the tasks that are frequently used in the cognitive, social, and affective neuroscience literatures link up with real-world outcomes such as cigarette smoking cessation and unhealthy food intake.
    a. Falk, E. B., Berkman, E. T., & Lieberman, M. D. (2012). From neural responses to population behavior: Neural focus group predicts population-level media effects. Psychological Science, 23(5), 439-445.
    b. Berkman, E. T., Dickenson, J., Falk, E. B., & Lieberman, M. D. (2011). Using SMS text messaging to assess moderators of smoking reduction: Validating a new tool for ecological measurement of health behaviors. Health Psychology, 30(2), 186-194.
    c. Falk, E. B., Berkman, E. T., Whalen, D., & Lieberman, M. D. (2011). Neural activity during health messaging predicts reductions in smoking above and beyond self-report. Health Psychology, 30(2), 177-185.

d. Berkman, E. T., & Lieberman, M. D. (2010). Approaching the bad and avoiding the good: Lateral prefrontal cortical asymmetry distinguishes between action and valence. Journal of Cognitive Neuroscience, 22(9), 1970-1979.

Complete List of Published Work in MyBibliography and Google Scholar:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40864077/
http://scholar.google.com/citations?user=jCxd8-UAAAAJ&hl=en

D. Research Support

Ongoing Research Support

R01 HD094831-01A1 Fisher, PI; Berkman, Co-I 02/02/19-01/31/24
RCT of FIND video coaching intervention for caregivers facing economic adversity
The objective of this project is to conduct a randomized effectiveness trial of the FIND (Filming Interactions to Nurture Development) parent coaching program in the context of a diverse sample of low-income families with children ages 12–36 months who are eligible for Early Head Start (EHS) but cannot be enrolled due to lack of program capacity.

R01 CA211224-01A1 Berkman, PI 08/01/17-07/31/22
Devaluing energy-dense foods for cancer control: Translational neuroscience
This study evaluates the mechanisms of action of two effective programs to increase intake of cancer-preventing foods and decrease intake of cancer-promoting foods. Though the programs differ in their proximal effects (one targets behavioral and the other targets cognitive processes), we hypothesize that both ultimately exert their effects by altering the ventromedial prefrontal cortical valuation system.

R01MH107418-02 Pfeifer, PI; Berkman Co-I 08/01/15-04/30/20
Puberty, neural systems for social processes, and early adolescent mental health: A longitudinal neuroimaging study
This study provides a comprehensive picture of the pubertal, neurodevelopmental, and social psychological changes occurring during early adolescence, and their relationship to the emergence of mental health problems, so that modifiable, developmentally specific risk factors can be identified as targets for early intervention and prevention efforts.

Completed Research Support

P50DA035763-04 Fisher, PI; Berkman, Co-I 07/15/13-04/30/18
Risk-taking and social contexts in CWS-involved youth: Underlying processes
The proposed Center provides a national resource in drug abuse prevention research, with the ultimate goal of reducing drug use and related outcomes for child welfare involved youth.

Pilot Project Award Berkman (PI) 09/01/16-10/31/17
Bezos Family Foundation
Motivational boost to enhance parenting buy-in
This pilot study tests the efficacy of an identity-based motivation intervention to enhance commitment to, engagement with, and perseverance in new parenting behaviors among a group of high-adversity parents enrolled in a parenting course.

R21 CA175241-01A1 Berkman (PI) 09/24/14-08/31/17
Reducing craving for cancer-promoting foods via cognitive self-regulation
The goal of this study is to compare the efficacy of an autonomy-boosting intervention to an information-only treatment as usual control for engaging cognitive control neural systems and improving self-regulation of craving for cancer-promoting foods such as energy dense carbohydrates and red meat.
Role: PI

R01 AG048840-01 Berkman (PI) 09/30/14-04/30/17

Tailored inhibitory control training to reverse EA-linked deficits in mid-life
This study tests the feasibility and efficacy of a personalized inhibitory control training protocol to increase proactive activity in inhibitory control-related neural systems and thereby reduce health-risking behaviors among a sample of mid-life adults who experienced high levels of early adverse experiences.
Role: PI

Frontiers of Innovation Award Berkman (PI) 04/01/14-12/31/15
Center on the Developing Child at Harvard University
Brain-based intervention to remediate the effects of early adversity on inhibitory control
This pilot study tests the efficacy of a customized inhibitory control training intervention in early adolescents with extensive early adversity who are at high risk for drug use and other health-risking behaviors.

Developmental Project Funds Berkman (PI) 09/01/12-08/31/14
University of Michigan Center for Excellence in Cancer Communications Research
National Institutes of Health / National Cancer Institute
Self-, peer-, and distant other-authored messages for cigarette smoking cessation
This pilot compared the effect of distance-from-self authorship on cigarette smoking cessation outcomes and identify specific neural and linguistic properties of messages that are predictive of these outcomes.

R43 HL110487-01 Mulvihill (PI) 08/01/12–4/30/14
Computer-based program to promote exercise among sedentary employees
Build upon and update an already proven to be efficacious, web-based exercise-promoting intervention that targets sedentary employees, and innovatively integrate that program within an employee’s daily workflow using Google Apps.

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Mills, Kathryn Leeann

eRA COMMONS USER NAME (credential, e.g., agency login): KLMILLS16

POSITION TITLE: Assistant Professor of Psychology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Portland State University	B.A.	04/2011	Psychology
University College London	Ph.D	06/2015	Neuroscience
Oregon Health & Science University	Postdoctoral	03/2016	Behavioral Neuroscience
University of Oregon	Postdoctoral	06/2018	Psychology

A. Personal Statement

Over the past nine years, the focus of my research has been to characterize functional and structural brain development. My lab applies longitudinal research methods and network analysis techniques to investigate the intertwined social, biological, and cognitive processes that underlie the development of skills needed to navigate the social environment. This program of research has not only contributed theoretically to our understanding of how brain development relates to cognition, behavior and well-being, but has also advanced the methodological practices of the field. As a recognized expert in longitudinal modeling of developmental neuroimaging data, I have been invited to present at several workshops on this topic, as well as co-authored a number of reviews and edited a special issue on the topic. Although I am in an early stage of my career, I have had extensive experience mentoring students and conducting educational workshops on longitudinal modeling, resting state functional connectivity, and open neuroscience. Further, an advocate for open science, I not only make my analytic tools accessible and freely available for other researchers to use through online repositories, but have trained several students in open science practices. As Dani Cosme's Co-Sponsor for her F99 training, I will oversee Dani's training in longitudinal modeling, as well as postdoctoral preparation in resting state fMRI and network analysis. I have worked with Sponsor Berkman for three years as a member of the Center of Translational Neuroscience. Together with Sponsor Berkman, we will ensure that Dani's F99 training builds a solid foundation from which she can become a leader in translational neuroscience, conducting cancer prevention research.

B. Positions and Honors

Positions and Employment

2015-2016 Research Fellow, Scottish Collaboration for Public Health Research and Policy
2015-2016 Postdoctoral Fellow, Fair Neuroimaging Lab, Oregon Health & Science University
2016-2018 Postdoctoral Scholar, Department of Psychology, University of Oregon
2017-2018 Research Associate, Oregon Research Institute
2018- Assistant Professor, Department of Psychology, University of Oregon

Other Experience and Professional Memberships

2010-2012 Society for Neuroscience
2010, 2012 Cognitive Neuroscience Society

2014 Society for Research on Adolescence
2015 British Neuroscience Association
2016 Society for Research in Child Development
2017 Society for Neuroscience
2016-2018 Guest Editor for Developmental Cognitive Neuroscience
2018- Editor for Collabra: Psychology

Honors

2008-2009 Underrepresented Researchers Mentoring Program, Portland State University, Portland, OR
2008-2011 Oregon Laurels Scholarship, Portland State University, Portland, OR
2009-2010 McNair Scholars Program Participant, Portland State University, Portland, OR
2011 Summa Cum Laude, Portland State University, Portland, OR
2011-2015 UCL Studentship for PhD Programme, University College London, London, UK
2011 Abstract selected by Society for Neuroscience as “Hot Topic”
2012 Full Scholarship CSHL Workshop on Biology of Social Cognition, Cold Spring Harbor, NY
2012 Guarantors of Brain grant for conference travel
2012 Best poster CSHL Workshop on Biology of Social Cognition
2012 Abstract selected by Society for Neuroscience for press conference
2012 Sully Scholarship for Division of Psychology and Language Sciences, UCL, London, UK
2014 New Perspectives and Future Directions in Social Neuroscience Workshop Attendee
2014 Wellcome Trust Small Arts Award
2014 Guarantors of Brain grant for conference travel
2014 UCL Graduate School student conference travel award, UCL, London, UK
2014 Travel award for HBM Satellite workshop
2015 Guarantors of Brain grant for conference travel
2015 British Neuroscience Association Postgraduate Prize

C. Contributions to Science

1. My research as an undergraduate began with a focus on examining resting-state functional connectivity MRI across development and between neurotypical and clinical populations (e.g. ADHD). This work was completed under the mentorship of Dr. Damien Fair at Oregon Health & Science University (OHSU). At this time, little was known about the functional architecture of the developing brain, and how this functional architecture might be different in children with developmental disorders. This work emphasizes the value of network-based approaches for understanding developmental disorders such as ADHD. Specific techniques used in this work include support vector based multivariate pattern analyses to identify individuals with specific phenotypic features. My role in these studies included data collection and analysis, as well as contributing to the writing of the manuscripts.
    a. Fair DA, Iyer S, Bathula D, Nigg JT, **Mills KL**, Dosenbach NUF, Schlaggar BL, Mennes M, Gutman D, Bangaru S, Buitelaar J, Dickstein DP, Di Martino A, Kennedy D, Kelly C, Luna B, Schweitzer JB, Velanova K, Wang Y-F, Mostofsky S, Castellanos FX, & Milham MP (2013). Distinct Neural Signatures Detected for ADHD Subtypes After Controlling for Micro-Movements in Resting State Functional Connectivity MRI Data. *Frontiers in Systems Neuroscience, 6*(80).
    b. Fair DA, Bathula D, **Mills KL**, Dias, TG, Blythe MS, Zhang D, Snyder AZ, Raichle ME, Stevens AA, Nigg JT, & Nagel BJ (2010). Maturing thalamocortical functional connectivity across development. *Frontiers in Systems Neuroscience, 4*(10).
    c. Fair DA, Posner J, Nagel BJ, Bathula D, Dias TG, **Mills KL**, Blythe MS, Giwa A, Schmitt CF, & Nigg JT (2010*).* Atypical default network connectivity in youth with ADHD*. Biological Psychiatry, 68*(12), 1084-1091.

2. I have conducted the analyses for several projects examining the relationship between functional connectivity development and phenotypic characteristics of children and adolescents. These projects have related individual differences in functional connectivity to cognitive-behavioral measures, including temporal discounting, impulsivity, and working memory capacity. My most recent work in this area includes the first longitudinal investigation of how functional brain organization relates to temporal discounting behavior in the transition into adolescence.

a. Anandakumar J*, **Mills KL***†, Earl E, Irwin L, Miranda-Dominguez O, Demeter DV, Walton Weston A, Karalunas S, Nigg J, & Fair DA (2018). Individual differences in functional brain connectivity predict temporal discounting preference in the transition to adolescence. Developmental Cognitive Neuroscience, 34, 101-113. (*shared first authorship) (†corresponding author)
b. **Mills KL**, Bathula D, Costa Dias TG, Iyer SP, Fenesy MC, Musser ED, Stevens CA, Thurlow BL, Carpenter SD, Nagel BJ, Nigg JT, & Fair DA (2012). Altered cortico-striatal-thalamic connectivity in relation to spatial working memory capacity in children with ADHD. *Frontiers in Psychiatry*, *3*(2).
c. Shannon BJ, Raichle ME, Snyder AZ, Fair DA, **Mills KL**, Zhang D, Bache K, Calhoun V, Nigg JT, Nagel BJ, Stevens AA, & Kiehl KA (2011). Premotor functional connectivity predicts impulsivity in juvenile offenders. *PNAS, 108*(27), 11241-11245.
d. Dias TG, Wilson VB, Bathula D, Iyer SP, **Mills KL**, Thurlow BL, Stevens CA, Musser ED, Mitchell SH, Nigg JT, & Fair DA (2013). Reward circuit connectivity relates to delay discounting in children with attention-deficit/hyperactivity disorder*. European Neuropsychopharmacology, 23*(1):33-45.

3. My work as a graduate student demonstrated that adolescence is a period of substantial development in both in terms of social navigation and brain structure. The empirical studies conducted as part of my graduate thesis provided support for the theory that adolescence is possibly a sensitive period to social signals in the environment, as this research provided evidence for the continued development of both cognitive skills and regions of the brain involved in social development between childhood and adulthood. I used longitudinal modeling in many of these projects to examine trajectories of brain development.
    a. **Mills KL**, Dumontheil I, Speekenbrink M, & Blakemore S-J (2015). Multitasking during social interactions in adolescence and early adulthood. *Royal Society Open Science*, *2*(11), 150117.
    b. **Mills KL**, Goddings AL, Clasen LS, Giedd JN, & Blakemore S-J (2014). The developmental mismatch in structural brain maturation during adolescence. *Developmental Neuroscience* 36(3-4), 147-60.
    c. Goddings AL, **Mills KL**, Clasen LS, Giedd JN, Viner R, & Blakemore S-J (2014). The influence of puberty on subcortical brain development. *NeuroImage*, 88, 242-51.
    d. **Mills KL**, Lalonde F, Clasen LS, Giedd JN, & Blakemore S-J (2014). Developmental changes in the structure of the social brain in late childhood and adolescence. *Social Cognitive and Affective Neuroscience, 9*(1), 123-31.

4. I have conducted several reviews to synthesize the current evidence on adolescent brain development. One review provided evidence for the hypothesis that adolescence is a time of heightened receptivity and sensitivity to complex social signals in the environment. Another review provided a critical examination of the scientific evidence for the hypothesis that Internet use is affecting brain develop in adolescence. My reviews of the methods and results of all longitudinal studies of brain development proposed best practices to move the field toward increased validity and reproducibility of findings.
    a. **Mills KL**, & Tamnes CK (2014). Methods and considerations for longitudinal structural brain imaging analysis across development. *Developmental Cognitive Neuroscience*, *9*, 172-190.
    b. Blakemore S-J, & **Mills KL** (2014). Is adolescence a sensitive period for socio-cultural processing? *Annual Review of Psychology*, *65*, 187-207.
    c. **Mills KL** (2014). Effects of Internet use on the adolescent brain: despite popular claims, experimental evidence remains scarce. *Trends in Cognitive Sciences, 18*(8), 385-387.
    d. Vijayakumar N, **Mills KL**, Alexander-Bloch A, Tamnes CK, & Whittle S (2017). Structural brain development: a review of methodological approaches and best practices. *Developmental Cognitive Neuroscience.*

5. During my doctoral training I initiated an international collaboration across several institutions to undertake the first to attempt to replicate the patterns of structural brain development across multiple independent longitudinal samples. We have published the results of our collaboration in three journal articles and have made our analysis scripts openly available.
    a. **Mills KL**, Goddings AL, Herting MM, Meuwese R, Blakemore S-J, Crone EA, Dahl RE, Güroğlu B, Raznahan A, Sowell ER, & Tamnes CK (2016). Structural brain development between childhood and adulthood: Convergence across four longitudinal samples. *NeuroImage, 141*, 273-281.
    b. Tamnes CK, Herting MM, Goddings AL, Meuwese R, Bartsch H, Blakemore S-J, Dahl RE, Güroğlu B, Raznahan A, Sowell ER, Crone EA, & **Mills KL** (2017). Development of the cerebral cortex

across adolescence: A multisample study of interrelated longitudinal changes in cortical volume, surface area and thickness. *Journal of Neuroscience, 37*(12), 3402-3412.

c. Herting MM, Johnson C, **Mills KL**, Vijayakumar N, Dennison M, Liu C, Goddings A-L, Dahl RE, Sowell ER, Whittle S, Allen NB, & Tamnes CK (2018). Development of subcortical volumes across adolescence in males and females: A multisample study of longitudinal changes. *NeuroImage*, *172,* 194-205.

Complete List of Published Work in Google Scholar:
https://scholar.google.com/citations?user=hZ-YQ3AAAAAJ&hl=en

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH Loan Repayment Program 07/01/2017 - 06/30/2019
Student loan repayment funded by NIMH Pediatric – Extramural program.
Role: Recipient

Completed Research Support

NSF BCS-1736406 Byrne (PI) 06/01/2017 - 05/31/2018
Modeling Developmental Change: Practical Integration of Advanced Neuroimaging and Statistical Methods
Organized and led a two-day workshop on best practices for processing, analyzing, modeling, and interpreting longitudinal neuroimaging data.
Role: Co-PI

PHS Fellowship Supplemental Form

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Introduction

1. Introduction to Application
(for Resubmission applications)

Fellowship Applicant Section

2. Applicant's Background and Goals for Fellowship Training*	ApplicantsBackgroundGoals.pdf

Research Training Plan Section

3. Specific Aims*	SpecificAims.pdf
4. Research Strategy*	ResearchStrategy.pdf
5. Respective Contributions*	RespectiveContributions.pdf
6. Selection of Sponsor and Institution*	SelectionSponsorInstitution.pdf
7. Progress Report Publication List (for Renewal applications)	
8. Training in the Responsible Conduct of Research*	ResponsibleConductResearch.pdf

Sponsor(s), Collaborator(s) and Consultant(s) Section

9. Sponsor and Co-Sponsor Statements	SponsorCoSponsorStatements.pdf
10. Letters of Support from Collaborators, Contributors and Consultants	Falk_LetterOfSupport.pdf

Institutional Environment and Commitment to Training Section

11. Description of Institutional Environment and Commitment to Training	DescriptionInstitutionalEnvironmentCommitmentTraining.pdf

Other Research Training Plan Section

Vertebrate Animals

The following item is taken from the Research & Related Other Project Information form and repeated here for your reference. Any change to this item must be made on the Research & Related Other Project Information form.

Are Vertebrate Animals Used? ☐ Yes ☑ No

12. Are vertebrate animals euthanized?

If "Yes" to euthanasia
Is method consistent with American Veterinary Medical Association (AVMA) guidelines?

If "No" to AVMA guidelines, describe method and provide scientific justification

13. Vertebrate Animals

PHS Fellowship Supplemental Form

Other Research Training Plan Information

14. Select Agent Research

15. Resource Sharing Plan

16. Authentication of Key Biological and/or Chemical Resources

Additional Information Section

17. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ☐ Yes ☑ No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s), using the registry information provided within the agency instructions. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s):

18. Alternate Phone Number:

19. Degree Sought During Proposed Award:

Degree:	If "other", indicate degree type:	Expected Completion Date (MM/YYYY):
PHD: Doctor of Philosophy		06/2021

20. Field of Training for Current Proposal*: 639 Social Psychology

21. Current or Prior Kirschstein-NRSA Support?* ☐ Yes ☑ No

If yes, identify current and prior Kirschstein-NRSA support below:

Level*	Type*	Start Date (if known)	End Date (if known)	Grant Number (if known)

22. Applications for Concurrent Support?* ☐ Yes ☑ No

If yes, describe in an attached file:

23. Citizenship*

U.S. Citizen — U.S. Citizen or Non-Citizen National? ☑ Yes ☐ No

Non-U.S. Citizen
- ☐ With a Permanent U.S. Resident Visa
- ☐ With a Temporary U.S. Visa

If you are a non-U.S. citizen with a temporary visa applying for an award that requires permanent residency status, and expect to be granted a permanent resident visa by the start date of the award, check here: ☐

24. ☐ Change of Sponsoring Institution — Name of Former Institution:*

PHS Fellowship Supplemental Form

Budget Section

All Fellowship Applicants:

25. Tuition and Fees*:

☐ None Requested ☑ Funds Requested

Year 1	$21,765.00
Year 2	$21,765.00
Year 3	$8,776.00
Year 4	$8,776.00
Year 5	$8,776.00
Year 6 (when applicable)	$8,776.00
Total Funds Requested:	$78,634.00

Senior Fellowship Applicants Only:

	Amount	Academic Period	Number of Months
26. Present Institutional Base Salary:			

27. Stipends/Salary During First Year of Proposed Fellowship:

a. Federal Stipend Requested:	Amount	Number of Months
b. Supplementation from Other Sources:	Amount	Number of Months
	Type (e.g.,sabbatical leave, salary)	
	Source	

Appendix

28. Appendix

APPLICANT'S BACKGROUND AND GOALS FOR FELLOWSHIP TRAINING

A. Doctoral Dissertation and Research Experience

Below I highlight key skills, methods, and research interests that will support the accomplishment of my training goals using **bold, underlined** typeface.

Neuroplasticity and interactions between cognition and emotion. I began my undergraduate studies as a biology major at Chapman University, with the aspiration of becoming a neuroscientist. My fascination with **neuroplasticity** led me to begin working in Dr. William Wright's marine neurobiology lab studying the evolutionary mechanisms of learning and memory. Inspired by the pioneering work by Eric Kandel, the first project I worked on investigated the neural basis of sensitization in sea hares (*Aplysia Californica)*. I learned how to ethically conduct animal surgery and carried out classical conditioning experiments. Whereas classic sensitization experiments typically use electrical shocks, this method lacks ecological validity. Because sensitization evolved in the natural world, we chose to study sensitization using touch and observed similarly enhanced withdrawal responses following tactile stimulation. Extending this line of work, I piloted a project using sub-lethal attacks by natural predators to induce sensitization in *Aplysia*, which informed later work using lobsters, ultimately published by my colleagues in *Learning and Memory*. Although the theoretical implications were striking, I realized that my passion lay in understanding neuroplasticity in humans and switched my major to psychobiology. My initial interest in the **interactions between cognition and emotion** was sparked by my undergraduate work in Dr. Connie Shears' cognitive psychology lab where I studied the effect of emotion on inference processing. I worked as part of a small team to develop stimuli, design experiments, recruit and run subjects, and analyze behavioral data. I won a travel grant to present this work at an international conference. While I lacked the means to investigate the neural correlates underlying these processes, it was a valuable introduction to psychological research and confirmed my longstanding sense that research was my calling.

Individual differences in emotional reactivity. To gain more experience with psychological research and prepare for doctoral studies, I began a master's degree in psychology at Stockholm University in Sweden. Here, I continued to refine my interests in emotion, cognition, and neuroplasticity. Through my coursework, I realized that it is not just emotion that affects cognition, but cognition also affects emotion; cognitive processes such as attention and appraisals (interpretations) modulate emotional responses. Because emotional responses are powerful drivers of behavior that can lead to maladaptive coping mechanisms, such as unhealthy eating and substance use, there is great potential to improve health and well-being by teaching individuals to control their emotional responses using cognitive strategies. Following this line of reasoning, I became interested in whether meditation could be used as a vehicle to **train emotion regulation and improve well-being**. Although I did not have the ability conduct a meditation intervention, I approached this question from an **individual difference perspective**. Together with my master's thesis advisor, Dr. Stefan Wiens, I developed a rigorous **psychophysiological experiment** to test whether emotional reactivity varies as a function of trait mindfulness. Prior research suggested that mindfulness meditation reduces emotional reactivity by facilitating disengagement from emotional stimuli, but it was unclear whether people with higher trait mindfulness actually exhibit decreased reactivity to emotional stimuli. To comprehensively characterize emotional reactivity, we used a **multi-method approach** and collected electrocortical brain activity (EEG), skin conductance, startle response, and self-reported responses to highly arousing emotional pictures. Across all measures, we did not find evidence for moderation by trait mindfulness, suggesting that either self-reported trait mindfulness is not related to spontaneous emotional reactivity or that the available questionnaires may not be valid measures of mindfulness. This work resulted in a first-author publication in *PLOS One*.

Neurodevelopmental trajectories of self and social processing across adolescence. Upon completing my master's thesis, I returned to the United States to immerse myself in the thriving social and affective neuroscience community and to gain experience with neuroimaging. I obtained a lab manager position at the University of Oregon working with Drs. Elliot Berkman and Jennifer Pfeifer. Splitting my time between their two labs afforded me the opportunity to work on a variety of projects, including large-scale prospective studies investigating topics like self-regulation and risk-taking in adolescent and adult populations who experienced early adversity. This experience was critical for my scientific development, both because it introduced me to the field of translational neuroscience and because it allowed me to develop priceless research skills. I gained experience with **experimental design**, functional neuroimaging (fMRI) **acquisition and optimization**, **programming** in a variety of computer languages, community participant **recruitment and retention**, as well as essential "soft skills" such as project management, troubleshooting, and on-the-fly problem solving.

Working with Dr. Pfeifer, an expert in developmental social neuroscience, convinced me that adolescence is a unique window of opportunity for interventions to help shape healthy habits and prevent engagement in health-risking behaviors. Working with Dr. Pfeifer, I had the unique opportunity to learn **fMRI preprocessing and analysis** using data from a 6-year **longitudinal study** on self and social development. Although human adolescence is characterized by major shifts in self and social processing, the specific neurodevelopmental trajectories of self and social evaluations are not well characterized. Further, these developmental effects are often subtle and not well-powered using traditional analytic methods. Because of this, I helped develop an innovative analysis technique to probe developmental effects across the whole brain while increasing power. We used a standardized parcellation atlas to divide the brain into 350 regions of interest (ROIs) rather than 70,000 voxels (volumetric pixels), extracted the mean signal within each ROI for each subject, time point, and condition, and used this data as inputs to a linear mixed effects model. This approach is significant because it substantially reduces the number of multiple comparisons and stabilizes effect estimates by averaging the signal across voxels in each ROIs. Our results showed expected increases in activation for self and social processing in their respective neural networks. However, we also showed that self-evaluations in the academic domain become highly salient, affirming the importance of academic identity during adolescence. To introduce this novel method to others, I was invited to present at the NSF-sponsored Modeling Developmental Change workshop. I also won a Jacobs Foundation Young Scholars Award to present this work at the Flux congress in the Netherlands. We are currently preparing this manuscript for publication and expect to submit in spring 2019. Overall, this was a formative experience, providing me with the skill set to pursue a doctoral degree in translational neuroscience, as well as revealing to me the incredible importance of taking a **developmental approach**. I also developed excellent working relationships with Drs. Berkman and Pfeifer and chose to continue working with them as a doctoral student.

The effect of choice on appetitive self-regulation. As a doctoral student, I continued my work on emotional self-regulation and began examining the ability to regulate **emotional responses to appetitive stimuli**. Although self-regulation to avoid goal-incongruent temptations is critical for healthy development, individuals who are otherwise capable often *choose not* to regulate. In most self-regulation tasks participants are explicitly told when to regulate, and thus these tasks only assess participants' abilities to regulate when prompted to do so. However, this approach lacks fidelity to the regulatory process outside the lab, where participants must decide for themselves whether and when to engage in regulation. To improve **ecological validity** and assess whether and how self-regulation may differ when individuals *choose* to regulate, Dr. Pfeifer and I designed a novel neuroimaging paradigm to test the hypothesis that choosing to regulate improves appetitive self-regulation for personally-craved foods. Participants used **cognitive reappraisal** to reframe their foods cravings and were either instructed when to regulate or chose when to regulate. Based on previous research showing that autonomy promotes intrinsic motivation and enhances self-regulation, we expected choice to facilitate regulation. However, we observed the opposite effect; choice actually disrupted regulation. To probe this unexpected result, I collaborated with Dr. Dagmar Zeithamova to employ **multivariate fMRI methods**. We found evidence that the disruption may be due to inefficient allocation of cognitive resources on choice trials, presumably because the choice itself demanded those resources. This work is important because it shows that standard task paradigms instructing individuals when to regulate may not generalize to behavior outside the lab, where they must first decide to regulate. This work resulted in a first-author manuscript at *Social Cognitive and Affective Neuroscience* and allowed me to further develop my expertise with **univariate neuroimaging analysis** and gain experience with **machine learning**. To further investigate the effect of choice on appetitive self-regulation, I designed a follow-up experiment and collected data from 117 participants while undergoing functional neuroimaging. I am currently in the process of submitting this study as a registered report.

Autonomy, appetitive self-regulation, and health-risking behaviors during the transition to college. **Designing effective interventions** to reduce collegiate substance use and other health-risking behaviors requires identification of risk factors that are amenable to change, such as appetitive self-regulation. Further, because there is a sudden increase in autonomy and decrease in regulatory scaffolding during the transition to college, it is important to understand how autonomous motivation interacts with regulatory ability. Extending the work cited above, I sought to investigate how individual differences in the ability to regulate appetitive motivations relate to substance use in college freshmen. I designed and carried out a year-long **longitudinal pilot study** to assess the ability of autonomous appetitive self-regulation to predict changes in substance use across freshman year. Prior to fall term, we assessed appetitive self-regulation ability and choice tendency with the task described above while participants were in the MRI scanner and measured self-reported **substance use** and engagement in other **health-risking behaviors**. Participants completed follow-up assessments each

quarter during freshman year to assess these measures. Our results indicated that autonomous self-regulation better predicted outcomes than either standard measures of appetitive self-regulation or other known predictors, such as gender, SES, or ethnicity. Dr. Pfeifer and I used this pilot data to write an R21 grant application to conduct this study in a large, well-powered sample, and it was funded by the National Institute on Drug Abuse. We collected neuroimaging data and baseline assessments from a large sample of incoming college freshman during the summer of 2018 and are currently tracking their health and well-being via quarterly self-report assessments. Leading this project has given me invaluable experience with project management, designing and conducting longitudinal studies, and critical experience with **grant writing**.

Eating behavior and reactivity, regulation, and valuation. Clarifying the mechanisms underlying **eating behavior** is essential for developing interventions to improve dietary habits and reduce the prevalence of overweight and obesity. Together with Dr. Berkman and others, I helped refine a framework for understanding the interplay between three key psychological processes involved in food choice–**cue reactivity, self-regulation, and valuation**. In contrast to predominant dual-process models, which emphasize the antagonistic relationship between reactivity and regulation, our framework proposes that subjective value plays a critical role in food choice, moderating the role reactivity and regulation play during decision making. We published a review of this work in the *Annals of the New York Academy of Sciences*. I also tested this model empirically in the context of an ecologically valid food decision making paradigm in which participants place monetary bids on healthy and unhealthy foods. I extracted estimates of neural activation from regions associated with reactivity, regulation, and valuation, and used **multilevel modeling** to test predictions of these two models on a trial by trial basis. The results showed evidence for the moderating role of subjective value, but did not support the dual-process account. This research adds critical evidence that refines models of self-regulation and eating behavior. I am the first author on this manuscript currently under review at *Social Cognitive and Affective Neuroscience.* Through this research, I've reviewed the neuroscientific literature on the psychological processes involved in human eating behavior and gained experience with **statistical model comparison**.

Doctoral Dissertation. The primary focus of my current research is on the relationship between **appetitive self-regulation** and health-risking, cancer-promoting behaviors, including unhealthy eating and substance use. Ultimately, I seek to improve our ability to predict real-world behavior using neural and behavioral data in order to identify risk and protective factors relevant to **cancer control**. Towards this goal, I have focused on improving the ecological validity of a task assessing appetitive self-regulation ability by incorporating choice into the paradigm and using it to predict substance use during freshman year. The findings from this work will constitute the first two chapters of my dissertation. The final chapter will focus on improving our ability to predict real-world behavior by enhancing the sensitivity and specificity of neural indicators of appetitive self-regulation. As outlined in the current project proposal for the F99 phase, I will pursue this goal by developing and validating a neural signature of craving reappraisal. Once created, this **neural signature** can be used in a variety of novel ways to advance the field, including assessment of spontaneous engagement in reappraisal, individual differences in craving reappraisal ability, and craving reappraisal intervention success. Ultimately, this work will reduce the prevalence of diet-related cancers by helping improve intervention development and efficacy. I have proposed my dissertation and plan to defend it in summer 2021.

B. Training Goals and Objectives

My long-term career goal is to become a leading cancer researcher in the field of translational neuroscience. The overarching objective of my research program is to leverage advanced multivariate neuroimaging techniques to build sensitive and specific neurobiological indices of target psychological processes, using task-based and task-free neuroimaging data, in order to more effectively evaluate whether, how, and for whom cancer-relevant health behavior change interventions are working. I plan to conduct rigorous, reproducible research that will help shape practice and policy. Ultimately, I believe this work will reduce the prevalence of cancer by helping people develop healthy habits and avoid engaging in behaviors, such as unhealthy eating, physical inactivity, and tobacco and substance use, that increase risk for a variety of cancers. Achieving these goals requires knowledge and skills in a variety of distinct domains. To develop these skills, I plan to build on my present skill set and acquire training in those domains I have not yet mastered. Specifically, my training goals are to develop expertise in intervention design, implementation, and evaluation using advanced longitudinal modeling techniques during the F99 phase, and in resting state fMRI and network analytic methods during the K00 phase.

F99 phase

Translational neuroscience. The goal of translational neuroscience is to leverage findings from basic research in neuroscience and psychology to develop and improve treatments to promote health and well-being. I plan to learn this approach in order to develop health behavior change interventions to reduce engagement in cancer-relevant behaviors. My goal is to learn how to design, implement, and evaluate a randomized controlled trial (RCT) of a novel craving reappraisal intervention to change eating behavior, and identify moderators that affect intervention efficacy. To do so, I am developing a neural signature of craving reappraisal using machine learning and multivariate neuroimaging methods under the mentorship of Dr. Zeithamova, and will complete this work prior to the start date of this award. During the F99 phase of this project, I will use this neural signature to evaluate the efficacy of the craving reappraisal intervention to improve healthy eating in overweight and obese adults at risk for developing diet-related cancers. Through Dr. Berkman's mentorship and R01, the parent grant for this project, I will receive training in intervention development for cancer control and longitudinal randomized control trial study design. Being awarded this fellowship will free me from my duties as a graduate research fellow and allow me to focus exclusively on my training aims. Rather than running participant sessions and operating the MRI scanner, I will be able to be involved in this project at a higher, more supervisory level and receive critical training that will propel me towards a successful career in academia. *I would not be able to accomplish all of my training aims, which are necessary to achieve my career goals, without the support provided by this fellowship.*

Advanced statistical techniques for longitudinal data. To evaluate intervention outcomes over time using the craving reappraisal neural signature, I will learn advanced statistical methods including multilevel modeling and structural equation modeling (SEM). I am well prepared for this aim, as I have used multilevel modeling in a number of analyses with nested data structures, and have taken a course in SEM. However, I have not used these techniques to do latent growth curve modeling or cross-lagged panel mediation models, which will enable me to assess mediated longitudinal change in intervention outcomes (e.g., healthy eating) with greater specificity than other approaches. This objective will be supported through coursework taught by Dr. Berkman and individual meetings with Drs. Mills and Berkman. Dr. Mills will provide hands on mentorship, assisting with the specification and programming of models in R using the lavaan package. Dr. Mills is an expert in longitudinal modeling with neuroimaging data, scientific computing, as well as resting state fMRI methods. Together with Dr. Berkman's expertise in translational neuroscience and cancer control, this mentorship team will help me achieve my doctoral training goals for the F99 phase, and launch me onto a successful path to pursue my postdoctoral training goals in the K00 phase.

Professional development. I will engage in critical professional development activities beyond the aforementioned training goals, including manuscript publication and presentations at professional meetings. To gain experience with grant management, I will participate in monthly meetings with the R01 leadership team. Further, to prepare me to pursue my postdoctoral training goals during the K00 phase, I will attend weekly resting state journal club meetings supervised by Dr. Mills, and conduct a systematic review of the literature on resting state fMRI applications to interventions together with Dr. Mills. This will facilitate the identification of K00 mentors and inform the refinement of my K00 training plan. I will select K00 mentors under the active guidance of Drs. Berkman and Mills. Dr. Berkman will help me generate a list of potential mentors with expertise in translational neuroscience who are currently running cancer-relevant health behavior change interventions, and Dr. Mills will help identify potential mentors with expertise in resting state fMRI and network science. A comprehensive list of specific activities related to these training goals is presented below.

K00 phase

Health behavior change intervention breadth. In order to achieve my long-term goal of developing and evaluating whether, how, and for whom cancer-relevant health behavior change interventions are working, I need to gain experience with a broad array of interventions and cancer-relevant outcomes. I plan to build on my experience designing, implementing, and evaluating an intervention to promote healthy eating, to gain exposure to health behavior change interventions targeting other modifiable behaviors, such as physical activity, or alcohol or tobacco consumption. In addition, because my intervention experience thus far has been limited to working with adults from a relatively homogenous population, I plan to work with mentors who take a developmental approach and have access to samples that are more representative of the racial, ethnic, and socioeconomic makeup of the United States. Ideally, I will pursue postdoctoral training in the context of an ongoing health behavior change RCT to reduce cancer risk in late adolescents or young adults, for whom unhealthy habits have not yet crystallized.

Resting state fMRI and network science. Though task-based fMRI is well-suited to identifying the neural underpinnings of specific psychological processes in the moment (i.e., more state-like features), task-

free, “resting state” fMRI reveals the connectivity of relatively more stable, intrinsic brain networks (i.e., more trait-like features) that may be more related to enduring patterns of health behaviors. Consequently, I plan to compliment my experience with multivariate and machine learning approaches to task-based fMRI to develop neural signatures from resting state functional connectivity patterns within and between established functional brain networks. Identifying network connectivity profiles that reliably index specific psychological process or are associated with intervention success and generalize to new samples will enable me to evaluate health behavior change interventions in a comprehensive fashion, spanning multiple temporal scales (state to trait). In order to achieve this objective, I will obtain training in how to acquire and preprocess resting state fMRI data using state of the art, open source tools, and how to control for critical signal artifacts from motion and other sources of physiological noise (e.g., pulse, respiration). I will also acquire theoretical training in graph theory and network science, and practical training on how to conduct network analyses with resting state fMRI data. To receive the best training possible, I plan to pursue these training goals under the supervision of mentors who are at the forefront of this field, developing innovative methods and tools.

Professional development. During the K00 phase, I will continue to engage in important professional development activities, such as presenting and publishing research, but will also gain further experience mentoring, teaching, and managing personnel. I will also participate in workshops to strengthen my writing and grantsmanship, and prepare a portfolio to enter the academic job market. This critical training will ensure that I am prepared to effectively handle the multifaceted demands of a career as a principal investigator.

C. Activities Planned Under This Award

The following didactic and pragmatic activities have been carefully selected to enable me to achieve my training goals. These activities will also promote my long-term career goal of becoming a leading independent researcher in the field of translational neuroscience studying cancer-relevant health behavior change.

F99 phase

1. **Translational neuroscience and evaluation of longitudinal RCT outcomes**
    a. **Intervention design:** Assist with design of RCT craving reappraisal intervention for NCI R01
    b. **Intervention monitoring:** Supervise staff to maintain fidelity with intervention protocol
    c. **Intervention evaluation:** Assess treatment effects and individual differences in treatment responsivity using advanced statistical and longitudinal modeling techniques
    d. Weekly individual meetings with Dr. Berkman
    e. Bi-weekly individual meetings with Dr. Mills
    f. Weekly project meetings with the NCI R01 team
    g. Monthly collaborative mentorship meetings with Drs. Berkman and Mills
    h. Bi-weekly Center for Translational Neuroscience brownbag to present and receive feedback
    i. Courses: Translational Neuro. (Fall 2019), Multilevel Modeling (Spring 2020), SEM (Fall 2017)
2. **Professional development**
    a. Prepare and publish planned first author manuscripts
        i. Paper 1: Development and validation of neural signature of craving reappraisal
        ii. Paper 2: Individual differences in reappraisal intervention success using neural signature
    b. Present research at lab meetings, brownbags, and conferences (e.g., OHBM, SANS, Flux)
    c. Monthly leadership team meetings with NCI R01 PI, co-Is, consultants, and full-time project staff
3. **K00 preparation**
    a. Weekly resting state fMRI journal club supervised by Dr. Mills
    b. Systematic review of literature on resting state fMRI in the context of interventions with Dr. Mills
    c. Generate list of potential K00 mentors with Drs. Berkman and Mills
    d. Identify K00 mentors and refine K00 training plan

K00 phase

1. **Health behavior change intervention breadth**
    a. Assist with an ongoing **RCT implementation** targeting cancer-relevant outcomes such as alcohol or tobacco consumption, or physical activity
    b. Gain experience with a wide array of methods for assessing **cancer-relevant outcomes** (e.g., ecological momentary assessment, accelerometer data)
    c. Apply a developmental approach to **tailor interventions** as a function of developmental stage
    d. Develop neurobiological indices using **representative samples** to facilitate generalizability
2. **Resting state fMRI and network science**

a. Gain experience **acquiring** resting state fMRI with real-time motion assessment (i.e., FIRMM)
b. Learn to **preprocess** resting state fMRI using cutting edge pipelines (e.g., XCP pipeline)
c. Gain familiarity with best practices to deal with **motion and physiological artifacts**
d. Extend current programming experience to **learn Python** in order to utilize state of the art tools
e. Complete coursework, bootcamps, and workshops (e.g., Indiana network science workshop, MIND summer camp) to learn the theoretical underpinnings of **graph theory** and network analytic methods
f. Hands on training with software for conducting **network analyses** (e.g., NiLearn, PyNets)
g. Practical training applying **machine learning methods** to resting state fMRI

3. **Professional development**
   a. Prepare and publish planned first author manuscripts
      i. Paper 1: Development and validation of task-free neural signatures
      ii. Paper 2: Individual differences in health behavior change intervention success
      iii. Paper 3: Comparison of neural signatures developed using task-based and task-free fMRI to predict intervention outcomes
   b. Present research at lab meetings, brownbags, and conferences (e.g., OHBM, SANS, Flux)
   c. Gain mentorship and personnel management experience by mentoring students in the lab
   d. Gain teaching experience by teaching workshops and classes (e.g., in fMRI or stats methods)
   e. Apply for tenure track faculty positions
   f. Write R21 grant application to launch faculty research

Timeline for proposed research training and activities, and percentage of time per year.

Phase	Year	Research & Manuscript Prep	Coursework	Teaching	Mentoring	Professional Development
F99	1	90%	5%	–	–	5%
	2	90%	–	–	–	10%
K00	1	80%	10%	–	–	10%
	2	80%	5%	–	5%	10%
	3	75%	–	5%	10%	10%
	4	75%	–	5%	10%	10%

F99 phase

Year 1	Year 2
RCT data collection	Complete Aim 1 analysis
Preprocess Aim 1 fMRI data	Identify K00 mentors
Model Aim 1 fMRI data	Refine K00 training plan and submit application
Complete coursework	Write and defend dissertation
F99 paper 1 manuscript preparation and submission	F99 paper 2 manuscript preparation and submission
Present at lab meetings, brownbags, and conferences	Present at lab meetings, brownbags, and conferences

K00 phase

Year 1	Year 2
Human subjects and RCR training	Training & coursework in health behavior change
Assist with ongoing health behavior change RCT	Assist with ongoing health behavior change RCT
Training, coursework, & workshops in resting state fMRI	Develop neurobiological indices using resting state fMRI
Training, coursework, & workshops in network science	K00 paper 1 manuscript preparation and submission
Analyze existing resting state fMRI data	Graduate & undergraduate mentoring
Manuscript preparation and submission	Present at lab meetings, brownbags, and conferences
Present at lab meetings, brownbags, and conferences	
Year 3	**Year 4**
Evaluate RCT using neurobiological indices	K00 paper 3 manuscript preparation and submission
K00 paper 2 manuscript preparation and submission	Write and submit R21 grant application
Compare predictive utility of task-based & task-free indices	Graduate & undergraduate mentoring
Graduate & undergraduate mentoring	Present at lab meetings, brownbags, and conferences
Present at lab meetings, brownbags, and conferences	Teach workshops and classes
Teach workshops and classes	Apply, interview, and negotiate tenure track position

SPECIFIC AIMS

Health behaviors, such as diet, sedentary lifestyles, and tobacco and alcohol consumption, increase the risk for developing various forms of cancer. Fortunately, these behaviors are modifiable and effective interventions have been developed to promote health behavior change. However, strong individual differences in treatment efficacy persist even in highly effective interventions. To understand why an intervention works for some people and not for others requires clearly defined mechanisms of change and sensitive and specific tools to evaluate individual differences in intervention targets. Functional neuroimaging (fMRI) is well suited to test theories of change because it can test competing mechanistic hypotheses that present the same overt behavior and can explain additional variance beyond behavior and self-report measures, which are more susceptible to self-presentational concerns and may not provide full information about what determines behavior.

The **overall objective** of this proposal is to develop a coherent research framework for creating reliable neurobiological indices that can assess 1) change in intervention targets and 2) individual differences in treatment response. I will then use these indices to predict cancer-relevant outcomes. This objective is well aligned with my **long-term goal** of becoming a leading investigator in the field of translational neuroscience, designing and evaluating interventions to reduce risk for cancers via health behavior modification. Achieving this long-term goal requires a multi-method approach using advanced neuroimaging and statistical techniques, with task-based and task-free neuroimaging data. I will achieve this objective through two specific aims, which provide **critical training** in translational neuroscience and advanced longitudinal modeling during the F99 phase, and in resting state functional neuroimaging and network analytic methods during the K00 phase.

Aim 1: The Dissertation Research Project. My dissertation evaluates the efficacy of an RCT to promote healthy eating and assess the degree to which cancer-relevant intervention outcomes are moderated by change in a neurobiological index (i.e., “neural signature”) of the intervention target, craving reappraisal. Craving reappraisal is a cognitive tool that shifts attention from the rewarding aspects of food to the costs of consumption, and effectively reduces craving for and subjective value of unhealthy foods. I will use data from a longitudinal RCT (R01 CA211224) assessing the efficacy of a four-week craving reappraisal intervention to reduce the value and consumption of unhealthy, cancer-promoting foods in overweight and obese adults. Neural measures of craving reappraisal ability and behavioral measures of food valuation and eating behavior are assessed pre and post, and outcome measures are assessed at 3- and 6-month follow-ups to evaluate the persistence of treatment effects. I am now developing and validating a neural signature of craving reappraisal using machine learning and multivariate neuroimaging techniques on existing data from our lab. This work is significant because it is the first neural index of craving reappraisal that generalizes across people, thereby increasing sensitivity to detect individual differences in reappraisal ability. Once validated, I will use this index to assess the degree to which 1) the reappraisal intervention causes change in the neural signature, and 2) individual differences in neural signature change predict outcomes. I expect that people with larger changes in the neural signature of craving reappraisal will show greater changes in food valuation and eating behavior.

F99 training goals: *Learn to design, manage, and evaluate a randomized control trial using advanced, multivariate task-based neuroimaging techniques. Gain further experience with advanced longitudinal modeling techniques to assess intervention outcomes and individual differences in treatment efficacy.*

Aim 2: The Postdoctoral Research Direction. Though task-based fMRI is designed to identify the neural correlates of specific psychological processes (i.e., state-like features), task-free resting state fMRI reveals the organization of relatively stable, intrinsic brain networks (i.e., trait-like features) that are more likely to relate to enduring patterns of health behaviors. To assess changes in brain networks related to health behavior change, I will use resting state fMRI data to identify reliable network connectivity profiles associated with 1) treatment success on average, and 2) individual differences in treatment response. Additionally, I will compare neurobiological indices derived from task-based and task-free fMRI to characterize the degree to which they account for overlapping or distinct variance and their relative utility in predicting cancer-relevant outcomes.

K00 training goals: *Learn resting state fMRI and network analytic methods. Gain experience targeting other modifiable health behaviors (e.g., physical activity, smoking, alcohol consumption) to reduce risk for cancer.*

RESEARCH STRATEGY

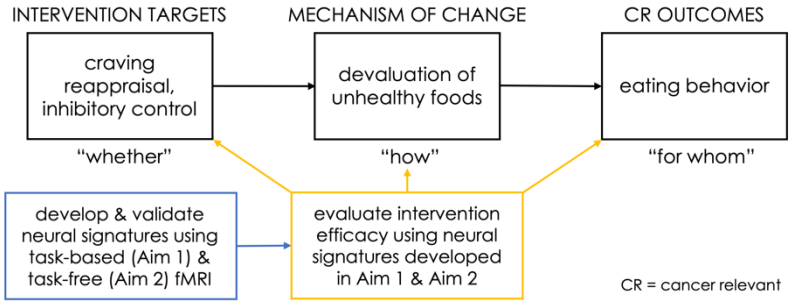
A. Significance

The overarching goal of this proposal is to leverage advanced multivariate neuroimaging techniques to build sensitive and specific neurobiological indices of target psychological processes, using task-based and task-free neuroimaging data. This will enable researchers to more effectively evaluate whether, how, and for whom cancer-relevant health behavior change interventions are working.

Preventable health-risking behaviors increase the risk for developing various forms of cancer. In total, it is estimated that 40-50% of cancer cases are associated with modifiable causes of cancer, such as overweight and obesity, poor diet, physical inactivity, alcohol and tobacco consumption, ultraviolet radiation, and resistance to vaccination[1,2]. For example, obesity is linked to various types of cancer, including endometrial, kidney, esophageal, colon, and liver cancer[3–6], whereas tobacco use associated with many forms of cancer, including as lung, larynx, mouth, and esophageal cancer[7], and is among the leading causes of preventable death[8]. In addition to the individual burden, these factors combined cost nearly 700 billion dollar per year in health-related expenses[9]. *It is therefore imperative to design effective preventative interventions to promote health behavior change and reduce cancer risk*.

The value of health behavior is a promising intervention target to reduce risk for cancer, but individual differences in treatment efficacy remain problematic. Recent psychological research has highlighted value-based decision making as an important factor for health behavior change[10–13]. Within this framework, healthy decisions, such as going to the gym, abstaining from unhealthy foods, or quitting smoking, are viewed as the result of a valuation process in which the subjective value from various inputs (e.g., effort, reward value, health value, social value) are integrated and evidence for each behavioral option (e.g., going to the gym or not) accumulates until one option reaches threshold and is enacted. Because subjective value for inputs can be modulated by social, affective, and cognitive processes to tilt the balance in favor of healthy behavioral choices[14–16], this framework suggests that there are myriad pathways to health behavior change mediated by changes in value (Figure 1). For example, the parent R01 for the F99 phase of this proposal is testing two distinct pathways to reduce the value of unhealthy foods in overweight and obese adults in order to improve eating behavior and concomitant cancer risk. One arm of this randomized control trial (RCT) focuses on training individuals to cognitively reappraise food cravings by emphasizing the personal costs of consuming unhealthy foods[17–21], whereas the other arm seeks to retrain automatic approach-related responses to unhealthy foods[22,23]. Although these training programs have disparate proximal intervention targets (i.e., cognitive reappraisal, inhibitory control), they share a common mechanism of change–devaluation of unhealthy foods. This framework has also been successfully applied to facilitate behavior change in other cancer-relevant domains, such as smoking cessation and physical activity[12,13]. However, individual differences remain a persistent problem even in highly effective interventions. *To further improve health behavior change interventions targeting value-based decision making, we require sensitive and specific tools to evaluate whether an intervention: 1) modifies proximal targets (e.g., are individuals getting better at craving reappraisal?), 2) operates via the theoretical mechanism of change (e.g., does valuation mediate the relationship between craving reappraisal and eating behavior?), and 3) is equally effective for all individuals.*

Figure 1. Conceptual model using examples from F99 phase parent R01



Multivariate neuroimaging can be used to develop sensitive and specific neurobiological indices of intervention targets. Even if an intervention has clearly specified targets, it remains difficult to assess the degree to which it "hits" the proximal target (e.g., craving reappraisal) and how individuals differ in target change. Functional neuroimaging (fMRI) is well suited to test theories of change because it can test competing mechanistic hypotheses that present the same overt behavior and can explain additional variance beyond behavior and self-report measures[24–28], which are more susceptible to self-presentational concerns[29] and may not provide full information about what determines behavior[30]. One predominant barrier to using fMRI to test theory is that there is not a one-to-one mapping between psychological constructs of interest and activity in any single brain region. For example, now-standard univariate results show that compared to food viewing,

reappraisal engages regions such as dorsolateral, ventrolateral, and dorsomedial prefrontal cortex[17–21]. However, these regions are involved in a variety of different cognitive processes, including planning, working memory, inhibition, and shifting attention[31], and therefore are unlikely to be specific indicators of reappraisal. In addition, because neuroimaging brain maps are comprised of thousands of individual voxels (volumetric pixels), a common approach to reduce the data for predictive modeling is to select one or several regions of interest (ROIs) and average the neural signal across the voxels within the ROI. However, this approach is limited in that it only uses a small fraction of the available data and the mean signal within an ROI is unlikely to generalize (e.g., across scan protocols or scanners). For these reasons, now-standard approaches are ill-suited for developing neurobiological indices. In contrast, assessing *patterns of activation or network connectivity* across the whole brain may be both more sensitive and generalizable. To develop neural indices that are sensitive and specific to a particular psychological process, researchers can capitalize on recent developments in multivariate neuroimaging methods and machine learning to analyze patterns of activity across the whole brain[32]. These predictive models, or *neural signatures*, have been employed to successfully classify a variety of psychological processes across individuals[28,33–36]. In addition to indexing a specific psychological process, because they use all available neural data, they may have greater sensitivity[32] and explain more variance in behavior than univariate ROIs[28,33]. Critically, because they are predictive models, once developed, these neural signatures can be shared among researchers and used to predict outcomes in new samples collected at different sites using different imaging protocols[37]. *Leveraging multivariate neuroimaging methods and machine learning techniques to create and validate neural signatures has significant promise to improve our ability to detect subtle changes in intervention targets and predict individual differences in intervention outcomes.*

Rationale for the proposed project and significance of the research contribution. The proposed research program (Figure 1) has the ability to significantly advance the field in several ways. First, developing sensitive and specific neural signatures using multivariate methods has the potential to substantially improve our ability to detect intervention-related change and individual differences. This, in turn, will enable researchers to more effectively evaluate whether, how, and for whom a health behavior change intervention is working. Second, by developing a coherent framework for developing and validating neural signatures, and openly sharing materials and analytic code, this research program will facilitate the development of neurobiological indices for any number of cancer-relevant intervention targets (e.g., food, tobacco, or alcohol craving, inhibitory control, attention, valuation) at any point along the continuum (e.g., prevention, treatment adherence). Third, this project produces sharable neurobiological indices that can be used on new and existing data, increasing the return on investment. This is important because neuroimaging studies are costly and new tools such as neural signatures can aid extraction of additional value. Fourth, developing this framework opens the door to a variety of novel and innovative analyses not currently possible. For example, it facilitates the measurement of spontaneous engagement of psychological constructs during more naturalistic, uninstructed contexts lacking a specific task (e.g., advertisement viewing). Because these circumstances more closely approximate the real-world, studying relevant processes in this way will likely improve our ability to predict behavior outside the lab. Last, this proposal takes a multi-method approach, integrating task-based (F99) and task-free (K00) fMRI to develop neural signatures. This is a critical objective because it is unclear whether intervention effects are best measured using task-based fMRI, which measures brain activity during specific psychological states, or intrinsic network connectivity, which approximates trait-like features of brain organization. Directly comparing the predictive utility of neural signatures developed from these data will provide essential information for researchers seeking to develop and evaluate cancer-relevant health behavior change interventions.

For this project, I will extend my current skill set to add critical training in translational neuroscience and advanced longitudinal modeling during the F99 phase, and in resting state fMRI and network analytic methods during the K00 phase. These goals are highlighted below in **bold, underlined** typeface.

B. Approach

Aim 1: The Dissertation Research Project

Overview

Cognitive reappraisal, or reframing a stimulus to change its affective meaning[38], effectively reduces food cravings and the value of unhealthy, cancer-promoting foods[17–21]. Therefore, training individuals to use cognitive reappraisal is a promising avenue to improve eating habits and reduce risk for cancer. The parent grant for the F99 phase of this project is testing this model in the context of a **longitudinal RCT** to improve

eating behavior in overweight and obese adults. However, standard methods for assessing change in intervention targets lack sensitivity and specificity. To bridge this critical gap and increase sensitivity to detect intervention-related change and individual differences, my dissertation extends current approaches by using **multivariate methods** to develop a whole-brain **neural signature** of craving reappraisal (in progress) and assess the degree to which change in neural signature expression is related to cancer-relevant intervention outcomes–food valuation and eating behavior–over the course of 6 months (F99 phase).

Progress report

Although the development of neural signatures is an exciting new direction in cognitive neuroscience[39], the best method for development remains unclear. For example, some studies have used machine learning to identify patterns of neural activity that are related to specific psychological constructs[33–35] and others have used whole-brain meta-analytic maps derived from univariate, subtractive methods[14,28,36] . Because a central goal of the F99 project is to create a robust measure of craving reappraisal that is sensitive and specific, and reliably generalizes to new data, I am currently testing numerous methods to develop the neural signature.

Data. To create the neural signature, I am using existing neuroimaging data from our lab (N = 173). To increase the generalizability of the results, participants from three studies ranging in age (18-46) and BMI (lean to obese) are included. All participants completed an fMRI craving reappraisal task developed in our lab[17,18,40].

Craving reappraisal task. Participants are trained to decrease their desire to consume personally-craved foods using cognitive reappraisal (e.g., by thinking about the negative health costs). Participants either passively view unhealthy craved foods ("look" condition) or reappraise their craving ("reappraise" condition). To maximize craving, participants select their most craved food from a number of unhealthy, cancer-promoting foods (e.g., barbeque, ice cream, processed meats). Each condition contains 20 trials with the task design specified in Figure 2.

Figure 2. Design of craving reappraisal task

Analytic strategy. Images were preprocessed using a standardized pipeline from the Center for Reproducible Neuroscience[41] and smoothed with a 6mm^3 FWHM smoothing kernel[42]. For each participant, general linear models were computed in SPM12[43], modeling each condition of interest (look, reappraise) versus baseline. This process yielded two whole-brain maps for each participant. Prior to group-level modeling, the sample was divided into training (N = 110), test (N = 28), and validation (N = 35) sets. In order to maximize out of sample prediction accuracy, I am using different classifiers, optimization parameters, and cross-validation schemes to create competing neural signatures within the training set. To avoid overfitting and increase generalizability, I compare model fit in the test set and iteratively test different algorithms and optimization parameters until the highest possible prediction accuracy in the test set is achieved. I will then select the best fitting model, apply it to the hold-out validation set, and use this accuracy value as the final test of out of sample accuracy. Since this model should only be applied to the validation set once, I report preliminary results in this proposal using the training and test sets only. To establish construct validity, I will compare the mean expression of this neural signature while participants in the validation sample view and reappraise personally-craved foods. For each subject, I will multiply the neural signature of craving reappraisal by the activation maps for the look and reappraise conditions (i.e., calculate the dot-product for look and reappraise for each subject). This process yields a single scalar value that will serve as the index of expression of the neural signature for each task condition. If the neural signature is specific to craving reappraisal, then participants should show greater expression of the signature during regulation trials than during look trials. To test this hypothesis, I will compare the mean expression across participants in the look and reappraise trials using a paired *t*-test ($p < .05$). I expect that the expression of the neural signature will be higher in the reappraise condition than in the look condition.

Preliminary results. Initial analyses comparing neural signature development using logistic regression, ridge, and support vector machine classifiers with 5-fold cross-validation in the training set show high out of sample prediction accuracy in the test set (accuracy range = 93-95%, sensitivity range = 96-100%, specificity range = 86-93%). With respect to construct validity (Figure 3), all three classifiers significantly differentiate between the look and reappraise conditions in the test set (*t* range = 7.13-8.65, *p*s < .001). These robust preliminary results establish the

Figure 3. (A) Example neural signature (B) Construct validity

feasibility of this approach. I am now finalizing the optimization of the neural signature of craving reappraisal and will complete this objective prior to the fellowship start date, September 1, 2019.

Work to be completed during F99 phase

The objective of this work is to use the neural signature of craving reappraisal to **evaluate the efficacy** of a craving reappraisal intervention to improve healthy eating in overweight and obese adults. I will assess the degree to which: 1) the intervention alters the (now developed) neural signature of craving reappraisal, 2) intervention-related change in expression of the neural signature is associated with change in the subjective value and consumption of unhealthy, cancer-promoting food, 3) the relationship between change in neural signature expression and eating behavior is mediated by change in subjective value, and 4) **individual differences** in expression change can predict change in these outcomes.

This project will provide essential training in how to design, implement, and evaluate an RCT testing the efficacy of two distinct health behavior change interventions to improve eating behavior and risk for diet-related cancers, as well methodological training in advanced statistical techniques for modeling longitudinal data.

Parent grant overview. The proposed research is a secondary analysis of data collected through the parent grant (R01 CA211224) funded by NCI. These data are completely separate from those used to develop the neural signature of craving reappraisal. The primary goal of the parent grant is to assess the efficacy of two novel interventions (craving reappraisal training and behavioral response training) to alter food valuation and reduce unhealthy eating in overweight and obese adults at risk for diet-related cancers. Participants complete a baseline MRI session, a 4-week craving **reappraisal training intervention,** behavioral response training intervention, or active control, a post-intervention MRI session, and follow-up assessments at 3 and 6 months. As of February 15, 2019, 67 participants have completed the baseline MRI session. The current proposal builds on the parent grant by analyzing neural data from the MRI sessions, as well as behavioral data from all 4 sessions to characterize the predictive validity of the neural signature currently being developed.

Participants and biological variables. Participants will be MRI eligible, overweight and obese adults (BMI 25-40), ages 18-60. Due to the physical constraints of the MRI machine, only participants weighing less than 550 lbs. will be included. I will use data from the first 150 participants who complete the protocol. We are currently enrolling 2-4 participants per week and so I expect to have this data by February 2020. Biological variables, such as age, sex, and body mass, that may moderate effects will be included as model covariates.

Procedure. Participants will complete 4 assessments with these measures at the following intervals:

Baseline MRI	4-Week Intervention	Post-Intervention MRI	Follow-Ups at 3 & 6 Months
Food valuation	Cognitive reappraisal training OR	Food valuation	Food valuation
Eating assessment	Behavioral response training OR	Eating assessment	Eating assessment
Craving reappraisal (MRI)	Active control training	Craving reappraisal (MRI)	

fMRI Data Acquisition & Analysis. MR scanning takes place at LCNI on a Siemens Skyra 3T magnet: a research-dedicated, whole-body MR system optimized for fMRI. Participants will complete the craving reappraisal task while in the MRI scanner. Data will be preprocessed and analyzed as specified previously.

Interventions. The interventions include in-person training and at home practice over the course of 4 weeks. There are 8 30-minute in-person sessions. The cognitive reappraisal intervention uses combination of interpersonal and computer-based methods to train participants to generate cognitive reappraisals and practice applying them. Participants receive feedback during these sessions and engage in speeded practice to help habitualize this behavior. At home practice consists of 7 15-minute exercises focused on using reappraisals in the natural environment. The behavioral response training intervention trains participants to inhibit approach responses toward unhealthy, cancer-promoting foods while also training them to approach healthy foods. The active control is a general (i.e., not food specific) attention and inhibitory control training intervention. All conditions are of equal duration and intensity.

Food valuation task. To measure individual subjective value of various foods, we adapted a validated willingness-to-pay task[15,24] (Figure 4). The task is an economic auction in which participants view images of 30 healthy and 30 unhealthy, cancer-promoting snack foods and determine how much they are willing to pay for each item. Participants are endowed with $1.50 to buy snacks during the task and told that one trial will be randomly selected and enacted. Bids greater than or equal to a randomly selected bid result in the participant getting the snack food, whereas lower bids result in participants receiving the money, but not the snack food. The optimal strategy is to bid the true amount one is willing to pay for each item.

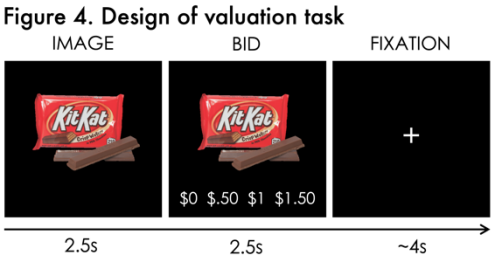


Figure 4. Design of valuation task

Eating assessment. At all assessments, eating behavior will be measured using NCI's Automated Self-Administration 24-hour Recall (ASA24). A composite score of diet quality (the "Healthy Eating Index") will be calculated for each participant at each assessment.

Analytic strategy and expected outcomes. To test these hypotheses, subjects will complete the same craving reappraisal task described above at the baseline and post-intervention sessions. For each subject and session, I will generate a map for the average activation on reappraise trials and multiply it by the craving reappraisal neural signature (i.e., calculate the dot-product for each subject and session). This process yields a single scalar value that will serve as the index of expression of the neural signature. For each participant, I will create a change score by subtracting the baseline expression from the post-intervention expression. First, I will compare mean change in neural signature expression as a function of intervention group using a one-way ANOVA. I expect that expression change will be significantly greater in the craving reappraisal intervention group then in the other two groups. Next, within the craving reappraisal group, I will assess the extent to which change in neural signature expression is associated with change in food valuation and eating behavior. Food valuation will be operationalized as the average bid value for the unhealthy, cancer-promoting foods in the food valuation task. Eating behavior will be operationalized as the ASA24 "Healthy Eating Index." Because I expect that the relationship between change in neural signature expression and eating behavior will be mediated by change in food valuation, I will also test this mediation model. To do so, I will use **latent growth curve modeling** and **cross-lagged panel mediation modeling**. These structural equation modeling techniques are used to assess latent growth in criterion variables over time and test longitudinal mediation, and will be implemented with the lavaan package[44] in R[45]. I expect that: 1) change in signature expression will be associated with devaluation and lower consumption of unhealthy food, 2) devaluation of unhealthy foods will mediate the relationship between neural signature change and eating behavior, and 3) individuals with the greatest increases in signature expression from baseline to post-intervention will show the greatest change in food valuation and eating behavior.

Potential problems and alternative strategies. If we experience attrition or are unable to acquire complete data (i.e., both 3- and 6-month follow-ups) for the targeted 150 subjects by February 2020, I will use all available data in statistical models to reduce potential attrition-related bias. Furthermore, as we may lack power to detect small effects in the SEM analyses, we will test the generalizability of effects in the full R01 sample (N = 300) once it has been collected.

Future directions. A natural next step is to apply the same approach to develop neural signatures for other relevant psychological constructs, such as valuation, craving, inhibitory control, and attention, using existing task-based fMRI data. I will use these neural signatures to test the efficacy of and individual differences in outcomes for the behavioral response training intervention. Another avenue I plan to pursue is to use the neural signature of craving reappraisal to estimate spontaneous regulation on a trial-by-trial basis during the food valuation task. This will allow us to assess the frequency with which individuals spontaneously control their cravings while viewing uneahlthy, cancer-promoting foods in a more ecologically valid context.

Timeline and benchmarks for success. To complete this aim over the course of two years, I have designated deadlines for the completion of data collection, preprocessing and analysis, and manuscript preparation. Neural signature development is underway and will be completed by the fellowship start date. Data collection and preprocessing will be completed during the first half of year one and the neural signature manuscript will be completed during the second half of year one. Analysis will be completed by the first half of year two, and the manuscript will be completed during the second half of year two.

Aim 2: The Postdoctoral Research Direction

Rationale. Whereas task-based fMRI is designed to identify the neural underpinnings of specific psychological processes in the moment (i.e., state-like features), task-free, "resting state" fMRI reveals the connectivity of relatively more stable, intrinsic brain networks[46] (i.e., trait-like features) that may be more related to enduring patterns of health behaviors. Resting state fMRI indexes low-frequency blood-oxygenation-level dependent signal and has revealed the existence of brain networks, whose component regions are reliably coactivated across a variety of contexts[47]. However, there is still substantial individual variability in functional brain organization[48,49] and this variability is associated with individual differences in personality, cognitive abilities, and behavioral tendencies[50–53]. In a clinical context, individual differences in brain organization are associated with psychiatric disorders, such as schizophrenia and major depression[54–56]. Consequently, *patterns of coactivation derived from task-free, resting state fMRI data are a complimentary source of information to identify neural signatures that vary across individuals and relate to health status*. However, to date, relatively few studies have used resting state fMRI to evaluate interventions[57–60] and it is not

yet commonly employed in the context of interventions targeting cancer-relevant health behavior change. Furthermore, although resting state fMRI has been used to predict individual differences in task-based fMRI[61], these sources of data are rarely compared directly to predict behavior outside the laboratory. Additionally, it is unclear whether neural signatures derived from task-based and task-free fMRI account for overlapping or distinct sources of variance, and in which contexts one approach might outperform the other. Therefore, *employing both neuroimaging methodologies to develop neural signatures may significantly improve our ability to detect intervention-related change in target processes.* The objective of this work is to extend the research program pursued in the F99 phase to derive neural signatures using task-free resting state fMRI and directly compare their utility for evaluating cancer-relevant health behavior change interventions and assessing individual differences in intervention outcomes. Through this, I will gain important conceptual and methodological training in resting state fMRI and network analytic methods. Together, this training will enable me to design and evaluate health behavior change interventions to reduce cancer risk using sensitive and specific neural signatures developed using this multi-method approach.

Approach. The goal of my research during the K00 phase remains the same as during the F99 phase: to leverage advanced multivariate neuroimaging techniques to build sensitive and specific neural signatures of target psychological processes to more effectively evaluate whether, how, and for whom health behavior change interventions are working. The major differences are that in the K00 phase I will 1) use resting state fMRI and network analytic methods to develop relevant neural signatures, 2) directly compare task-based and task-free neural signatures to evaluate intervention efficacy and individual differences, and 3) expand my experience with cancer-relevant health behavior change interventions beyond eating behavior. **Resting state fMRI** can be used to index dynamic fluctuations in coactivation between brain regions, rather than static coactivation associated with a particular psychological process measured using task-based fMRI. Researchers employ **graph theory** to characterize different properties of functional brain organization, such as efficiency, modularity, and centrality, and variability in network properties are associated with individual differences in personality and health status [51,54]. Furthermore, machine learning techniques can be applied to resting state fMRI to develop generalizable neural signatures that predict individual differences in new samples[62,63]. During the K00 phase, I plan to build on my experience with machine learning and multivariate neuroimaging to 1) identify **network connectivity profiles** from resting state fMRI that are reliably associated with relevant intervention targets (e.g., cognitive reappraisal, inhibitory control, attention), 2) assess intervention-related change in network connectivity, and 3) characterize the degree to which individual differences in network reconfiguration are related to cancer-relevant outcomes, such as healthy eating, alcohol consumption, or smoking cessation. Further, with the overarching goal of generating new hypotheses that can inform future directions, I will also identify network connectivity profiles that are associated with intervention success and compare these profiles across various interventions to determine the degree to which there are generalized network changes that underlie intervention efficacy, irrespective of intervention type. I plan to pursue this training in an environment that will allow me to broaden my intervention training to investigate other interventions targeting cancer-relevant health behaviors, such alcohol consumption or tobacco use. However, I also have access to resting state fMRI data from the F99 parent R01, which would enable me to immediately pursue these goals if data collection at the postdoctoral institution is not yet complete when I arrive.

Mentors and institution. Achieving these aims is only possible in a postdoctoral training location that houses a team of mentors who have expertise in resting state fMRI and network analytic methods, as well as expertise in designing and evaluating cancer-relevant health behavior change interventions. Ideally, these mentors would have existing collaborations in the context of an intervention trial to reduce cancer risk that includes both task-based and task free neuroimaging, or be open to collaboration and have sufficient funding to support this line of research. In addition, mentors must have a strong track record of training postdoctoral scholars who go on to tenure-track faculty positions at R1 universities. Mentors should also have proven experience procuring grant funding to help me refine my grant writing skills. In addition to practical requirements, such as access to an MRI suite and target populations, the institution should be collaborative, and have a strong focus on translational neuroscience. Amazingly, I have identified at least four sites that fulfill each of these requirements: University of Pennsylvania (Drs. Emily Falk, Danielle Bassett, Theodore Satterthwaite; see Falk Letter of Support), Oregon Health and Science University (Drs. Damien Fair, Kristen Mackiewicz Seghete), Indiana University (Drs. Peter Finn, Olaf Sporns, Richard Betzel), University of Pittsburgh (Drs. Kirk Erickson, Peter Gianaros, Timothy Verstynen). My current sponsors have professional connections with the faculty in each of these institutions and will facilitate introductions, as outlined in the Sponsor and Co-Sponsor statements. I will arrange meetings with potential mentors online or at conferences and finalize my postdoctoral training plan with the selected mentors during year two of the F99 phase.

RESPECTIVE CONTRIBUTIONS

Development of Research Training Plan

This research training plan was developed in close collaboration with my mentor Dr. Elliot Berkman and co-mentor Dr. Kathryn Mills and designed specifically to enable me to achieve my long term goal of becoming a leading independent investigator in the field of translational neuroscience, designing and evaluating interventions using multivariate neuroimaging and advanced statistical methods to reduce risk for cancers via health behavior modification. The training plan for the F99 phase is motivated by my dissertation research, which will likely be funded as an F31 by NCI (F31CA232357, 9th percentile). To gain broader experience with cancer-relevant health behavior change interventions and resting state fMRI as a postdoctoral researcher, I met with Drs. Berkman and Mills to discuss how best to procure this training. I then wrote an initial draft of the K00 proposal and training plan, and Drs. Berkman and Mills provided several rounds of feedback digitally and in person.

Roles in Accomplishing the Proposed Work

I am the primary author on the proposed research training plan and will take the lead role in the research described in the plan. I will join the leadership team of Dr. Berkman's R01 to design the cognitive reappraisal intervention and will supervise the intervention staff to maintain fidelity between the design and implementation. The project coordinator and other graduate students funded by the grant will be responsible for subject recruitment and data collection. I will be responsible for preprocessing the neural and behavioral data, and applying the neural signature of craving reappraisal to this data.

With guidance from Drs. Berkman and Mills, I will conduct the latent growth curve modeling and cross-lagged panel mediation modeling outlined in Aim 1. Dr. Berkman will provide conceptual training related to multilevel modeling and structural equation modeling, and Dr. Mills will provide practical training specifying and implementing models in the statistical programming language, R. Dr. Mills will help prepare me for the K00 phase by providing introductory theoretical training in resting state fMRI via the weekly journal club she supervises, hands-on training on the implementation of cutting-edge resting state fMRI processing pipelines (Ciric et al., 2018), and by collaborating with me on a systematic review of resting state fMRI applications to intervention studies. These training activities will help ensure that I'm well prepared to pursue postdoctoral training during the K00 phase.

Drs. Berkman and Mills will provide critical feedback on analytic preregistrations and manuscripts related to this proposal. They will also be actively involved in the process of identifying my K00 mentors. Specifically, Dr. Berkman will help me generate a complete list of potential mentors with expertise in translational neuroscience who are currently running cancer-relevant health behavior change interventions, and Dr. Mills will help identify potential mentors with expertise in resting state fMRI and network analysis. Once potential mentors have been identified, Drs. Berkman and Mills will facilitate introductions between myself and these mentors, and provide continued support as I refine the specifics of my K00 training plan.

SELECTION OF SPONSOR AND INSTITUTION

Sponsors. These sponsors were selected to provide the optimal mentorship to meet the proposed training goals. Dr. Berkman is an Associate Professor in Psychology and Co-Director of the Center for Translational Neuroscience, with expertise in translational neuroscience for cancer control, functional neuroimaging, and behavioral approaches to cancer prevention. Dr. Berkman combines these techniques to design and refine interventions to improve health and well-being, and helped pioneer the "brain-as-predictor" approach, leveraging neural data to predict real-world health outcomes and identify novel candidate psychological targets. Furthermore, over the past four and a half years, Dr. Berkman and I have developed a productive working relationship, co-authoring three journal articles. Dr. Berkman has served on each of my advising committees and is an excellent mentor (he has won several awards for mentorship and teaching). His mentorship style strikes the perfect balance between autonomy and guidance, critical feedback and support, facilitating my development as an independent scientist. Dr. Mills is an Assistant Professor in Psychology with expertise in advanced statistical approaches to modeling longitudinal fMRI data, resting state fMRI, network analysis, and scientific computing. Dr. Mills uses longitudinal modeling to characterize functional and structural brain development, and resting state fMRI to examine functional brain organization in childhood and adolescence. She takes an individual differences approach, integrating longitudinal methodology with network analytic approaches to relate brain cognition and development. I have worked closely with Dr. Mills since she started at the University of Oregon as a postdoctoral researcher in 2016. She is a fabulously attentive and pedagogical mentor, and a strong advocate for her trainees. As a postdoc and into her transition to Assistant Professor, Dr. Mills and I developed a great relationship and have organized several neuroimaging hackathons together. As Co-PI for the NSF-sponsored Modeling Developmental Change workshop, Dr. Mills invited me to present and we continue to collaborate on training workshop proposals (e.g., R25MH120869-01). Dr. Mills and Berkman's combined expertise will ensure that I receive excellent training in translational neuroscience broadly, and intervention design and evaluation using advanced statistical techniques specifically. This mentorship team is exceptionally well-positioned to prepare me to pursue my postdoctoral training aims.

Institution. The University of Oregon is the ideal setting for this work because of the innovative, interdisciplinary opportunities offered here. A distinctive feature that makes it an ideal fit for the proposed training is the Center for Translational Neuroscience (CTN). The CTN, which is co-directed by my sponsor Dr. Berkman, is a research center within the Department of Psychology that fosters an intellectual community on campus around translational neuroscience and provides concrete resources such as award support, pilot funds, and project management resources. The CTN's mission is to leverage knowledge from neuroscience to improve health and well-being, promote resilience, and mitigate the negative effects of early adversity. The CTN emphasizes research approaches that advance the identification of mechanisms of change and moderating factors within interventions, and is home to core faculty with extensive expertise in intervention design and evaluation. The CTN provides training for graduate students through formal mentoring, as well as through colloquia and bi-weekly brownbags. The Department of Psychology has a vibrant intellectual cultural, offering rigorous coursework and providing students with ample opportunities to learn cutting edge methods. For example, it hosts the bi-weekly methodological brownbag as well as a formalized programming seminars, in which students learn data science and open science practices. The department places strong value on interdisciplinary collaboration, which is formalized in the Supporting Area Project (SAP) requirement. In the SAP, students are mentored by faculty in a different area, helping facilitate the development of novel ideas and fruitful collaborations. Finally, UO is home to the Lewis Center for Neuroimaging (LCNI). LCNI is designed to facilitate high-quality neuroimaging research and houses a research-dedicated MRI scanner, employs several full-time staff, and provides training to graduate students formally as courses and informally as workshops.

K00 phase. Several factors will be critical for determining a postdoctoral institution during the K00 phase. First, it is essential that I pursue postdoctoral training with a team of mentors who have expertise in designing and evaluating cancer-relevant health behavior change interventions, as well as resting state fMRI and network analysis. Ideally, these mentors would have existing, productive collaborations around interventions to reduce cancer risk utilizing both task-based and task free neuroimaging. Second, mentors should have experience applying a developmental approach, as intervention efficacy may be constrained by developmental capacities. Third, mentors must have a strong track record of training postdoctoral scholars who go on to tenure-track faculty positions at R1 universities. Fourth, in addition to practical requirements, such as access to an MRI suite and target populations, the institution should be collaborative, and have a strong focus on translational neuroscience. I have identified at least four research groups around the US that meet these criteria (see Falk Letter of Support) and present a detailed plan for identifying postdoctoral mentors in Aim 2 of the Research Strategy.

TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH

Previous training

This project will strictly adhere to all human subjects procedures set forth by the University of Oregon's Office for the Protection of Human Subjects. Further, all research proposals will be submitted to and reviewed by the UO's Institutional Review Board before any data is collected. Each year, a renewal application will be submitted until the project has been completed. All researchers working on the project will complete ethics training through the Collaborative Institutional Training Initiative, which must be renewed bi-annually. All researchers using the UO Lewis Center for Neuroimaging (LCNI) will also complete the required safety course and test to demonstrate understanding of the responsible conduct of MRI research, which must be renewed yearly. The parent grant for this project has been approved by the UO Institutional Review Board.

As a graduate student, I have completed two ethics courses. First, I have completed ethics training through the Collaborative Institutional Training Initiative (CITI). This is a web-based program is designed to educate and test researchers on ethical issues in human subjects research. I have completed the course for Social-Behavioral-Educational Researchers, as well as the course for Responsible Conduct of Research for Social and Behavioral Sciences. Each course include modules on specific topics, and I have completed modules for the following topics: history and ethical principles, federal regulations for protecting human subjects, informed consent, defining human subjects, assessing risk, conflicts of interest, privacy and confidentiality, research with children, international research, research misconduct, data management, authorship, peer review, mentoring, using animal subjects in research, collaborative research, and research involving human subjects. Researchers are required to be recertified bi-annually. I last completed recertification on July 12, 2018 and will recertify prior to expiration on July 11, 2020. Second, I have completed ethics training through the UO psychology department winter 2016. All first year graduate students are required to take a course in research ethics as part of the first year seminar program. This course is 10 weeks long and covers ethical issues in the following domains: data acquisition, management, and ownership, questionable research practices, research fraud, publication and authorship, ethics of research with human subjects, non-human animal research, conflicts of interest, peer review, and mentoring. Each class is 80 minutes and consists of lecture and group discussion. Weekly readings are assigned and students also complete two short reflection papers. I have also completed MRI operator training through LCNI in March 2016. This training included 40 hours of supervised training by the LCNI Director Dr. Fred Sabb, MR physicist, Dr. Jolinda Smith, and MRI technician, Scott Watrous. MRI operator status is maintained through yearly written quizzes and by operating a minimum of one scan per month. To date, I have completed over 100 hours operating the MRI scanner.

Ongoing and future training

During the F99 phase, I will continue my training in the responsible conduct of research in several ways. First, I will recertify my CITI training every two years. Second, I will complete the NIH Research Ethics Training program online (https://researchethics.od.nih.gov/). To more fully engage with these topics and their application to ongoing research, I will lead a quarterly ethics discussion at our lab meeting. Each quarter during this training grant, I will complete one to two of the training modules and facilitate a 45 minute discussion on the topic, supervised by Sponsor Berkman. One to two hours of preparation are expected prior to each discussion. Third, ethical issues are a standing agenda item in our monthly R01 leadership meetings led by Sponsor Berkman. At these hour-long meetings, our team discusses issues related to voluntary consent, privacy and confidentiality, harm reduction, and risk assessment and management. These discussions are often centered around specific incidents that have arisen or are likely to arise and therefore provide excellent training for how to practically deal with ethical issues on a research project. Fourth, I will regularly attend our department's bi-weekly hour-long methodological brownbag where faculty and students discuss ethical topics related to scientific integrity, reproducibility, replicability, and generalizability. More specifically, I will receive training on issues such as preregistration, power, data sharing, and secondary data analysis. This training will help ensure I am adequately trained to conduct research in an ethical fashion after I have finished data collection. Fifth, I have previously volunteered to lead discussions on preregistration and data management in the ethics course that all first year graduate students in psychology are required to take, and I will continue to volunteer while on this training grant. For this, I expected to spend two hours preparing and 80 minutes presenting each year. During the K00 phase, I will develop a plan with my K00 mentors to continue training in a similar fashion tailored to the institution and resources available.

SPONSOR AND CO-SPONSOR STATEMENTS

A. Research Support Available

Dr. Berkman's support

FUNDING SOURCE	ID NUMBER	TITLE	PI	DATES	ANNUAL DIRECTS
NIH	*R01 CA211224	Devaluing energy-dense foods for cancer control: Translational neuroscience, NCT03557710	Berkman	07/01/17 – 06/30/22	$435,960
NIH	R01 HD094831	RCT of FIND video coaching intervention for caregivers facing economic adversity	Fisher	02/01/19 – 01/31/24	$423,751
NIH	R01 MH107418	Puberty, neural systems for social processes, and early adolescent mental health: A longitudinal neuroimaging study	Pfeifer	08/01/15 – 04/30/20	$418,653

* Note that R01 CA211224 is the parent grant for the data collection and analysis proposed in Aim 1. This grant will backstop Dani's work on this project in the event of a shortfall on the F99/K00. We are one year into data collection on the project and are recruiting 2-4 participants per week. The parent grant proposes to collect pre-post data on 300 participants in the first 4.5 years. Therefore, we are confident that we will have N = 150 for Dani to use for Aim 1 by the first half of year 1 of the proposed training period.

Dr. Mills' support

FUNDING SOURCE	ID NUMBER	TITLE	PI	DATES	ANNUAL DIRECTS
University of Oregon CAS	N/A	Start-up funds ($657,300)	Mills	07/01/18 – 06/30/21	N/A
NIMH	R25 MH120869-01	ABCD Workshop on Brain Development in Relation to Mental Health (pending)	Mills	04/01/19 – 03/31/20	$103,365

B. Sponsor's/Co-Sponsor's Previous Fellows/Trainees

Dr. Berkman's previous trainees

Dr. Berkman has previously sponsored 4 predoctoral fellows and 1 postdoctoral fellow.

NAME	TIME IN LAB	CURRENT POSITION / ORGANIZATION
May, Lisa	2010-2017 (predoctoral)	Manager, Center for Translational Neuroscience, University of Oregon
Calcott, Rebecca	2011-2017 (predoctoral)	Postdoctoral Scholar, DAAD Fellowship, University of Regensberg
Giuliani, Nicole	2011-2015 (postdoctoral)	Assistant Professor, College of Education, University of Oregon
Kahn, Lauren	2012-2018 (predoctoral)	Center Manager / Research Scientist, University of Oregon
Livingston, Jordan	2012-2018 (predoctoral)	Postdoctoral Scholar, University of Toronto

Dr. Mills' previous trainees

Dr. Mills is a junior faculty member. She has previously mentored high school, undergraduate, and graduate students on resting state fMRI methods. This includes mentorship of a high school student (who transitioned into an undergraduate), on a project recently published in a peer-reviewed neuroimaging journal (Anandakumar, Mills et al., 2018). She has not yet served as the primary mentor for predoctoral trainees but is currently mentoring several predoctoral trainees.

NAME	TIME IN LAB	NOTE
Jeya Anandakumar	2015-2018 (undergraduate)	Undergraduate (sophomore), Portland State University
Jessica Flannery	2016-current (predoctoral)	NSF GRFP recipient; Dissertation supervision
Theresa Cheng	2016-current (predoctoral)	OSLER NIH TL1 recipient; Supporting Area Project supervision
Karlena Ochoa	2018-current (predoctoral)	Supporting Area Project supervision
Adam Pettitt	2018-current (predoctoral)	Supporting Area Project supervision
Angela Lee	2018-current (predoctoral)	Supporting Area Project supervision

C. Training Plan, Environment, Research Facilities

Dr. Berkman's (sponsor) training plan

This proposal seeks support for Dani to complete her doctoral training in social and developmental psychology at the University of Oregon, where the F99 will allow her to learn and apply a range of innovative methodological approaches and statistical tools that would otherwise not be feasible. I direct the Social and

Affective Neuroscience Laboratory and co-direct the Center for Translational Neuroscience (CTN; http://ctn.uoregon.edu) at the University of Oregon. The CTN is a research center that promotes translational neuroscience by supporting an intellectual community, providing formalized pre- and postdoctoral training, and housing pre- and post-award infrastructure. Translational neuroscience is the interdisciplinary field that applies knowledge and methods from human and animal neuroscience to improve health and well-being. The University of Oregon is the ideal site for Dani to complete her F99 training because of the *strong infrastructure for all aspects of her training plan*, including a highly productive and collaborative translational neuroscience group (Elliot Berkman, Kathryn Mills, Jennifer Pfeifer, Philip Fisher, Nicholas Allen, Maureen Zalewski, Elizabeth Skowron, and others), and a strong neuroimaging group with training and specializations in multivariate methods (Dagmar Zeithamova, Brice Kuhl, Robert Chavez) who collaborate with the translational neuroscience group. The CTN and the Department of Psychology are also on the forefront of teaching and implementing open science practices. For example, we offer a seminar in open and reproducible science and have specifically mentioned that we consider open science practices in the evaluation of new faculty candidates in each of the 4 most recent faculty searches in Psychology.

Completed training. The University of Oregon Doctoral Program in Psychology is highly collaborative and encourages an interdisciplinary approach that exposes students to a wide range of topics through core coursework, small seminars, informal brownbag series, lab meetings, as well as other intellectual opportunities. The primary goal of the program is to develop outstanding researchers with high quality training combined with substantive and methodological breadth. Towards this goal, students complete “core” courses in three of the five areas in our program (i.e., developmental, social/personality, clinical, systems neuroscience, cognitive neuroscience), as well as a year-long comprehensive sequence in statistics during the first two years of the program. Dani has completed these requirements, selecting core coursework in developmental, social/personality, and cognitive neuroscience. To receive further training in support of the career goals outlined in this proposal, Dani has completed additional coursework in: adolescent development, brain decoding, grant writing, machine learning, data science, and structural equation modeling, and has developed her teaching and computer programming skills as a facilitator for the Data Science Club. Students are also required to complete three major requirements. During their first year, students design, conduct, and write up an original research study, and present their project to the department in the fall of second year. To support intellectual breadth and foster interdisciplinary collaboration, students complete a “supporting area” project, in which they are mentored by a faculty member from a different area and complete a research project under their guidance. By the end of fourth year, students must also complete a major preliminary examination, in which they integrate knowledge from a relatively broad area of psychology through written and oral presentation. Dani has successfully completed all major requirements and successfully proposed her dissertation in November 2018.

Training plan. Dani’s long-term goal is to become an independent translational neuroscientist who designs and evaluates interventions to change cancer-related behaviors using advanced multivariate neuroimaging methods. The objectives of her training plan therefore are to (1) develop skills to conduct rigorous and reproducible cutting-edge research in the field of translational neuroscience using task-based and task-free neuroimaging data and (2) publish and present scientific findings, building a track record in order to successfully compete for academic positions. These objectives will be met in this F99/K00 as Dani completes two interrelated Training Aims, which are to develop expertise in translational neuroscience and advanced statistical methods for modeling longitudinal data.

The team that Dani has assembled for the F99 is exceptionally well suited to provide the proposed training. Dr. Mills and I are faculty members in the Department of Psychology and collaborate on several projects including an R01 and T32 to be submitted in the coming months. Several other faculty in the department will also provide support, including Dr. Pfeifer, who is Dani’s primary advisor in the program, and Dr. Zeithamova, who is mentoring Dani in machine learning applications to neuroimaging (see letters). My expertise is in applying a translational neuroscience approach to develop and refine behavior change efforts in the area of cancer control. For example, the parent R01 is a randomized controlled trial (NCT03557710) that tests the hypothesis that two effective interventions for dietary change (cognitive reappraisal and behavioral response training) both operate by altering the same underlying reward valuation system. If this is true, then other interventions that are known to influence this system might also change diet, and it might be possible for people to be assigned to the most effective intervention ideographically based on which intervention was most likely to influence the valuation system for that individual. I have completed two NIH-funded trials that used neuroimaging to index whether and how interventions for behavior change - especially cancer-related behavior - target underlying neurobiological systems. This makes me uniquely suited to provide expertise in translational

neuroscience for cancer control and supervise Dani as she gains clinical trial experience. Dr. Mills has expertise in advanced statistical approaches to modeling longitudinal neuroimaging data, resting state fMRI, and network analysis. Dr. Mills will provide mentorship to Dani in the application of these techniques. Together, we provide a unique and complementary blend of expertise related to Dani's training goals in translational neuroscience and advanced statistical methods, and are well-positioned to help Dani secure a competitive position as a postdoctoral fellow in the K00 phase of this award.

I will provide specific training in translational neuroscience, and particularly the development, conduct, and assessment of longitudinal interventions that utilize human neuroimaging. With F99 support, Dani would be able to immerse herself deeply in the leadership and supervision of the parent R01 that is now under way (funding began August 2017). Dani would attend leadership team meetings; help design and implement the pre- and post-intervention neuroimaging assessment; help design and implement the cognitive reappraisal arm; assist with the delivery and fidelity monitoring of the intervention; and learn to supervise research staff and manage grant budgets. Critically, Dani will be centrally involved in the neuroimaging analyses to test whether the intervention arms altered neural activation in the reward valuation system and whether those changes mediated behavioral effects. As part of those analyses, Dani will work with me on the longitudinal analyses including latent growth curve modeling, group-by-time longitudinal modeling, and intent-to-treat analyses. Dani will also take the lead in grant preparation (e.g., R03, R21) for follow-up projects related to her interests, supported by preliminary data gathered as part of her F99 training project. Dani will be first author on at least one manuscript per year related to her F99 project and/or the parent project.

Dani and I will continue to interact extensively to accomplish her training in translational neuroscience. The mentorship will primarily occur during our weekly one-on-one meetings in which I will provide regular assessments of her progress and specific guidance of additional steps she could take or changes that need to be made to accomplish her training aims. We will also interact in weekly project meetings with the staff and monthly project leadership meetings, which are attended by the PI, co-Is, consultants, and full-time project staff. Dani will learn about planning, budgeting, and staff supervision in the leadership meetings. Also, as my lab follows the Agile system for project management, we all work in the same shared space and have brief, scheduled check-ins three to four times per week. We also have numerous informal meetings throughout the course of each two-week "sprint" as well as longer, scheduled meetings at the beginning and end of each sprint. For example, in one sprint we might plan all intervention assessment activities in a three-hour planning meeting, and then the entire team would dedicate two full weeks to working only on assessment, meeting each morning to discuss accomplishments since the previous meeting, work plans until the next one, and barriers. We would then meet for a two-hour meeting at the end of the sprint to take stock of our progress. Finally, I will also provide Dani with regular, clear, and prompt feedback and guidance on her writing as she prepares manuscripts and grant proposals related to her project. In sum, F99 support will allow Dani to dedicate herself to learning to design, manage, analyze, and report a longitudinal translational neuroscience trial.

In terms of formal pedagogy, Dani has already finished the structural equation modeling seminar offered in the Psychology Department Fall 2017. She will complete the translational neuroscience graduate seminar that I teach in the Fall of 2019, and will take my graduate multilevel modeling seminar in the Spring of 2020. Dani will also attend and present regularly in our CTN brownbag series. The CTN brownbag is a standing bi-weekly meeting of the CTN group that is attended by the core CTN faculty (Berkman, Pfeifer, Fisher) and several additional faculty (Mills, Skowron), as well as graduate students and postdocs in those labs. The CTN brownbag series is an ideal way for Dani to learn about a variety of approaches and problems in translational neuroscience, as well as to receive regular feedback on her own project as it progresses.

K00 mentor identification. Dr. Mills and I will work with Dani select to identify and connect with a set of postdoctoral mentors in an environment where she will thrive. I will help Dani generate a comprehensive list of potential mentors with expertise in translational neuroscience who have ongoing cancer-relevant health behavior change interventions. Dr. Mills will help identify potential mentors with expertise in resting state fMRI and network science. We will also assist Dani in generating a set of institutional requirements necessary to pursue her K00 training aims and make introductions to mentors at institutions that fulfill these requirements.

Research environment. My main lab room occupies approximately 400 sq. ft. on the 2nd floor of the Lewis Integrative Sciences Building (LISB), which also houses our 8 small (100 sq. ft) run rooms. The full-time project manager for the parent R01 has an office in the main lab room. My office, my lab and Dr. Mills' lab, as well as the neuroimaging facility, the Lewis Center for Neuroimaging (Sabb, Director), are located on the LISB. As noted above, though I have my own office, my students and I work together in the main lab room during regular business hours. Our run rooms were designed for individual neuropsychiatric testing, and each contain a computer equipped with the necessary software to acquire behavioral task data (e.g., cognitive reappraisal,

food valuation) and self-report questionnaires. Each run room also has a medical grade scale and measuring tape to measure BMI. A “BodPod” air displacement measurement device to calculate body fat percentage is housed in a separate, larger (~200 sq. ft.) room that is dedicated for that purpose. The LISB has 5 parking spaces dedicated for research subjects. Research participants come to our 2nd floor run rooms for the consenting process and initial task and questionnaire completion, then have a biometric assessment across the hall, and finally enter the imaging facility one level below. The co-location of participant space, research lab space, and faculty office space greatly facilitates supervision, mentorship, and collaboration because informal, face-to-face interactions can occur as needed. Also, the CTN administrative staff (e.g., project management and grants management personnel) are also housed in the LISB, and the CTN brownbags take place in the neuroimaging center conference room on the 1st floor. Thus, nearly all training activities take place literally under the same roof, and all project personnel are within steps of each other.

Dr. Mills’ (co-sponsor) training plan.

First and foremost, I will provide Dani with specific mentorship in advanced statistical techniques for modeling longitudinal data while she pursues Research Aim 1. I am recognized as an expert in longitudinal modeling of developmental neuroimaging data and have been invited to present at several workshops on this topic, and have co-authored a number of reviews as well as edited a special issue on the topic. Despite being at an early stage of my career, I have already had extensive experience mentoring students and conducting federally sponsored educational workshops on longitudinal modeling. I also have over 8 years of experience running statistical models in programming languages such as R, which enables the use of state of the art modeling tools such as lavaan and facilitates reproducibility. To compliment the conceptual training Dani will receive with Dr. Berkman through formal coursework, I am exceptionally well-suited to provide Dani with practical training and support while she implements the latent growth curve and cross-lagged panel mediation analyses in R using lavaan.

I will also work with Dani to establish a strong foundation in resting state fMRI methods during the F99 training phase to ensure that she is poised to take full advantage of her K00 training. Dani will attend the weekly Resting State Journal Club that I have led for the past three terms. During these 90-minute meetings, trainees discuss both foundational and cutting-edge research articles using resting state fMRI, and gain a practical introduction to common analytic tools and pipelines. Trainees are from diverse areas on campus, including prevention science and clinical, developmental, social, and cognitive neuroscience, which engenders a lively and inclusive discussion on topical issues regarding this methodology and its application. Several students who completed my Network Analysis graduate seminar attend the journal club, so we frequently discuss network analytic methods applied to resting state functional connectivity data. To further enable Dani to hit the ground running as postdoctoral researcher during the K00 phase, I will mentor her as she conducts a systematic review of the literature on resting state fMRI applications to intervention contexts. I have experience conducting and publishing systematic reviews, and have authored several high-impact review papers. Together, the goal of these training activities is to ensure Dani has substantive knowledge of the theoretical bases of resting state fMRI methods and current best practices in order to enter postdoctoral studies with a well-developed training plan and select a training environment that will enable her to make the most of her K00 training.

Research environment. The Developmental Cognitive Neuroscience suite, which is occupied by both my lab and Dr. Pfeifer’s lab, is located on the first floor of the Lewis Integrative Sciences Building (LISB), and measures approximately 1800 sq. ft. Graduate students in Dr. Pfeifer’s lab, including Dani, and my lab share offices within this suite. In addition to the three graduate office spaces in this suite, there is also one large room where graduate students and postdoctoral researchers regularly work together in a collaborative environment. When I am not teaching or holding office hours, I spend my time working in this larger collaborative space. There are several individual testing rooms within the suite, a large room for research assistants, a large meeting room, as well two additional offices for lab staff and a waiting room. The Resting State Journal Club that I lead meets in the large meeting room within the Developmental Cognitive Neuroscience suite.

Coordination between co-sponsors

Both Dr. Mills and Berkman are members of the Department of Psychology and Center for Translational Neuroscience. We have an excellent working relationship and regularly collaborate. For example, while a postdoctoral scholar, Dr. Mills led the Center for Translational Neuroscience brownbag series with guidance from Dr. Berkman. Furthermore, Dr. Berkman and Mills are Co-Investigators on several grants, including an R01 and T31, that will be submitted this year. In terms of specific roles on this project, Dr. Berkman is

responsible for making sure all proposed F99 training and research activities are carried out on schedule and providing practical training in translational neuroscience and conceptual training in advanced statistical methods. Dr. Mills is responsible for practical training to implement the longitudinal modeling analyses in R, as well as introducing Dani to the literature on resting state fMRI to scaffold her transition to the K00 phase. Formally, we will interact during the the monthly mentorship meetings with Dani. In the mentorship meetings, Dr. Berkman and Dr. Mills will provide specific feedback on past performance and plan concrete future goals for Dani's work on the project and her overall career progress. Finally, because of our co-location in LISB and dedication to this project, we both are available to Dani in person and digitally as needed.

D. Number of Fellows/Trainees to be Supervised During the Fellowship

Dr. Berkman's trainees
Dr. Berkman will supervise three predoctoral trainees in addition to Dani. Rita Ludwig is supported by a university fellowship, and Brendan Cullen and Krista DeStasio are both supported by NSF GRFPs.

Dr. Mills's trainees
Dr. Mills will supervise one additional predoctoral trainee in addition to Dani (to be determined). Dr. Mills' incoming predoctoral trainee will be supported by her startup funds.

E. Applicant's Qualification and Potential for a Research Career

Dr. Berkman's (sponsor) assessment

Dani is exceptionally well prepared for F99/K00 training. I know Dani well because I have been her co-advisor in our doctoral program (along with Dr. Jenn Pfeifer) since 2015, and she was our lab manager for a full year before that. She is easily one of the best students in our department in terms of aptitude, productivity, and trajectory, and is well on her way to a tenure-track position at a research university. Dani functions at the level of a postdoc in her productivity, her ability to evaluate the literature, generate hypotheses to advance the field, independently seek funding to support her work, and analyze and report her data in a rigorous, open, and ethical way. I have no doubt that F99/K00 training will further propel Dani along her path to becoming an independent, federally-funded researcher in the area of cancer control by providing her with a unique blend of training and research opportunities in translational neuroscience that would not otherwise be available.

Dani has long shown a strong dedication to science in general and translational neuroscience in particular. Dani contacted me about our program in 2014 and traveled to Eugene twice (once from Sweden!) to meet with my colleagues and me, so she's quite committed to her training. She applied when we opened a lab manager position and was easily our top choice among a pool of about three dozen promising researchers. She began working full time at the University of Oregon (splitting her hours between my lab and Jennifer Pfeifer's Developmental Social Neuroscience lab) in the summer of 2014. Our initial impressions of her as an unusually bright, dedicated, and mature researcher were strongly and repeatedly confirmed.

Though Dani was an outstanding lab manager, her real passion is for the substantive psychological questions. When she applied to graduate school, we naturally did everything we could to keep her here, and feel fortunate to have succeeded. For her "First Year Project" (FYP), she conducted an ambitious longitudinal neuroimaging study of the transition to the college freshman year. This project involved scanning the entire sample in a short window before their first year began, then conducting intensive surveys throughout the academic year. The paper that she first-authored about this project was accepted at a top-tier journal.

This project illustrates several of Dani's notable qualities that have enabled her success so far and support our belief that Dani is exceptionally well prepared to transition to the K00 phase en route to becoming a productive, independent investigator. First and foremost, Dani wants her science to have an impact. The study uses a brain-as-predictor approach to be able to extract as much predictive information as possible about subsequent behavior from the fMRI data. Initial analyses revealed that activation in a network of self-regulation regions during autonomous (vs. exogenous) regulation predicted increases in substance use over the following 4 months. Using these preliminary data, Dani assisted Dr. Pfeifer in writing an R21 proposal to NIDA to follow-up on this result in a larger, riskier sample and with better assessment of drug use, which got funded last year and is now in progress. So, Dani is already an experienced and successful grant writer.

The second quality that her FYP illustrates is Dani's advanced statistical and coding skills. We began our interrogation with standard univariate analyses, contrasting activity during regulation with passive viewing, and during high- with low-autonomy regulation. Dani wanted to dig deeper and do more than just the bare minimum required for a publication. She built regions-of-interest using a priori parcellation maps based on resting-state functional connectivity. She ported the data into R because she was learning that language and

wanted to force herself to practice it more. She built whole-brain visualizations of the parcellation results into very cool 3D animations. Inspired by coursework in brain decoding, Dani applied multivariate pattern analysis (MVPA) to train a classifier to distinguish brain activity during regulation from passive viewing. Interestingly, the classifier had greater rates of accuracy during low- than high-autonomy regulation, possibly indicating more similarity between regulation and passive viewing in the high autonomy condition. We never would have obtained that result it if not for Dani's inquisitiveness and ability. That set of analyses perfectly sets the stage for more in-depth training in that family of methods; Dani is 100% ready for the next phase in her career.

The F99 is the perfect way for Dani to build on her already formidable skill set in translational neuroscience and longitudinal neuroimaging research. She has clearly demonstrated an aptitude for these things and crafted a well-conceived plan to take advantage of the strong resources at UO to elevate her training to the next level. F99/K00 support ensures a clear path for Dani to continue her stellar development as an independent scientist, and the training laid out in her proposal guides that development toward a career of innovative, significant work. Dani possesses the intellectual, statistical, and methodological skills on par with the best postdoctoral scholars I've worked with, plus her work is benefitted by her conscientiousness, smarts, and a strong personal dedication to and interest in conducting open and ethical science. I have no doubt that Dani will continue to flourish as a scholar in her graduate career (F99), postdoc (K00) and well beyond.

Dr. Mills' (co-sponsor) assessment

Without exception, Dani Cosme is the most promising graduate student I have had the opportunity to work with, and she is particularly well-suited to benefit from the F99/K00 program. Her maturity, industriousness, and intelligence are evident in her developmental trajectory as a scientist. I have worked with Dani for three years, beginning when I joined the Department of Psychology at the University of Oregon as a postdoctoral researcher in March 2016. I was surprised to learn that she was in her first year of doctoral training, as she already operated at the level of an advanced doctoral student: mentoring other students, managing several projects, and applying novel statistical approaches to these projects. I remember in one of our first lab meetings, Dani was working through a significant roadblock in her work examining longitudinal changes in task-based fMRI—there wasn't a software program readily capable of conducting these analyses across the whole brain. Coming from a different background as Dani, I suggested she utilize an approach common in resting state functional connectivity MRI: apply a parcellation to the whole brain. Within a short amount of time, Dani had reviewed the literature and developed a novel method using a parcellation approach to extract and visualize developmental changes in brain activation in a longitudinal dataset. This is just one example illustrating how well-prepared Dani is to integrate knowledge from task-based and task-free (resting state) functional neuroimaging for her proposed F99/K00 project.

In the time that I have known her, Dani has repeatedly demonstrated her aptitude for learning new statistical techniques and research methodologies, as well as her dedication to open and reproducible research. She has been a facilitator in the UO Data Science Club for several years, helping her fellow graduate students understand and apply advanced statistical approaches such as machine learning and multivariate pattern analysis. Dani was the most junior scientist to present at the 2017 Modeling Developmental Change workshop sponsored by the NSF. She presented her work on modeling developmental changes in longitudinal fMRI data, and made her presentation, tutorial, and code accessible and publicly available for all to use. Because Dani is both actively engaged in developing the resources needed to model longitudinal fMRI data and demonstrates an aptitude for teaching others how to use these resources, I have invited her to be part of applications for future workshops on this topic, including an Organization for Human Brain Mapping educational course. It should be noted that Dani herself has also taken an active role in organizing educational workshops to teach her peers. Last year she organized a one-day workshop on best practices for reproducible neuroimaging as part of the broader Brainhack Global event. Her track record of making the tools that she has built accessible to other researchers, and teaching others how to use these tools, suggests that she is both able, and committed, to sharing the neural signatures that she develops during her F99/K00 fellowship period.

Dani is also well-poised to execute her proposed training plan because she is already fluent in several programming languages, including Shell scripting, MATLAB, and R. Along with myself and a few others, Dani was one of the first users (alpha testers) of the University of Oregon's High Performance Computer Cluster, and is experienced with running large numbers of analyses efficiently through cluster computing. Her quick uptake of new programming languages suggests she will readily achieve her K00 goal of learning Python. Overall, Dani is exceptionally well equipped to achieve the training goals laid forth in this proposal and become a leader in the field of translational neuroscience, conducting rigorous and impactful research to prevent cancer.

Emily Falk, Ph.D.
Associate Professor of Communication, Psychology and Marketing
falk@asc.upenn.edu
Phone: 215-869-8873

February 17, 2019

Dani Cosme
Department of Psychology
1227 University of Oregon
Eugene, Oregon, 97403

To Whom it May Concern,

I am writing to give my enthusiastic support for Ms. Dani Cosme's NCI Predoctoral to Postdoctoral Fellow Transition Award (F99/K00) proposal, "*A multi-method translational neuroscience approach to cancer prevention via health behavior change.*"

Dani's innovative proposal to use multivariate neuroimaging to develop objective neurobiological indices of target psychological processes has the potential to significantly improve our ability to detect intervention effects and individual differences in health behavior change interventions to reduce cancer risk. Due to the multifaceted nature of this approach, she requires a unique team of mentors and resources to enable her to achieve her postdoctoral training goals. Specifically, she is seeking further training in intervention design, implementation, and evaluation in the context of interventions targeting modifiable health behaviors (e.g., sedentary lifestyles, alcohol and tobacco consumption) that are known risk factors for a variety of cancers, as well as methodological training in resting state functional neuroimaging and network analysis methods.

I am writing to affirm that the University of Pennsylvania would be an excellent environment for Dani to pursue her training plan and that I would gladly mentor her as a postdoctoral fellow.

My research program focuses on understanding how persuasive messaging facilitates behavior change at the individual, group, and population level, and I have substantial expertise in predicting behavior change using functional neuroimaging. At present, much of my research focuses on health communication and linking neural responses to health messages to cancer-relevant behavioral outcomes. I have extensive experience designing and executing

randomized controlled trials targeting cancer-relevant health behaviors, including physical activity, alcohol consumption and tobacco use, and evaluating interventions using functional neuroimaging. Furthermore, I have productive, ongoing collaborations with leaders in the field of network science and resting state neuroimaging, including my colleague at the University of Pennsylvania, Dr. Danielle Bassett, who is a Co-Investigator on the project described below.

Although my lab has conducted numerous studies that are relevant to Dani's interests, our recently launched, federally funded, large-scale longitudinal intervention targeting alcohol consumption in college students is an optimal project for her to pursue her postdoctoral training aims. The goal of this project is to understand the neural processes underlying individual change in alcohol consumption, as well as how individual change impacts alcohol consumption within an individual's social network. For this interdisciplinary collaboration, we will recruit 800 college students from the University of Pennsylvania and Columbia University. All participants will complete assessments of alcohol-related attitudes and behaviors three times over the course of one year. After the first assessment, a subset of 240 students will undergo functional neuroimaging and be randomized to one of three intervention conditions which focus on deliberately altering appetitive responses to alcohol cues using cognitive strategies. They will be trained to either use mindfulness, perspective-taking, or focused attention to control their cravings for alcohol, and will receive text messages reinforcing the strategy for 30 days. During this time, we will also measure daily alcohol consumption and mood via text message. Once everyone has completed the intervention, we will reassess alcohol-related attitudes and behaviors in the full sample to investigate the relationship between individual change and social network change. At the scanning session, we will acquire structural, resting state, and task-based neuroimaging scans.

This study is an ideal opportunity for Dani to pursue postdoctoral training for several reasons. First and foremost, Dani will gain experience with cancer-relevant health behavior change interventions to reduce alcohol consumption. This experience will extend her already substantial knowledge of craving regulation via cognitive reappraisal, to include new cognitive strategies and intervention outcomes. She will also learn new methodologies for intervention implementation and assessment using text messaging, and can apply her knowledge of advanced longitudinal modeling techniques in this rich dataset. Second, Dani can use the resting state functional neuroimaging data collected as part of this project to pursue her postdoctoral research aim of identifying reliable network connectivity profiles that are associated with intervention success and individual differences in intervention outcomes under the mentorship of Dr. Bassett, who is a Co-Investigator on this study. In addition to Dr. Bassett, the University of Pennsylvania is home to a thriving interdisciplinary community of researchers studying brain organization using resting state functional neuroimaging, and developing tools and methods for analyzing resting state data. Last, because we have already begun scanning on this project, Dani will be able to hit the ground running and begin analyzing data as soon as she arrives. Finally, we will

also have data from two other R01s that NCI has funded (one focused on physical activity and another focused on smoking). These projects are also directly relevant to Dani's training goals. She will be welcome to work with those datasets and I will work closely with her to advance her training goals. In short, I cannot imagine a training environment better suited to Dani's goals.

With her expertise in craving regulation, her strong background in advanced neuroimaging and statistics methods, and her passion for translational neuroscience, I would be thrilled to have Dani pursue postdoctoral training as part of our lab. I believe she is an excellent candidate for this fellowship and the training goals in this proposal will enable her to launch a successful career as an independent cancer researcher, designing and evaluating health behavior change interventions using multivariate neuroimaging.

Sincerely,

Emily Falk, Ph.D.

DESCRIPTION OF INSTITUTIONAL ENVIRONMENT AND COMMITMENT TO TRAINING

Educational Information. University of Oregon, Psychology Doctoral Program, Developmental and Social/Personality focus. The psychology doctoral program is a research and scholarly degree with the expectation that students will engage in research throughout their graduate career. Our program is highly collaborative and encourages an interdisciplinary approach that exposes students to a wide range of topics through small seminars, informal brownbag series, lab meetings, and a variety of other opportunities. The primary goal of the program is to train outstanding researchers with high quality training combined with substantive and methodological breadth.

Within our developmental area, our program offers extensive coverage of development during infancy, childhood, and adolescence, with some additional interest in aging. Topics strongly represented include cognitive development, socioemotional development, developmental psychopathology, developmental social and affective neuroscience, theory of mind, perspective taking. These connect with research on self-evaluation; affective and appetitive motivations; and decision-making. Another area within development includes research on infant processing of action; language; and the statistical properties of everyday visual, linguistic, and musical environments. Shared across the developmental area is also the shared interest in social contextual effects on infant, child, and adolescent well-being, ranging from the “micro” (familial and peer influences, early adversity) to the “macro” (cultural and global contexts of development).

Within our social/personality area, one will find an intellectually diverse research approach to understanding intrapersonal and interpersonal processes and individual differences. Current research topics include: Emotion and motivation; self, identity, and social cognition; groups, networks, and organizations; culture, values, and worldviews; personality structure and development; and, decision making and risk perception. Research in these areas draws upon a wide range of methods, including individual, dyadic, and group methods, psychophysiology, neuroimaging, neuroendocrinology, experience sampling, longitudinal studies, surveys, computational methods, and field studies.

The Center for Translational Neuroscience is a mutlidisciplinary research Center housed within the Department of Psychology. The CTN functions as an intellectual community for translational neuroscience that bridges several departments including Psychology, Biology, Human Physiology, and Education. The mission of the CTN is to translate knowledge from basic neuroscience and apply it to improve well-being, promote resilience, and mitigate the effects of early adverse experiences. The CTN focuses on training at the undergraduate, graduate, postdoctoral, and junior faculty levels in neuroscience-informed approaches to prevention and intervention. The University of Oregon Graduate School also offers a Graduate Specialization in Translational Neuroscience through the CTN. Doctoral students are eligible to receive a Specialization in Translational Neuroscience if they take a set of courses and complete a Translational Neuroscience Research Project. More details about the CTN are provided in the Facilities and Other Resources document.

The Department of Psychology at the University of Oregon encourages multidisciplinary collaborations with students and colleagues from other areas of psychology and other academic departments.

Requirements, Milestones, Timing.

Requirement	Completion Deadline
Data Analysis I, II, III	End of spring term, first year
First Year Research Series including Ethics	End of spring term, first year
Departmental Core Sequence (3 of 5 core courses)	End of spring term, second year
First-Year Research Requirement	November 15, second year
Supporting Area Requirement	October 15, fourth year

Major Preliminary Examination	October 15, fourth year
Advancement to Candidacy	After completion of the above
Doctoral Dissertation & Final Oral Defense	Expected within six years
Doctorate of Philosophy	Awarded after completion of all of the above, within seven years

During their time in our program, the majority of our doctoral students serve as teaching assistants, research assistants, or sole instructor throughout most of their academic career.

Doctoral students are evaluated on several levels: Final course grades, performance on major requirements (First Year Research Project, Supporting Area Requirement, Major Preliminary Examination), as teaching/research assistants or course instructor. Although doctoral students meet regularly with their Advising Committee, only once each academic year will they evaluate and formally report on the student's progress in the program.

Danielle Cosme is a fourth year doctoral student in the developmental and social/personality areas in psychology. She has already Advanced to Candidacy and proposed her dissertation research.

Information is provided by Lori Olsen, UO Department of Psychology Graduate Secretary.

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved	● Yes ○ No
Is the Project Exempt from Federal regulations?	○ Yes ● No
Exemption Number	❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8
Other Requested Information	

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Devaluing Foods to Change Eating Behavior	Yes

Section 1 - Basic Information (Study 1)

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

1.1. Study Title *

Devaluing Foods to Change Eating Behavior

1.2. Is this study exempt from Federal Regulations * ❍ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	❍ No
1.4.b. Are the participants prospectively assigned to an intervention?	● Yes	❍ No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	● Yes	❍ No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	● Yes	❍ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- Overweight and Obesity
- Cancer

2.2. Eligibility Criteria

For the sample used in Aim 1, the following criteria will be used:

Inclusion Criteria:
- overweight to obese range (BMI 25-40)

Exclusion Criteria:
- metal implants (e.g., braces, permanent retainers, pins)
- metal fragments, pacemakers or other electronic medical implants
- claustrophobia
- weight > 550 lbs.
- women who are pregnant or believe they might be pregnant
- people who have been diagnosed with past or current medical, psychiatric, neurological, eating disorders, or are taking psychotropic medications
- urine screen to exclude participants who are acutely intoxicated
- screen for handedness

Beyond these criteria, participants will be recruited without exclusions based on gender, race, or ethnicity, so our sample will reflect the diversity in the local population (Lane County, Oregon) with regard to gender, race, and ethnicity.

2.3. Age Limits	Min Age: 18 Years	Max Age: 60 Years
2.4. Inclusion of Women, Minorities, and Children	InclusionWomenMinoritiesChildren.pdf	
2.5. Recruitment and Retention Plan	RecruitmentRetentionPlan.pdf	
2.6. Recruitment Status	Recruiting	
2.7. Study Timeline	StudyTimeline.pdf	
2.8. Enrollment of First Subject	04/02/2018	Actual

INCLUSION OF WOMEN, MINORITIES, AND CHILDREN

Enrollment will be based on the data from the first 150 participants that have completed the intervention in the parent grant. The target population of the parent grant will consist of 300 individuals between ages 18 and 60 and will be equally balanced between males and females. Children aged 18-20 will be included in the sample, but are considered legal adults in the state of Oregon. They will provide informed consent using procedures approved by our institutional ethics board. Participants will be recruited for the parent grant without exclusion based on gender, race, or ethnicity. Thus, the subject population is anticipated to reflect the percentages in the local population of Eugene, Oregon (Lane County) with regard to gender, race, and ethnicity, as indicated in the Planned Enrollment Report. According to the 2010 census, Eugene is 7.8% Hispanic/Latino, 1% American Indian/Alaskan Native, 4% Asian, 0.2% Native Hawaiian/Pacific Islander, 1.4% Black/African American, and 85.8% White. We have taken this demographic information into account when creating our Inclusion Enrollment Report. We will oversample the Hispanic/Latino, Asian, Native American/Alaskan Native, Black/African American, and Native Hawaiian/Pacific Islander populations so as to collect data from a more diverse sample of participants. This oversampling is reflected in the Inclusion Enrollment Report.

RECRUITMENT AND RETENTION PLAN

Below is the Recruitment and Retention protocol from the parent grant, R01 CA211224.

Recruitment plan

The primary recruitment tools will be advertisements placed in the Eugene/Springfield *Register-Guard* daily and the *Eugene Weekly* newspapers, on Craigslist, Google, and Facebook, in direct mail and email campaigns, radio stations, bus posters, and on flyers in and around the Eugene/Springfield area, including community centers, pools, churches, and libraries. Additional advertisement for this study may occur via ads placed in other newspapers (e.g., *The Oregonian*) or on online message boards. These methods have been used successfully in the past by the research team to recruit large and representative community samples including samples of overweight and obese individuals. Our minority recruitment plan is to post flyers in physical and online settings that involve high percentages of ethnic minority individuals. In addition, all recruitment posters will contain pictures of adults who are of ethnic minority. These procedures will enable us to recruit samples that are more ethnically diverse than the general population in our region.

Retention plan

We will use the following strategies to maximize participant retention. First, participants will be assigned one staff person to be the “point person” for scheduling and the main interventionist. Second, participants will be compensated $60 per session for the baseline and endpoint sessions, $30 for each of the three follow-ups, and $100 throughout the training sessions. Participants will be paid $10 per session plus a max bonus of $20 for at-home work. We have successfully achieved response rates of 94% using a similar incentivization schedule for completion. Third, they will provide names, addresses, phone numbers, and e-mail addresses of 3 people who “will always know where you are” for tracking purposes; this info will be updated every 6 months. Subjects who move will be invited to complete assessments during visits back to Eugene, which minimizes attrition. These procedures that have resulted in retention rates of 84-95% through 3 yr follow-up in randomized trials of obesity and eating disorder prevention and treatment interventions (Stice et al., 2011, 2013, 2015).

STUDY TIMELINE

Below is the study timeline from the parent grant, R01 CA211224.

Recruitment and data collection will begin in the second half of Year 1 and continue through the first half of Year 4. Consistent with the current productivity of the research team, participants will be recruited at the pace of approximately 4-5 per week. This will yield a full sample of N = 330 (allowing 10% attrition) by the end of Month 54 at the latest, even accounting for academic breaks and 50% slower summer recruitment. Data cleaning of behavioral measures and preprocessing and first-level modeling of fMRI data will be ongoing throughout this period. All data will be collected and ready for group-level analysis by the end of Month 54. Group-level analysis, interpretation, and write-up will occur during Months 48–60.

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	Eugene, Oregon

Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ❍ Yes ● No

Enrollment Location Type* : ● Domestic ❍ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s): Eugene, Oregon

Comments: Planned enrollment for Aim 1; based on the parent R01 planned enrollment.

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	1	1	0	0	2
Asian	5	5	0	0	10
Native Hawaiian or Other Pacific Islander	1	1	0	0	2
Black or African American	2	2	0	0	4
White	53	53	8	8	122
More than One Race	4	4	1	1	10
Total	66	66	9	9	150

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	ProtectHumanSubjects.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	○ Yes ● No ○ N/A
If yes, describe the single IRB plan	
3.3. Data and Safety Monitoring Plan	DataSafetyMonitoringPlan.pdf
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	● Yes ○ No
3.5. Overall structure of the study team	OverallStructureStudyTeam.pdf

PROTECTION OF HUMAN SUBJECTS

Below is the Protection of Human Subjects protocol from the parent grant, R01 CA211224. Addendums pertinent to this proposal are *italicized*.

1. Risks to Human Subjects

A. Human Subjects Involvement, Characteristics, and Design

Characteristics of the subject population. Our goal of the parent grant is to obtain usable data from 300 adult participants. These participants will be overweight or obese adults between the ages of 18 and 60, inclusive. In the previous experience of the research team, the loss of usable data resulting from study noncompliance, attrition, or excessive movement in the scanner is less than 10%. Therefore, our recruitment goal is to enroll 330 participants (165 females, 165 males) in the study. From this, we estimate that we will have usable data from 150 male and 150 female participants. *The current proposal will use the data from the first 150 participants collected.*

Involvement. All participants will make between 11 and 13 visits to the Lewis Integrative Sciences Building (LISB) at the University of Oregon: two to the Lewis Center for Neuroimaging (LCNI; “baseline” and “endpoint” sessions) and 9-11 to the Social and Affective Neuroscience (SAN) Laboratory (6-8 training sessions and 3 follow-ups at 3-, 6-, and 12-months post baseline). The baseline and endpoint sessions will take place approximately 30 days apart. The intervention sessions occur between the baseline and endpoint sessions. *The current proposal will only use data from the baseline endpoint MRI sessions and the 3 and 6 month follow ups.*

Participants will be recruited via physical and digital ads and online postings (e.g., on bus advertisements, newspapers ads, at grocery stores and markets, via direct mailing, radio, and on Craigslist, Google, and Facebook) then screened for eligibility over the phone. To be eligible, participants must meet the sample criteria in terms of age and BMI status, absence of medical, psychiatric, neurological, and eating disorders, absence of tobacco and substance use, be psychotropic medication-free, not be dieting (past 6 months, current, or planned for the following 6 months), and also be safe to enter the magnetic resonance imaging (MRI) scanner.

At the baseline and endpoint sessions, participants will be situated in the fMRI scanner at LCNI to complete four behavioral tasks that will involve inhibitory control (e.g., pressing buttons rapidly to some stimuli and withholding them to others), cognitive reappraisal (e.g., viewing images of appetitive foods and thinking about them in a different way to make them seem less appealing), and valuation (e.g., bidding on various foods to be purchased from an endowment provided by the experimenter). Before the tasks, participants will complete a brief questionnaire about the kinds of healthy and unhealthy foods that the participants find palatable and eat regularly. Participants will also complete a urine toxicology screen for a range of illicit substances at both sessions. Participants will be told during the phone screening and at the pre-session that drug tests will be used to ensure sobriety at the time of the scan.

Between the baseline and endpoint sessions, participants will be randomized to one of two interventions for changing food valuation (a behavioral or cognitive training) or a generic inhibitory control training involving non-food stimuli. Participants will be scheduled for 6-8 training sessions (depending on their condition) to take place across the following 4 weeks, between the baseline and endpoint sessions. Participants will return to the lab at 3-, 6-, and 12 months following the baseline session for follow-ups to measure long-term intervention effects on the proximal processes (behavioral responses and cognitive reappraisal), on valuation, and on eating and body composition. In these sessions, participants will complete all self-report and task-based behavioral measures as in the baseline and endpoint sessions, and also have their body fat assessed with the BodPod, BMI, and waist-to-hip ratio. There will be no neuroimaging in these sessions. *The current proposal will only use data from the 3 and 6 month follow ups.*

Sampling plan. Participants will be recruited for the parent grant without exclusions based on gender, race, or ethnicity. Thus, our subject population will reflect the percentages in the local population (Lane County, Oregon) with regard to gender, race, and ethnicity, as indicated in the Targeted/Planned Enrollment Table. Because of the high Caucasian population of Lane County, we will oversample minorities to increase the generalizability of our findings. Participants who cannot undergo an MRI scan will be excluded from the proposed research. These MRI contraindications include metal implants (e.g., braces, permanent retainers, pins) or metal fragments, pacemakers or other electronic medical implants, claustrophobia, and weight greater than 550 lbs. We will perform this screening twice, once during the telephone screening and again immediately before the baseline scan to ensure that no answers had changed since the original screening. Although there

are no known risks of MRI to a developing fetus, female participants who are pregnant or believe they might be pregnant will be excluded, per the policy of the Institutional Review Board of the University of Oregon. However, participants will not disclose their pregnancy status; female participants will be told during the screening that if they are pregnant or believe that they might be pregnant should withdraw from the study.

Because the purpose of the proposed research in the parent grant is to identify mechanisms and moderators of food valuation interventions among people at elevated risk for food-related cancers, we will screen participants to have BMI in the overweight to obese range (25-35). We will not exclude individuals who report current psychiatric, neurological, or substance use disorders, but will exclude those who do not pass a urine toxicology screen during either of the fMRI sessions to ensure that the neuroimaging data are as homogeneous and reliable as possible. We will also exclude individuals who meet any of the MRI contraindications described above (e.g., claustrophobic, pregnant).

Rationale for involvement of special vulnerable populations (children). Because the purpose of the proposed research in the parent grant is to study eating and weight change in adults as defined by state law, we will recruit children ages 18-20. The rationale is that their weight status confers cancer risk even at that young age.

Assignment to study group. The proposed research in the parent grant empirically tests a randomized, controlled trial of mediators and moderators of an eating and weight change intervention for adults who are at elevated risk for eating-related cancers. Therefore, we will randomly assign participants into three equal groups: behavioral training, cognitive training, or active control. Study groups are expected to be matched for age, sex, and SES.

Collaborating sites. All data will be collected at the University of Oregon. Parent grant Co-I Stice is located at the Oregon Research Institute, and his role in the study to oversee the delivery of the interventions, which take place at the University of Oregon. Dr. Stice will also provide a BodPod for the study, which will be re-located to the University of Oregon. Thus, all research activity involving human subjects takes place at the University of Oregon.

B. Study Procedures, Materials, and Potential Risks

Research materials and data collected from human subjects. Data will be obtained from participants using questionnaires, physiological assessments (i.e., height, weight, body fat %), behavioral (task) sessions, and MRI scans. Data will be obtained solely for research purposes.

Access to identifiable private information. To protect individually identifiable private information, each participant will be assigned a numerical identifier. This numerical identifier will be attached to all data collected from participants, including questionnaires, behavioral task performance, MRI data, and biometric assessments. This numerical identifier will ensure the strictest participant confidentiality.

Collection, management, and protection of data. Dr. Berkman, who will match data to numerical identifiers, will maintain the list of numerical identifiers. Participants' numerical identifiers, names, phone numbers, body composition data, behavioral or MRI data, and survey responses will never all appear in the same file. To ensure the strictest participant confidentiality, electronically stored data will be password protected and paper data will be stored in locked file cabinets in the Dr. Berkman's office. Access to all data will be limited to the key investigators and the project coordinator for this study. Any data being analyzed will be stripped of identifying information. Only group-based analysis will be reported in publications, not information about individuals.

Potential risks to subjects. The proposed research in the parent grant poses risk that is generally mild, and at most minimal, in severity. The safety of MRI has been evaluated during the past 20 years, and no short-term effects have been observed. However, the long-term effects of MRI on the body are not fully known. Individuals with claustrophobia may find the MRI equipment too confining, which may cause anxiety. The MRI scanner makes loud noises, which could be damaging to the ears if not protected with earplugs. In addition, a person cannot have an MRI if they have any metal in or near their brain. There are also possible risks for participants if metal is drawn to the magnet while a participant is within or near the bore. Accordingly, participants will be asked to leave all jewelry and metal objects outside of the scanning room, and no loose metal objects will be allowed near the magnet. We exercise careful safety procedures outlined by the LCNI and have never had an adverse event while performing more than 600 scans. Regarding surveys and behavioral tasks, participants may find some of the experimental tasks or questionnaires to be boring or difficult. There is also a slight risk that research records (e.g., surveys, MRI data) might be obtained by persons not authorized to do so, though it is unlikely that our records will contain sensitive information, because participants with psychiatric disorders will be excluded at baseline.

Alternative treatments and procedures. There are no alternative treatments or procedures beyond those outlined in the parent grant. However, subjects are always reminded that they may stop their participation in the experiment at any time, with no adverse consequences.

2. Adequacy of Protection Against Risks

A. Informed Consent and Assent

Process for obtaining informed consent. Eligibility will be determined using a telephone screening interview. This interview will be conducted by phone by the project manager after participants have received information about this study, have had a chance to ask any questions, and have expressed the desire to participate in the study, as detailed in the following section. Ethically and legally acceptable procedures will be followed for the identification and recruitment of participants. No form of coercion will be applied.

Circumstances under which consent will be sought and obtained. Participant consent will be solicited in a private setting during the participant's first visit to UO ("baseline") by a trained and certified member of the research team. Under no circumstances will coercion be applied to obtain informed consent, and participants will be thanked for their participation in the study and compensated on a prorated basis for their time regardless of whether they choose to continue in the research study. Potential participants will be given the opportunity to discuss their participation with family, friends, or other advisors prior to signing the consent form. If needed, all participants will be allowed to terminate their participation after giving consent but before completing the study.

B. Protections Against Risk

Procedures for protecting against or minimizing potential risks. We will minimize any discomfort associated with engagement in the study by informing participants about what to expect prior to participation. There are no known adverse effects resulting from exposure to MRI. The only known risk of MRI scanning is that of bringing metal objects into the scanner room or dislodging any implanted metal objects. To prevent this from occurring, participants are carefully screened prior to having an MRI scan. Participants with any history of surgery involving metal objects or implants are excluded from the study. Also, the MRI scanning procedure requires that the participant be as still as possible while lying in a small, partially enclosed space. Although the fMRI session will be about 90 minutes long, participants will be required to hold still only for periods of up to 9 minutes each. The other primary risk of MRI scanning is psychological, that is, fear of the unfamiliar MRI environment or annoyance with the loud noise. This can be mitigated by allowing the participants to become familiar with the scanner environment in our mock scanner suite before the actual MRI scan, and reducing noise by wearing earplugs. Participants may find some experimental tasks to be boring or difficult, but they will be given multiple breaks to ease fatigue. Participants will communicate with the MR technologist via an intercom system and may trigger an audible alarm at any time to stop the MR session if he or she is uncomfortable or anxious. In addition, all imaging center staff and the project manager will participate in safety training annually. All scans will be conducted with at least two team members present, an MRI technologist and a researcher, all of whom will have been MR safety-certified and extensively trained.

As part of informed consent procedures, participants will be advised that the MRI scans will not provide "diagnostic" results and that the MRI technicians at the LCNI are not medically trained and would not be able to provide a medical interpretation of the MRI data. They will also be advised that project staff would advise them if incidental or anomalous findings are discovered (Illes et al., 2004), encourage them to contact their primary care physician, and provide a report of the relevant findings. Specifically, if the MRI technician perceives a potentially concerning abnormality, the UO neuroimaging center policy (for all users) is as follows. Participants will not be informed of potential abnormalities until these images are reviewed by a licensed clinical radiologist; potentially abnormal images will be sent for review via secure transmission to a radiologist at a partner hospital (UCLA Medical Center); the radiologist will inform LCNI staff of results; if positive results are found, participants will be contacted by the LCNI director, informed of the procedure and the finding, and advised to contact a medical professional.

As mentioned earlier, all personal information will be stored in locked file cabinets in Dr. Berkman's office, with access limited to the key investigators and the project coordinator for this study. All potential subjects will be assigned an ID number upon receipt of their contact information so that no personal identifiers will appear on any subsequent form, assessment, questionnaire, behavioral task, MRI scan, or text message. Access to the code linking the subject name to the identification number will be strictly limited to Dr. Berkman. All key investigators will complete the NIH Protection of Human Subjects: Computer-Based Training Program before any of the funded research activities begin.

3. Potential Benefits of the Proposed Research to Participants and Others

Participants are not guaranteed to obtain any direct benefit from participation in this project (other than a picture of their brain, acquired during the MRI scan). However, participants assigned to any of the groups might experience reductions in desire for cancer-risk foods, increases in desire for healthy foods, and changes in body fat, along with associated reductions in cancer risk. All participants will be informed of study hypotheses upon completion of the study, so that all participants may benefit from the intervention arm that shows the greatest effect on eating and body composition, and at a minimum improve knowledge regarding the effect of our interventions on eating and weight, and their underlying mechanisms. Furthermore, by becoming involved in this project, participants will be contributing to the advancement of translational neuroscientific research for cancer risk reduction. Also, the MRI scan may reveal an undiagnosed problem that would be beneficial for the participant to know about. As described earlier, if the MRI technician perceives a potentially concerning abnormality, the UO neuroimaging center policy (for all users) is to refer those cases to a neuroradiologist for review. If the findings are determined to have clinical significance, the participant will be notified by the UO neuroimaging center.

4. Importance of the Knowledge to Be Gained

This study will greatly advance scientific understanding of the mechanisms and moderators of interventions to change eating patterns and reduce weight. There is robust evidence that behavioral and cognitive interventions can change food intake and/or weight, but those changes are not durable. An impediment to making progress in improving the interventions is that their underlying mechanisms are unknown. Thus, establishing the mechanisms of these interventions will ultimately allow scientists to make them more effective. Additionally, detailed knowledge about the individual difference moderators of treatment effectiveness will allow treatment providers to triage at-risk individuals to one intervention or another that may be more effective for a given person or group based on a personalized profile that is known to respond to particular treatment mechanisms. Furthermore, better knowledge about how interventions operate will enable the development of more efficient interventions that could targeted the specified system while using fewer resources than interventions that are currently available.

DATA AND SAFETY MONITORING PLAN

The PI will gain clinical trial experience through the parent grant, R01 CA211224, under the supervision of the Sponsor Berkman, who is lead investigator of the clinical trial. The independent Data and Safety Monitoring Board is located at the Oregon Research Institute. The Safety Monitor is Emma Lee Junior, M.D.

OVERALL STRUCTURE OF THE STUDY TEAM

For the parent grant R01 CA211224, all administration, enrollment, and data collection will be conducted at the University of Oregon under the leadership of Sponsor Berkman. The independent Data and Safety Monitoring Board is located at the Oregon Research Institute. For more information concerning the structure of the study team, please see the parent grant.

Section 4 - Protocol Synopsis (Study 1)

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

Type	Name	Description

4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ❍ Yes ❍ No

4.2.e. Intervention Model

4.2.f. Masking ❍ Yes ● No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

4.4. Statistical Design and Power

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? ❍ Yes ❍ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
The form does not have any delayed onset studies			

SUMMARY STATEMENT

PROGRAM CONTACT:
Susan Perkins
240-276-5630
perkinsu@mail.nih.gov

(Privileged Communication)

Release Date: **07/12/2019**
Revised Date:

Application Number: **1 F99 CA245811-01**

COSME,DANIELLE
University of Oregon
1227 University of Oregon
Eugene, OR 974031227

Review Group:	**ZCA1 RTRB-R (A1)** **National Cancer Institute Special Emphasis Panel** **Predoctoral to Postdoctoral Fellow Transition Award (F99/K00)**
Meeting Date:	**06/03/2019**
Council:	**AUG 2019** ***PCC:*** **S9TR**
Requested Start:	**09/01/2019**
Project Title:	**A multi-method translational neuroscience approach to cancer prevention via health behavior change**
	***Requested*: null**
Sponsor:	
Department:	**Psychology**
Organization:	**UNIVERSITY OF OREGON**
City, State:	**EUGENE OREGON**
SRG Action:	**Impact Score:41**
Next Steps:	**Visit https://grants.nih.gov/grants/next_steps.htm**
Human Subjects:	**30-Human subjects involved - Certified, no SRG concerns**
Animal Subjects:	**10-No live vertebrate animals involved for competing appl.**
Gender:	**1A-Both genders, scientifically acceptable**
Minority:	**1A-Minorities and non-minorities, scientifically acceptable**
Age:	**7A-Only Adults, scientifically acceptable**

RESUME AND SUMMARY OF DISCUSSION: The applicant proposes training in neuropsychology as it relates to cancer prevention and control. Her goal is to develop reliable neurobiological indices of target psychological processes in order to improve detection of intervention-related change and individual differences in cancer patients. Her thesis project is expected to have a significant impact on the field of cancer-relevant health behaviors. She has already made significant progress and she has published one first-author paper stemming from her Ph.D. research, one paper also as first-author is under review, and one is under preparation. She has defined the neural signature that she will use by applying a novel statistical approach that she developed. Preliminary data support the utility of the signature to differentiate the appraise condition. The letters of recommendation are each very strong and describe the applicant as an outstanding student, productive, and talented, with advanced statistical and coding skills. Her solid history of commitment to research since an undergraduate student and her master's degree in psychology are additional strengths for this applicant. The sponsor and co-sponsors have substantial and relevant track-record mentoring Ph.D. students and have complementary expertise in the field of neuropsychology, behavioral sciences, clinical trials, statistical methods, and imaging. However, no cancer investigator in behavioral sciences is included in the mentoring team. The research plan employs an interdisciplinary approach to determine why interventions to modify cancer risk factors (smoking, diet, activity) are not equally-effective across individuals. If successful, this research plan will likely lead to strong publications. The applicant will learn many new techniques and she provides a training plan that is consistent with her goal of becoming a cancer researcher. In the K00 phase, the applicant proposes to explore the relationship between resting state functional magnetic resonance imaging (fMRI) to examine trait-like features that may relate to the patterns of health behavior and more likely reflect a real-world process. The University of Oregon, the Lewis Center for Neuroimaging (LCNI), and the Center for Translational Neuroscience have each suitable equipment and facilities, as well as other outstanding faculty and students with whom the applicant can interact. The strong candidate, the clear engagement of the sponsor/co-sponsor, and the skill development that will result from the proposed research and training mitigate the moderate weaknesses in the design of the research plan, in which no specific cancer outcome is addressed. Also, the training in health behavior interventions and in cancer research are insufficient for the goals proposed. Nevertheless, overall, it is likely that the activities described in this application, will provide moderate training to advance the applicant's research independence.

DESCRIPTION (provided by applicant): Health behaviors, such as poor diet, lack of physical activity, and tobacco and alcohol consumption, increase risk for developing various forms of cancer. These behaviors are modifiable and effective interventions have been developed to promote health behavior change. Critically, however, behavior change interventions do not work equally well for all people. To understand why an intervention works for some individuals and not for others requires clearly defined neurobiological mechanisms of change and sensitive and specific tools to evaluate individual differences in intervention targets. This application seeks to develop a coherent research framework to produce reliable neurobiological indices that can effectively index change in cancer-relevant intervention targets and individual differences in treatment responsivity. Maximizing sensitivity and generalizability requires a multi-method approach that applies advanced neuroimaging and statistical techniques to task-based and task-free fMRI data. I will receive training that will enable me to achieve this objective, including translational neuroscience and advanced longitudinal modeling during the F99 phase, and resting state fMRI and network analytic methods during the K00 phase. My dissertation evaluates the efficacy of an RCT to promote healthy eating and estimates the degree to which cancer-relevant intervention outcomes are moderated by change in a neurobiological index (i.e., "neural signature") of the intervention target, craving reappraisal. I used machine learning with task-based fMRI to develop a whole-brain signature that is specific to craving reappraisal and has up to 95% out of sample prediction accuracy. This result is significant because it is the first objective measure of craving reappraisal that generalizes across people, thereby increasing sensitivity to detect individual differences in reappraisal ability. In the F99 phase of this application, I will assess the degree to which the reappraisal intervention is associated with change in this neural signature, and whether individual differences in neural signature change predict intervention outcomes. In the K00 phase, I will extend

this research program to develop neural signatures using task-free resting state fMRI, which may reflect more enduring patterns of health behaviors. To characterize changes in brain networks related to cancer-relevant health behavior change interventions, I will identify reliable network connectivity profiles associated with treatment success and individual differences in treatment responsivity, and directly compare the predictive utility of neural signatures derived from task-based and task-free fMRI. This research program has the potential to substantially improve our ability to detect intervention-related change and individual differences and enable researchers to more effectively evaluate whether, how, and for whom health behavior change intervention is working. Additionally, by developing this framework for creating and validating neural signatures, and openly sharing materials and analytic code, this research program will facilitate the development of neurobiological indices for any number of cancer-relevant intervention targets at any point along the cancer continuum.

PUBLIC HEALTH RELEVANCE: Health behavior change interventions can reduce modifiable cancer risk factors such as unhealthy eating, lack of physical activity, and substance use, but interventions are not equally effective for all individuals. This project will leverage novel multivariate neuroimaging techniques to develop reliable neurobiological indices of target psychological processes in order to improve detection of intervention-related change and individual differences. The knowledge gained from this application will enable researchers to more effectively evaluate whether, how, and for whom interventions targeting cancer-relevant health behaviors are working.

CRITIQUE: The written critiques of individual reviewers are provided in essentially unedited form in this section. Please note that critiques and criteria scores, prepared prior to the review meeting, may not have been revised following discussions at the meeting. The "Resume and Summary of Discussion" section summarizes the final opinions of the review committee.

CRITIQUE 1

Fellowship Applicant:	2
Sponsor:	2
Research Training Plan:	3
Training Potential/Developmental Plan:	2
Institutional Environment & Commitment to Training:	2

Overall Impact/Merit: Applicant has outstanding academic record and research experience, which gives her excellent potential to be an independent investigator. The sponsors are an excellent match for this applicant, are very well-published and have external funding in the topic area. A minor issue is one of the co-sponsors has a relatively brief history of collaboration with the sponsor and applicant. Another weakness is that the team does not include expertise in nutrition and dietary behavior change interventions. The training plan is clear and detailed and will lead to attaining the aims proposed. A minor concern is that there should be more training in machine learning. The environment is strong for supporting this research.

1. Fellowship Applicant

Strengths

- Applicant has outstanding training in neuroscience – she has a master’s degrees from both Stockholm University and from the University of Oregon in psychology and she is currently a doctoral student at the University of Oregon, expecting to graduate in 2021.
- Applicant has at least 3 first author papers in good journals, and several other coauthored papers.

- Letter writers just rave about her promise as a scientist – one said she was 'the best doctoral I have ever worked with' and another said: 'she is on a superstar' trajectory'.
- Applicant also has an F31 application with 9th percentile that is likely to be funded.

Weaknesses

- No major weaknesses.

2. Sponsors, Collaborators, and Consultants

Strengths

- The sponsor, Dr. Berkman, is the Associate Director of the University of Oregon Center for Translational Neuroscience.
- Dr. Berkman is a Stanford- and UCLA-trained neuroscientist, with a focus on neurocognitive bases of cancer-relevant health goals.
- Dr. Berkman is Principal Investigator of 1 R01 research grant and Co-Investigator of two R01 research grants and would be a very strong mentor.
- Applicant has 3 papers with Dr. Berkman, including at least one paper published and under review.
- Co-Mentor, Dr. Mills is trained at University College London and University of Oregon and has strong training and publications in neuroscience.

Weaknesses

- Dr. Mills is more junior than Dr. Berkman and recently started at the University of Oregon. A minor issue is that she does not appear to have published with either Dr. Berkman or the applicant, although they are working on an R01 research grant and a T31 fellowship to be submitted in 2019.

3. Research Training Plan

Strengths

- The applicant will use neuroimaging techniques to focus on understanding why interventions to modify cancer risk factors (smoking, diet, activity) are not equally-effective across individuals, with an ultimate goal of identifying ways to match individuals to interventions.
- Applicant will learn SEM and multilevel modeling, which is appropriate, given training goals.
- A training goal is to learn to conduct an RCT related to dietary behavior.
- Applicant has a nice plan to transition from the F99 to the K00 phases and identifying new mentors and sites for the K00 period; applicant has identified 4 universities that meet her criteria, which is very strategic (applicant even includes a letter from Dr. Emily Falk at the University of Pennsylvania, one of those sites).
- This work is guided by a conceptual model of a mechanism of change for eating behavior.

Weaknesses

- The mentoring in neuroscience is very strong, but several of the key questions involve health behaviors, such as dietary behavior. The mentoring team is heavy on neuroscience and has less experience for dietary behavior or nutrition. This is a limitation because the F99 phase goal is to develop a dietary behavior change intervention.
- Applicant has interest in machine learning during the K00 phase and more training on that topic would be desirable.

- The ability of neuroscience applications to change dietary behavior in the real world has not been fully-justified in the application.

4. Training Potential

Strengths

- The applicant's goal is to become a leading translational neuroscientist and the training plan is well-developed and will contribute to that goal.
- Appropriate milestones are set for this training period

Weaknesses

- No major weaknesses.

5. Institutional Environment & Commitment to Training

Strengths

- The University of Oregon has an excellent environment for this project. The Center for Translational Neuroscience appears to be a strong place to support this work.
- The Lewis Center for Neuroimaging (LCNI) appears to be a top-notch facility, with a large amount of equipment, appropriate for this project and the letter of commitment from the Chair of Psychology and Sponsored Project Rep note she has access to all of the equipment at the LCNI.

Weaknesses

- The description of the Center for Translational Neuroscience is very meager – what is the amount of laboratory space, what equipment is available?

ADDITIONAL REVIEW CRITERIA

Protections for Human Subjects

Acceptable Risks and Adequate Protections

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Acceptable

Inclusion Plans

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Acceptable
- Inclusion/Exclusion Based on Age:

Vertebrate Animals

Not Applicable (No Vertebrate Animals)

Biohazards

Not Applicable (No Biohazards)

ADDITIONAL REVIEW CONSIDERATIONS

Training in the Responsible Conduct of Research

Acceptable

Comments on Format (Required):

Comments on Subject Matter (Required): Acceptable

Comments on Faculty Participation (Required): Acceptable

Comments on Duration (Required): Acceptable

Comments on Frequency (Required): Acceptable

Applications from Foreign Organizations

Not Applicable

Select Agents

Not Applicable (No Select Agents)

Resource Sharing Plans

Acceptable

Budget and Period of Support

Recommend as Requested

CRITIQUE 2

Fellowship Applicant:	2
Sponsor:	2
Research Training Plan:	1
Training Potential/Developmental Plan:	5
Institutional Environment & Commitment to Training:	1

Overall Impact/Merit: The overarching goal of the applicant is to become an expert in translational neuroscience to facilitate cancer prevention. In this application, the applicant plans to pursue this goal by developing neurobiological indices that will help promote healthy eating during the F99 phase. In this phase, the applicant will develop skills to assess an intervention for craving reappraisal by applying advanced statistical techniques and longitudinal modeling, using fMRI data available through an ongoing randomized clinical trial (RCT) directed by the applicant's primary sponsor. She will evaluate changes in a neural signature that she developed. In the K00 phase, the applicant proposes to explore the relationship between resting state fMRI to examine trait-like features that may relate to the patterns of health behavior and more likely reflect a real-world process. The applicant is exceptionally well-prepared to perform neuro-translational research. Impressively, the applicant has defined the neural signature that she will use by applying a novel statistical approach that she developed. Preliminary data support the utility of the signature to differentiate the appraise condition. The F99 phase training provides the applicant with the opportunity to learn advanced statistical techniques and the opportunity to learn how to design, implement, and evaluate behavior change interventions in an RCT, applying a

translational neuroscience approach. The applicant presents well-formulated specific aims for the F99 and K99 phases, with well-defined milestones. The K00 phase complements the approach proposed in the F99 phase. The applicant has identified four potential institutions appropriate for the K99 phase. A moderate weaknesses in this application is that it does not directly address a cancer outcome. A weakness in the mentoring team is that it does not include a cancer investigator in behavioral sciences.

1. Fellowship Applicant

Strengths

- The applicant is currently a doctoral candidate in the Department of Psychology at the University of Oregon and has focused her studies on translation neuroscience with a focus on appetitive self-regulation. Her long-term goal is to become an independent investigator in cancer research to improve health behavior using neural and behavioral data. She also received a master's degree in psychology from Stockholm University.
- Her academic performance is outstanding and she is first-author on two peer-reviewed manuscripts related to her research goals.
- The candidate is notably well prepared for the proposed training having developed a promising neural signature with a novel statistical approach that she developed
- In this application, she has specified two years of work on her dissertation in the F99 phase and 4 years in K00 phase, which include further advanced statistical training, experience in the conduct of a research project involving data processing and analysis, manuscript preparation, professional development, and mentoring.
- The applicant's graduate training has prepared her for the F99 phase through relevant course work and experience with project management, data collection analysis.

Weaknesses

- The applicant does not specifically-address her training related to health behavior interventions.
- The applicant does not appear to be grounded in cancer research.

2. Sponsors, Collaborators, and Consultants

Strengths

- Dr. Berkman is the primary sponsor for the applicant dissertation work in the F99 phase and is exceptionally-qualified as the principal investigator of the parent grant from which the training data will be derived. He also has an excellent track-record in mentoring students.
- Dr. Mills will also advise the applicant in the area of advance statistical methods related to the longitudinal data analysis well-qualified.
- Collectively, the mentoring team offers expertise in the analysis and interpretation of findings in translational neuroscience research.

Weaknesses

- A weakness is the mentoring team does not include a behavioral science in the field of cancer prevention research or else an expert population scientist in cancer research.

3. Research Training Plan

Strengths

- The dissertation addresses an important health behavior related to cancer risk, with the ultimate goal to reduce obesity through behavioral interventions, taking a novel neuroscience and neuroimaging approach.
- Novel preliminary data generated by the applicant are presented that support her ability to conduct the research proposed.
- The scientific aim for both the F99 and K00 phases - Aim 1 - to address longitudinal data in a RCT study. The K00 phase is complementary by incorporating data from trait-like features and course-work in in health behavior change. Each are consistent with the applicant's research goals. Together, the applicant will be well-prepared for an independent career in cancer research.
- The applicant will receive data analysis skills and bioethics training through didactic training. Additional training relevant to the goals of the applicant with occur through working with mentors inducing experience in the design and conduct of a RCT. Other critical milestones include the development the neural signature.
- The applicant's dissertation is clearly distinct from that of the research of the primary sponsors and other mentors.

Weaknesses

- Although the research proposed is novel, it does not incorporate cancer as an outcome.

4. Training Potential

Strengths

- Structured and regular meetings are planned with each sponsor separately and together. This should optimize the communication and coordination with the training. The applicant will attend various laboratory meetings, discussion groups, and conferences relevant to the dissertation research.
- The training plan for the F99 phase is well-designed by including the applicant with additional experience in data collection and data processing.
- The training plan includes milestones for both the F99 and K00 phases. A timeline for analysis completion, followed by manuscript preparation and publication is provided.
- The primary sponsor is appropriate and provides access to relevant data resources from her ongoing study. The research plan appears to be distinct from Dr. Berkman's primary goal as it is focused on development of a neural signature and testing whether it predicts behavior change.
- The applicant is clearly well-qualified to conduct and successfully complete the F99 phase. This is evident by her involvement in the management of the study funded by the sponsor's parent grant, where she has demonstrated the capability for developing and processing data relevant to her dissertation project.
- The process to identify an appropriate postdoctoral position is promising for making the transition to independence.

Weaknesses

- A foundation in cancer research is nor provided.

5. Institutional Environment & Commitment to Training

Strengths

- The environment at the University of Oregon's Department of Psychology appears to be exceptional in support the applicant's research and training. This is apparent with the

Developmental Cognitive Neuroscience suite at the University of Oregon, along with the expertise of the faculty that are well-matched with the training goals of the applicant.

- The doctoral program fosters an interdisciplinary approach.

Weaknesses

- None noted.

ADDITIONAL REVIEW CRITERIA

Protections for Human Subjects

Acceptable Risks and Adequate Protections

- Informed consent is obtained and there appears to be minimal risk involved for the participants. There is potential benefit in developing healthy eating habits.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Unacceptable

- This is not clearly stated in the current application but may have been described in the parent grant.

Inclusion Plans

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Not applicable
- Inclusion/Exclusion Based on Age: Distribution justified scientifically
- The participants are aged 18-20 and are considered adults. The age reflects an appropriate time to intervene on eating habits to be most effective.

Vertebrate Animals

Not Applicable (No Vertebrate Animals)

Biohazards

Not Applicable (No Biohazards)

ADDITIONAL REVIEW CONSIDERATIONS

Training in the Responsible Conduct of Research

Acceptable

Comments on Format (Required):

- The applicant has completed online CITI Training and ethics training within her department in the form of a course. Future training will be through updates of the CITI training and an NIH ethics course as well as discussion with the primary sponsor.

Comments on Subject Matter (Required):

- The training includes ethics training. as well as data sharing responsibilities.

Comments on Faculty Participation (Required):

- The primary sponsor will participate in supervised discussions.

Comments on Duration (Required):

- Quarterly modules are followed by 45 minutes of discussion. Bi-weekly hour-long sessions where bioethics is discussed The applicant will also lead discussion that will be approximately 3 hours in preparation and presentation combined.

Comments on Frequency (Required):

- Quarterly training modules and bi-weekly meetings.

Applications from Foreign Organizations

Not Applicable

Select Agents

Not Applicable (No Select Agents)

Resource Sharing Plans

Unacceptable

- Not included

Budget and Period of Support

Recommend as Requested

CRITIQUE 3

Fellowship Applicant:	5
Sponsor:	5
Research Training Plan:	5
Training Potential/Developmental Plan:	5
Institutional Environment & Commitment to Training:	5

Overall Impact/Merit: Ms. Danielle Cosme's research project is "A multi-method translational neuroscience approach to cancer prevention and health behavior change". Ms. Cosme is an extremely well-trained statistician and coding expert and has considerable expertise in functional MRI/neural signatures. However, her background and research to cancer prevention is substantially distant because of the expectation that her research could determine cancer causation. Both the research training plan and her training potential, while strong in measurement, is flawed in terms of their relationship to cancer. Likewise, expecting human subjects to make 11-13 visits to participate in this research seem overly optimistic, without the assurance that this is realistic. Her research also neglects to consider pregnancy as a condition when weight gain is expected.

1. Fellowship Applicant

Strengths

- Danielle Cosme is a Ph.D. student, with advanced statistical and coding skills. She has worked as a laboratory manager and is very skilled in the use of functional MRI.
- She assisted Dr. Pfeifer in writing a R21 that was funded.
- The applicant has published in neurodevelopment and eating behaviors.

Weaknesses

- The applicant does not have any training in cancer, e.g., no courses taken.

2. Sponsors, Collaborators, and Consultants

Strengths

- Dr. Berkman, the sponsor, is the Principal Investigator of a NCI-funded R01 research grant on devaluing energy-dense foods for cancer control: Translational neuroscience. Dr. Berkman and Ms. Cosme co-authored at least two papers together.
- Letters of reference are glowing.

Weaknesses

- Both the sponsor, Dr. Elliott Berkman and the co-sponsor, Dr. Kathryn Mills, are assistant professors. Dr. Mills is an early-stage investigator, having just been appointed assistant professor in 2018. Dr. Mills has no funded research. She lists pending research support from a R25 MH.
- If Ms. Cosme is working as a Ph.D. student in Dr. Pfeifer's laboratory, why is not Dr. Pfeifer not part of the F99 committee?

3. Research Training Plan

Strengths

- Ms. Cosme has extremely strong and sophisticated statistical skills.
- If successfully conducted, the research could result in detecting whether intervention-related behavior change occurs using neural signatures.
- The plan for her dissertation and post-doctoral experience is described clearly and demonstrates sophisticated emphasis on precision and mechanisms. It is consistent with her stage of research development.
- The plan is sufficiently distinct from her sponsor's.
- The applicant has considered alternatives if the primary plan is not workable.
- The applicant has identified at least four sites that could provide her with an appropriate place for fellowship training.

Weaknesses

- Despite the potential of measuring whether intervention-related behavior change, e.g., eating behavior, occurs, the neural signatures will not predict whether cancer is averted.
- There are no linkages or interactions with the OHSU or any NCI cancer center during Ms. Cosme's training during either the F99 or the K00 phases.
- It is unclear what the dependent variable for how the intervention will be evaluated beyond changing eating behavior.
- Alcohol or tobacco consumption or physical activity are behaviors and not "cancer-relevant outcomes". Thus, the time frame is not sufficient if cancer is a detectable outcome.

- The dissertation research project is flawed. Cancer requires a long time to develop and even so, there could be many confounders as to its etiology. The applicant has not presented a time-line to predict when cancer could occur within the life-span of a dissertation, at least not for a two-year time period.
- Participants will need to make 11-13 visits as part of the dissertation research. It is unclear how realistic this will be.
- There do not appear to be attention to whether women who are pregnant and need to gain weight are eligible for the study.
- Food-related cancers are not defined.

4. Training Potential

Strengths

- The program may provide the applicant with adequate experience in statistical and coding as it applies to functional MRI.

Weaknesses

- However, relevance to cancer is conspicuously-missing, with no expertise from cancer experts in her dissertation committee.
- As a result, the training will not lead to cancer-relevance and the dependent variables are not directly linked to cancer.

5. Institutional Environment & Commitment to Training

Strengths

- The University of Oregon has considerable facilities in neuroimaging and neuroscience, especially the Center for Translational Neuroscience.

Weaknesses

- Conspicuously missing in the list of the facilities and other resources is mention of the NCI designated cancer center that will be called upon as a resource in Oregon.

ADDITIONAL REVIEW CRITERIA

Protections for Human Subjects

Unacceptable Risks and/or Inadequate Protections

- No special exclusions are listed for pregnant women.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Not Applicable (No Clinical Trials)

Inclusion Plans

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution not justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Not applicable
- Inclusion/Exclusion Based on Age: Distribution justified scientifically

- The race/ethnicity is based on recruiting from Eugene, OR and will not be representative of the nation.

Vertebrate Animals

Not Applicable (No Vertebrate Animals)

Biohazards

Not Applicable (No Biohazards)

ADDITIONAL REVIEW CONSIDERATIONS

Training in the Responsible Conduct of Research

Unacceptable

Comments on Format (Required):

- The format includes both online and in person.

Comments on Subject Matter (Required):

- Whether the required subject matter is included is unclear.

Comments on Faculty Participation (Required):

- Faculty participation in the F99 period is exemplified by Dr. Berkman leading meetings on ethnical issues.

Comments on Duration (Required):

- Duration proposed is unclear.

Comments on Frequency (Required):

- Frequency is unclear.

Applications from Foreign Organizations

Not Applicable

Select Agents

Not Applicable (No Select Agents)

Resource Sharing Plans

Unacceptable

- This reviewer could not find the Resources Sharing Plan.

Budget and Period of Support

Recommend as Requested

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: ACCEPTABLE

INCLUSION OF WOMEN PLAN: ACCEPTABLE

INCLUSION OF MINORITIES PLAN: ACCEPTABLE

INCLUSION ACROSS THE LIFESPAN PLAN: ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Footnotes for 1 F99 CA245811-01; PI Name: Cosme, Danielle

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-14-074 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-074.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.