BIOGRAPHICAL SKETCH

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NAME: Mackey, Sean, MD, PhD

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

POSITION TITLE: Redlich Professor of Anesthesiology & Pain Medicine; Neurosciences; and Neurology; Chief, Division of Pain Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pennsylvania, Philadelphia, PA	BSE	05/1986	Bioengineering
University of Pennsylvania, Philadelphia, PA	MS	12/1986	Bioengineering
University of Arizona, Tucson, AZ	PhD	12/1994	Electrical Engineering
University of Arizona, Tucson, AZ	MD	05/1994	Medicine
Stanford University Medical Center, Stanford, CA	Residency	07/1998	Anesthesiology, Perioperative & Pain Medicine
Stanford University Medical Center, Stanford, CA	Fellowship	07/1999	Pain Medicine

A. Personal Statement

By way of introduction, I am the Chief for the Stanford Division of Pain Medicine. I also oversee the research mission as the Director of the Stanford Systems Neuroscience and Pain Lab (our Pain Division's research group). I have a broad background in engineering, pain medicine, neuroimaging, outcomes and clinical neuroscience. I am PI on several NIH grants (two R01s, K24 and T32) and Co-I on two other R01s. I currently have an NIH K24 award, which provides with me with sufficient time and resources to provide mentoring for junior investigators. I also have an NIH T32 for postdoctoral trainees and a formal system in place to guide mentoring and evaluation. Finally, I hold two research endowments that provide the discretionary monies to help support trainees for novel spinoff projects that may come out of the project in this grant.

I currently serve as a primary mentor for several current recipients of NIH career development K awards at Stanford (Dr. Kenneth Weber [K23]; Dr. Maisa Ziadni [K23]; Dr. JT Kong [K23]; Dr. Eric Sun [K08]), Dr. Lola Falasinnu [K01]; Dr. Behnaz Jarrahi [K25]), primary mentor for several T32 awardees and have recently transitioned several of my mentees from a K99/R00 or K23 to tenured faculty positions and R level funding (Dr. J Younger, Dr. K Martucci, Dr. J. Hah). I have also mentored over 100 junior clinicians (including anesthesiologists, pain medicine physicians, neurologists, physiatrists, and psychologists). I will provide trainees with important advice on grantsmanship, research innovation, and development as a future leader and mentor research areas of interest. I have a documented track record in performing productive research, mentorship grants management, and am well positioned to provide valuable mentorship for trainees.

Ongoing and recently completed projects that I would like to highlight include:

R01NS133305 PI: Weber, Co-I: Mackey **07/2023-06/2028**

Dermatomal Mapping with Spinal Cord Functional Magnetic Resonance Imaging

To use spinal cord functional magnetic resonance imaging (fMRI) to test hypotheses central to dermatomal maps, advance our knowledge of spinal cord sensory processing in healthy and injured states, and provide preliminary validation of diagnostic markers for radiculopathy while improving our spinal cord fMRI methods.

R01NS128478 PI: Weber, Co-I: Mackey **05/2023-01/2028**

MRI-Derived Neuromuscular Signatures to Predict Surgical Response in Degenerative Cervical Myelopathy
To use simultaneous brain-spinal cord functional MRI with hand motor tasks and forearm muscle MRI to characterize the mechanisms of hand dysfunction in degenerative cervical myelopathy and then develop neuromuscular signatures of hand function that predict surgical outcomes in degenerative cervical myelopathy.

PCORI # PCS-2021C1-22347 PI: Beth Darnall, Co-I: Mackey **04/2022-03/2027**
Comparative Effectiveness of Online Cognitive Behavioral Therapy vs. an Online Single-Session Pain Relief Skills Class for Chronic Pain
To create a 6-site, national, pragmatic, randomized comparative effectiveness trial of two evidence-based and online-delivered behavioral treatments for chronic pain.

R61/R33 NS118651 PI: Mackey **09/2020-08/2025**
Prognostic biomarkers for high-impact chronic pain: Development and Validation
To discover and validate biomarker signatures for high-impact musculoskeletal chronic pain.

K24 NS126781 PI: Mackey **09/2021-08/2024**
Mentoring in Discovery and Validation of Clinical Chronic Pain Biomarkers
To provide support for mentoring junior investigators in patient oriented chronic pain biomarkers

1U24AR076730-01 PI: Mackey **10/2021-05/2024**
Back Pain Consortium (BACPAC) Research Program Data Integration, Algorithm Development and Operations Management Center (Operational)
To inform a precision medicine approach to the treatment of chronic low-back pain (cLBP) using a multi-site, sequential, multiple assignment randomized trial (SMART) to evaluate four evidence-based interventions.

PCORI #1610-37007 PI: Beth Darnall, Co-I: Mackey **02/2018-01/2024 (NCE)**
Comparative Effectiveness of Pain Cognitive Behavioral Therapy and Chronic Pain Self-Management within the Context of Opioid Reduction
Implement a multistate comparative effectiveness trial to assess impact of behavioral therapies on voluntary opioid weaning

2U01FD005978-06 UCSF-Stanford CERSI PI: Mackey **09/2021-08/2024 (NCE)**
UCSF-Stanford Center of Excellence in Regulatory Science and Innovation (FDA)
Grant Award #63 *Development, Implementation, and Evaluation of an Open Source Software Program to Support Patient-based Estimation of Clinically Meaningful Levels and Change Scores for Patient Reported Outcome Measures*.

R01 NS109450 Multi-PI: Sean Mackey (Contact), Gary Glover **09/2018-08/2024 (NCE)**
Characterization of central pain mechanisms using simultaneous spinal cord-brain functional imaging
To characterize brain, brain stem and spinal cord contributions of ascending facilitation and descending modulation in acute and chronic pain using neuroimaging of the entire central nervous system

2U01FD005978-06 UCSF-Stanford CERSI PI: Mackey **09/2019-08/2024 (NCE)**
UCSF-Stanford Center of Excellence in Regulatory Science and Innovation (FDA)
Grant Award #40 *Characterizing Risk-Benefit Tradeoff in Opioid-based Chronic Pain Treatment*
To help patients, clinicians, and regulators understand how patients assess the tradeoff between benefits and risks in making the best choices for opioid use in chronic pain.

R01 DA 045027 Co-I: Sean Mackey; PI: Jennifer Hah **08/2018-07/2024 (NCE)**
Psychological Risk Factors for Persistent Opioid Use and Prevention of Chronic Opioid Use and Misuse After Surgery: Postoperative Motivational Interviewing and Guided Opioid Weaning
To test a novel intervention to reduce postoperative opioid use and characterize psychological risk factors for persistent use of opioids following surgery

T32 DA035165 PD: Mackey **07/2013-06/2024**
Interdisciplinary Research Training in Pain and Substance Use Disorders
Postdoctoral training program in pain and/or substance use disorders research

Chris Redlich Professorship in Pain Research **09/2009 – Forever**
This endowment supports pain medicine research efforts.

Dodie and John Rosekrans Pain Research Endowment Fund **2001 – Forever**
This endowment supports pain medicine research efforts.

R01AT008561 Multi-PIs: Mackey and Darnall **09/2015-05/2023 (NCE)**

Single Session Pain Catastrophizing Treatment: Comparative Effectiveness & Mechanisms
Develop and validate a short daily pain catastrophizing measure and compare effectiveness of a brief, single-session pain catastrophizing treatment against an 8-session CBT class.

R01 HD082200 PI: Beth Darnall, Co-Investigator: Sean Mackey 09/2015-03/2022
Maternal Chronic Pain: Risk for Pain and Poor Outcomes in Children
This longitudinal, multi-site study is examining the intergenerational transmission of chronic pain in high-risk children of mothers with current chronic pain.

K24 DA029262 PI: Mackey 03/2015-04/2021
Neuroimaging and Mentoring in Translational Pain Research
To provide support for mentoring junior investigators in patient oriented pain research

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019-2020 Vice-Chair, National Academy of Medicine Committee on Temporomandibular Dysfunction Pain
2015-2017 Clinic Chief (Interim), Stanford Pain Management Center, Stanford Univ. Medical Center, Stanford, CA
2015-2016 Past-President, American Academy of Pain Medicine
2014-2016 NIH Healthy People 2020 Chronic Pain Workgroup
2014-2015 Immediate President, American Academy of Pain Medicine
2013- Committee Member, National Comprehensive Cancer Network, Adult Cancer Pain
2012- Redlich Professor, Anesthesiology & Pain Medicine, Neurosciences and (by courtesy) Neurology, Stanford Univ. Medical Center, Stanford, CA
2012-2016 Co-Chair, NIH Oversight Committee of the National Pain Strategy Task Force
2012-2013 Committee Member, NIH Pain Consortium Chronic Low Back Pain Research Task Force
2012-2016 Co-Chair, NIH Prevention and Care Working Group for the National Pain Strategy Task Force
2011-2013 Committee Member, NIH Interagency Pain Research Coordinating Committee
2008-2012, 2016 National Institute on Drug Abuse, Career Award Scientific Review Committee
2007-2019 Program Director, Clinical Pain Medicine Fellowship Program, Stanford University, Stanford, CA
2007-2012 Associate Professor. Anesthesiology, Perioperative and Pain Medicine, Neurosciences and (by courtesy) Neurology, Stanford Univ. Medical Center, Stanford, CA
2007- Chief – Division of Pain Medicine, Stanford University Dep. Anesth., Stanford, CA
2004-2007 Associate Director – Pain Medicine Division, Stanford University Dep. Anesth., Stanford, CA
2002- Director, Stanford Systems Neuroscience and Pain Lab
2000-2006 Founder and Director - Regional Anesthesia Services, Stanford Dep. of Anesthesiology
1999-2007 Asst. Prof. Anesthesia & Pain Management, Stanford University Medical Center, Stanford, CA
1998-1999 Fellow, Pain Management, Stanford University Medical Center, Stanford, CA
1997-1998 Chief Resident, Anesthesia, Stanford University Medical Center, Stanford, CA
1996-1998 Resident, Anesthesia, Stanford University Medical Center, Stanford, CA

Honors

2020 American Academy of Pain Medicine, Robert G. Addison, MD Award
2019 American Academy of Pain Medicine, Presidential Commendation
2017 American Academy of Pain Medicine, Distinguished Service Award
2016 American Pain Society Fordyce Award
2015 NIH Director's Award
2012 Top 1% Pain Medicine Physicians in America, US News & World Report Guide to Top Doctors
2012 American Academy of Pain Medicine, Presidential Commendation
2010 Ellis Cohen Achievement Award, Stanford Department of Anesthesia
2008, 2012 American Pain Society Clinical Center of Excellence Award
2002, 2004-2016 Top Doctors in America published in "Guide to Top Doctors"
1994 Eta Kappa Nu Electrical Engineering Honor Society

C. Contributions to Science (from over 200 peer-reviewed publications)

1. Collaborative Health Outcomes Information Registry (CHOIR) and Big Data for Pain and Opioids: My research and personal mission has been to use high-quality data from the real-world patients we care for to inform our clinical assessments and tailor treatments. For 20 years I sought different approaches to optimize capture of quality data in clinical settings. After many failures, I developed an open source, open platform, learning health system (LHS) in 2012 called CHOIR. CHOIR is designed to provide a deep phenotype of every patient coming to a clinical encounter across multiple domains of physical, psychological and social functioning. It serves as a platform for point of care decision making, longitudinal patient tracking, comparative effectiveness research and large simple trial designs. We have characterized over 50K unique patients and over 200K longitudinal samples. We have disseminated CHOIR beyond Stanford to other clinical specialties (Pediatrics, Surgery, Chronic Fatigue, Family Medicine, Gastrointestinal Medicine, Psychiatry, and others) and academic institutions nationally and internationally (Canada and Israel).

a. Bhandari, R. P., Feinstein, A.B., Huestis, S.E., Krane, E.J., Cohen, L.L., Kao, M.C., Darnall, B.D., **Mackey, S.** Pediatric-Collaborative Health Outcomes Information Registry (Peds-CHOIR): a learning health system to guide pediatric pain research and treatment. *Pain* 2016;157(9): 2033-2044. PMCID: PMC4988911
b. Harle, C., Listhaus, A.,…**Mackey, S**., Carek, P., Fillingim, R., Hurley, R. Overcoming barriers to implementing patient-reported outcomes in an electronic health record: a case report. *Journal of the American Medical Informatics Assc*. 2015:ocv085. DOI: 10.1093/jamia/ocv085. PMCID: PMC5009936
c. Hoang, N., Hwang, W., Katz, D., **Mackey, S**., Hofmann, L. Electronic Patient-Reported Outcomes: Semi-Automated Data Collection in the Interventional Radiology Clinic. *Journal of the American College of Radiology.* October 2018. ISSN 1546-1440, DOI: 10.1016/j.jacr.2018.08.033. PMID: 30297246
d. Rosenberg, G., Shearer, E., Zion, S., **Mackey, S**., Spain, D., Weiser, T. Implementation Challenges Using a Novel Method for Collecting Patient-Reported Outcomes After Injury. *Journal of Surgical Research*. 2019 Sep, Volume 241, Pgs. 277-284. doi.org/10.1016/j.jss.2019.04.008. PMID: 31042606

2. Novel Insights from Real-World Patients using CHOIR as a Learning Health Systems (LHS): LHS leverages an integrated digital infrastructure to provide data-based and coordinated care that is available just-in-time to the clinician and that is centered on the patient. Additionally, there is increasing interest in the use of real-world data/real world evidence (RWD/RWE) to represent a much broader and more diverse patient experience compared to the traditional RCTs. I have enabled CHOIR as a platform for gaining insights from large numbers of real-world patients Further, expansion of RWD/RWE allows for very large sample sizes that promote the detection of infrequent events, treatment-treatment interactions, and better account for heterogeneity of treatment effects. LHSs are critical to advancing RWD/RWE to inform patient care and to advance more generalizable knowledge. Finally, we have used this RWD/RWE to gather unique insights on modifiable factors mediating our patients' magnitude, burden and persistence of chronic pain, opioid and cannabis use. These insights serve as targets to develop future treatments for pain.

a. Sturgeon, J. A., Darnall, B. D., Kao, M. C., **Mackey, S. C**. (2015). Physical and psychological correlates of fatigue and physical function: a Collaborative Health Outcomes Information Registry (CHOIR) study. *J Pain, 16*(3), 291-298 e291. doi:10.1016/j.jpain.2014.12.004. PMCID: PMC4352393
b. Sturgeon, J., Khan, J., Hah, J., Hilmoe, H., Hong, J., Ware, M., **Mackey, S**. Clinical Profiles of Concurrent Cannabis Use in Chronic Pain: A CHOIR Study. *Pain Medicine.* 2020 March 31, doi: 10.1093/pm/pnaa060. PMCID: PMC685692
c. Khan, J., Hah, J., **Mackey, S**. Effects of smoking on patients with chronic pain: a propensity-weighted analysis on the Collaborative Health Outcomes Information Registry. *Pain.* 2019 Oct, 160(10): 2374-2379. Doi: 10.1097/j.pain.0000000000001631. PMCID: PMC6768701
d. Hah, J.M., Sturgeon, J.A., Zocca, J., Sharifzadeh, Y., **Mackey, S.C**. Factors associated with prescription opioid misuse in a cross-sectional cohort of patients with chronic non-cancer pain. *J Pain Res*. 2017 10:979-987. doi: 10.2147/JPR.S131979. PMCID: PMC5422534

3. Using Real-World Data from LHSs (CHOIR) for Rapid Prototyping: CHOIR is a flexible platform allowing rapid data capture from large numbers of real-world patients. We have used this approach to generate pilot data for subsequent grant submissions (e.g. Sharifzadeh et al, using CHOIR to rapidly test Dr. Darnall's single-session intervention to generate pilot data for our current NIH R01). We also use this rapid, iterative approach to test treatment effectiveness in real-world patients, validation of patient-reported outcomes in specific clinical settings and identify targets for subsequent treatment interventions (e.g. catastrophizing, social functioning, self-efficacy).

a. Darnall, B., Sturgeon, J., Kao, M., Hah, J., **Mackey, S.** From Catastrophizing to Recovery: a pilot study of a single-session treatment for pain catastrophizing. *J of pain research*. 2014; 7:219. PMCID: PMC4008292
b. Barad, M., Sturgeon, J., Fish, S., Dexter, F., **Mackey, S**., Flood, P. "Response to BotulinumtoxinA in a Migraine Cohort with Multiple Comorbidities and Widespread Pain". *Regional Anesthesia & Pain Medicine.* 2019 Jun;44(6):660-668. doi: 10.1136/rapm-2018-100196. PMCID: PMC8541790
c. You, D., Hah, J., Collins, S., Ziadni, M., Domingue, B., Cook, K., **Mackey, S**. Evaluation of the Preliminary Validity of Misuse of Prescription Pain Medication Items from the Patient-Reported Outcomes Measurement Information System (PROMIS)® 11 March 2019. Pgs. 1925-1933, doi.org/10.1093/pm/pnz001. PMCID: PMC6784744
d. Karayannis, N.V., Baumann, I., Sturgeon, **Mackey, S.C**. The Impact of Social Isolation on Pain Interference: A Longitudinal Study. *Ann Behav Med*. 2018 Apr 12. PMCID: PMC6301311

4. National Pain Policy Work: I have been active in national leadership to help guide and shape our approach to pain. My efforts started with membership on the Institute of Medicine committee that published the *Relieving Pain in America* report. The IOM report presented a high-level blueprint of the state of our country's assessment and care of those in pain. I then Co-Chaired the HHS/NIH *National Pain Strategy* which served as a strategic action plan building off the recommendations from the IOM Pain Report. In both these efforts, we called for the improvement in the collection of quality data for pain prevalence, burden, treatment effects and costs in real-world patients. I have since been President of the American Academy of Pain Medicine which has also set improvement in quality data collection as one of its missions. Finally, I was Vice-Chair of a recent National Academy of Medicine Committee on Temporomandibular Disorders which also called for the need for national efforts to collect high-quality pain data. All of these leadership efforts align with my research efforts and are addressed in our current proposal.

a. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington (DC): National Academies Press (US); 2011. PMID: 22553896
b. **Mackey, S.** *et al.*, "National Pain Strategy: A Comprehensive Population Health Level Strategy for Pain," (National Institute of Health, Bethesda, MD, 2011).
c. **Mackey, S**., Kao, M. Managing twin crises in chronic pain and prescription opioids. BMJ. 06 March 2019 364: l917. doi: 10.1136/bmj.l917. PMID: 30842099
d. Dahlhamer, J., Lucas, **Mackey, S**., DeBar, L., Kerns, R., Von Korff, M., Porter, L., Helmick, C. Prevalence of Chronic Pain and High-Impact Pain Among Adults – United States, 2016. *Morbidity and Mortality Weekly Report.* Sept 14, 2018, doi:10.15585/mmwr.mm6736a2. PMCID: PMC6146950

5. Brain Neuroimaging of Pain and Development of Brain Based Biomarkers of Pain: I have made significant contributions to our understanding that chronic pain can become its own disease, not just a symptom of another condition. Central neuroimaging has advanced our appreciation that pain is a subjective experience involving the brain. Our work in the following areas has shaped these advances: characterizing the neural correlates of the individual differences in pain perception due to fear, anxiety and catastrophizing; empathy of pain; cortical plasticity due to chronic pain, abnormal neuroplasticity due to chronic opioid use, and the intersection of reward and analgesic systems. Recently, my work has been focused on translating spinal cord and brain neuroimaging from a tool used to characterize spinal cord/brain systems related to pain, to that of a true diagnostic/prognostic/predictive biomarker for acute and chronic pain.

a. Martucci, K. T., Shirer, W.R.,…**Mackey, S**. The Posterior Medial Cortex in Urologic Chronic Pelvic Pain Syndrome: Detachment from Default Mode Network. A Resting-State Study from the MAPP Research Network. *Pain*. 2015; 156(9):1755-64. PMCID: PMC4545714
b. Martucci, K., MacNiven, K., Borg, N., Knutson, B., **Mackey, S**. Apparent Effects of Opioid Use on Neural Responses to Reward in Chronic Pain. *Scientific Report* 2019 9(1) 9633. PMCID: PMC6610070
c. **Mackey, S.**, Greely, H., Martucci, K. Neuroimaging-Based Pain Biomarkers: Definitions, Clinical and Research Applications, and Evaluation Frameworks to Achieve Personalized Pain Medicine. *PAIN Reports.* July/August 2019. PMCID: PMC6727999
d. Ung, H., Brown, J., Johnson, K., Younger, J., Hush, J., **Mackey, S**. Multivariate classification of structural MRI data detects chronic low back pain. *Cereb Cortex* 2012 24(4):1037-1044. PMCID: PMC3948494

Complete List of Published Work in MyBibliography: here