# UCSF Awarded $12M Research Grant to Improve Cancer Outcomes

SPORE Grant from National Cancer Institute provides resources for translational research into genomic, biochemical, and environmental drivers of cancers outcomes.

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The UCSF Helen Diller Family Comprehensive Cancer Center announced today the awarding of a Specialized Programs of Research Excellence (SPORE) grant by the National Cancer Institute (NCI) for a combined program focused on cancer outcomes. The program will receive $12 million over five years to improve cancer health outcomes across populations by investigating the interplay of tumor biology with individual risk factors and external drivers of health.

The SPORE grant supports three translational research projects that focus on three types of cancer with well-known differences in clinical outcomes: meningioma (a type of brain tumor), prostate cancer, and breast cancer.

The cancer outcomes SPORE grant is co-led by Susan M. Chang, MD, neuro-oncologist and UCSF professor-in-residence in the UCSF Division of Neuro-Oncology in the Department of Neurological Surgery, a principal investigator in the Brain Tumor Center, and co-leader of the UCSF Neurologic Oncology Program in the Helen Diller Family Comprehensive Cancer Center; and Franklin W. Huang, MD, PhD, a medical oncologist and associate professor in the Division of Hematology and Oncology, principal investigator of the SFVA/UCSF Precision Oncology Center of Excellence, and a Chan Zuckerberg Biohub Investigator.

“The infrastructure for our SPORE grant is designed to leverage the expertise and resources at the cancer center to encourage and promote translation of innovative, impactful ideas,” said Chang. “We also aim to sponsor interdisciplinary collaborations and provide an effective framework for mentoring and nurturing the next generation of investigators with an interest in improving cancer outcomes across populations.”

## Hard-to-treat brain tumors

One research project will investigate the genomic and biochemical mechanisms underlying differences in meningioma outcomes. Many high-grade meningiomas (grades 2 and 3) are resistant to currently available treatments and have higher recurrence rates in some patient

populations. This project aims to establish the generalizability of DNA methylation and gene expression biomarkers for managing disease across patient populations.

Led by David Raleigh, MD, PhD, a radiation oncologist and the Robert and Ruth Halperin Endowed Chair in Meningioma Research at UCSF, and Nancy Ann Oberheim Bush, MD, PhD, a neuro-oncologist and the Wendy Olson Wood-Smith Endowed Professor in the Departments of Neurology and Neurological Surgery, this project will define the molecular architecture of meningiomas across external drivers and personal risk factors; identify the role that a progesterone receptor protein (PGRMC1) plays in driving meningioma growth; and develop new therapies to block PGRMC1. The project also leverages collaborations with investigators from the University of Alabama at Birmingham, Northwestern University, Duke University, and Baylor College of Medicine.

## A better way to predict prostate cancer outcomes

Another research project will examine interactions between genetic and environmental drivers of prostate cancer outcomes. Some patient populations face a higher burden of more aggressive, deadly prostate cancer. The project focuses on the interactions between stress, inflammation, and immune pathways within the tumor microenvironment and how both genetic and environmental factors contribute to these differences in patient outcomes.

This project, led by Huang and Matthew Cooperberg, MD, MPH, the Helen Diller Family Chair in Urology and co-leader of the UCSF Prostate Cancer Program, will identify how adverse external factors drive differences in immune activation and the development of more aggressive types of prostate cancer; create a comprehensive molecular atlas that maps the immune cell profiles in prostate cancer across populations; and develop machine-learning models to predict which men are at the highest risk for aggressive prostate cancer. UCSF co-investigators include Li Zhang, PhD, William Chen, MD, Stacy Kenfield, ScD, and David Quigley, PhD, who will also collaborate with investigators from Boston University.

## How our genes influence our immune system response to cancer

The third project seeks to understand the drivers of response-predictive inflammatory states underlying differences in health outcomes in patients with breast cancer. The tumor immune microenvironment influences patient outcomes for many tumors, including breast cancer. Many features of the tumor immune microenvironment vary across different populations. This project studies how genomic variants and combinations of variants — called polygenic risk scores — affect the tumor immune microenvironment and contribute to differences in treatment response.

This project, led by Jennifer Rosenbluth, MD, PhD, and Elad Ziv, MD, with co-investigators Kimberly Badal, PhD, and Rosalyn Sayaman, PhD, and colleagues at City of Hope, will identify the specific tumor immune microenvironment pathways by which inherited genetic factors affect response to targeted treatments, chemotherapy agents, and immunotherapies. It will also examine whether

differences in exposure to adverse external factors across patient populations influence the tumor immune microenvironment and predict breast cancer recurrence and treatment response.

“By bringing together a diverse and multi-disciplinary group of investigators, this cancer outcomes SPORE will accelerate highly impactful translational research with the potential to significantly improve clinical outcomes for meningioma, prostate cancer, and breast cancer treatment,” said Huang.

In addition to the research projects, an administrative core led by Chang, Huang, and Raleigh will supervise the activities of the program. A biospecimen/pathology core led by Joanna Phillips, MD, PhD, with co-directors C.K. Cornelia Ding, MD, PhD, and Alexander Borowsky, MD, (of UC Davis), and a community outreach/engagement core directed by Samuel Washington, MD, and Scarlett Lin Gomez, PhD, MPH, provide specialized expertise in service of the main research projects. The Career Enhancement Program, managed by Shawn Hervey-Jumper, MD, provides support for early career investigators, and the Developmental Research Program, managed by Iona Cheng, PhD, MPH, supports innovative high-risk, high-reward pilot projects. A multidisciplinary team of internal and external scientific advisors, patient advocates, and the members of the Community Advisory Board provide overall guidance on the direction of the SPORE grant.

The NCI established the Specialized Programs of Research Excellence (SPORE) in 1992 to promote interdisciplinary, translational research focused on cancers of specific organs or on groups of highly related cancers. To be awarded an NCI SPORE grant, investigators must have a track record of peer-reviewed research studies that include moving translational studies to human clinical trials to promote interdisciplinary, translational research focused on cancers of specific organs or on groups of highly related cancers.

In addition to the cancer outcomes SPORE, UCSF has SPORE grants in prostate cancer, brain tumors, and pediatric malignancies.

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