

D

DETAILS

N

NEWS

A

AWARDS

VOLUME XVI Fall 2022

## Focus on Research

### When Good Bacteria Go Astray

We've all heard about good bacteria and bad bacteria. In some cases, good bacteria leave their natural environment and enter a place where they can do damage, even though they are just trying to survive.

Barbara Bensing, PhD, an NCIRE-supported investigator, studies how sugar linkages (O-glycan structures) on human proteins help determine whether, and where, bacteria can attach, survive, and thrive in their human hosts.

Bensing studies a variety of streptococcus bacteria that normally reside in the mouth, a habitat for trillions of bacteria of over 700 species. Most are helpful or harmless bacteria and able to surmount the bad and potentially harmful bacteria.

Ideally, balance and harmony would rule this biological community. Good bacteria would do their job, including warding off invading pathogens and keeping our immune system finely tuned.

“But there are instances when good bacteria get into the wrong environment, and then become accidental pathogens,” said Bensing, a UCSF Assistant Professor of Medicine and SFVAHCS Research Microbiologist. For example, streptococci that normally live in plaque, or on our teeth or gums, can routinely enter the bloodstream. In some cases, these bacteria can take hold in a new anatomical site before they can be cleared by the immune system.

In earlier work with Paul Sullam, MD, another NCIRE-supported scientist, and UCSF Professor of Medicine,



*Barbara Bensing, PhD*

*Assistant Professor, Department of Medicine, UCSF  
Research Microbiologist, Division of Infectious  
Diseases, SFVAHCS*

Bensing identified a family of proteins, “adhesins,” on the surface of streptococci that help the organisms bind to host surfaces. She found that the adhesins help the bacteria attach to O-glycan structures on human platelets and serum proteins that deposit on damaged heart valves. If the streptococci begin to grow in this new location, they can cause the rare but life-threatening condition known as infective endocarditis. This process may be an accidental consequence of how these bacteria

survive in their native habitat.

### O-glycan structures mediate colonization

Bensing continues to delve into the workings of streptococcus bacteria. Not only are they culprits in infective endocarditis, but the bacteria colonize teeth and gums, which may have implications for oral health. In studying the molecular biology of streptococci, she hopes to uncover how mucus-forming proteins in our saliva help promote a healthy consortium of microbes, including beneficial streptococci, and ward off those that cause cavities, tooth decay and gum disease.

Bensing's current research focuses on a sugar-modified protein in saliva – MUC7. Until now, the function of MUC7 has not been well defined. It is a lubricant and surfactant that coats the surfaces of teeth and gums. It likely has a protective role by helping clear out pathogens in the oral cavity, but Bensing wants to find out if MUC7 influences whether beneficial or harmful microbes will survive in the mouth. Her research project assesses if differences in MUC7 sugars, called O-glycans, affect the type of streptococcus bacteria that settle into teeth and gums.

In her study, Bensing is comparing O-glycan structures from saliva of people with periodontitis and age-matched healthy controls (see figure). Already she found that good, health-promoting MUC7 has bigger, branched sugar structures (5 or more monosaccharide units, or simpler sugar units), compared to disease-promoting MUC7, which has smaller sugar structures (only 2 or 3 monosaccharide units).

In the periodontitis saliva, Bensing is trying to determine whether decreased expression of some structures and increased expression of others may instigate a loss of protective microbes, and at the same time invite pathogens to stick around.

Bensing is also looking at periodontitis in mouse models of this disease to see if similar phenomena occur in vivo.

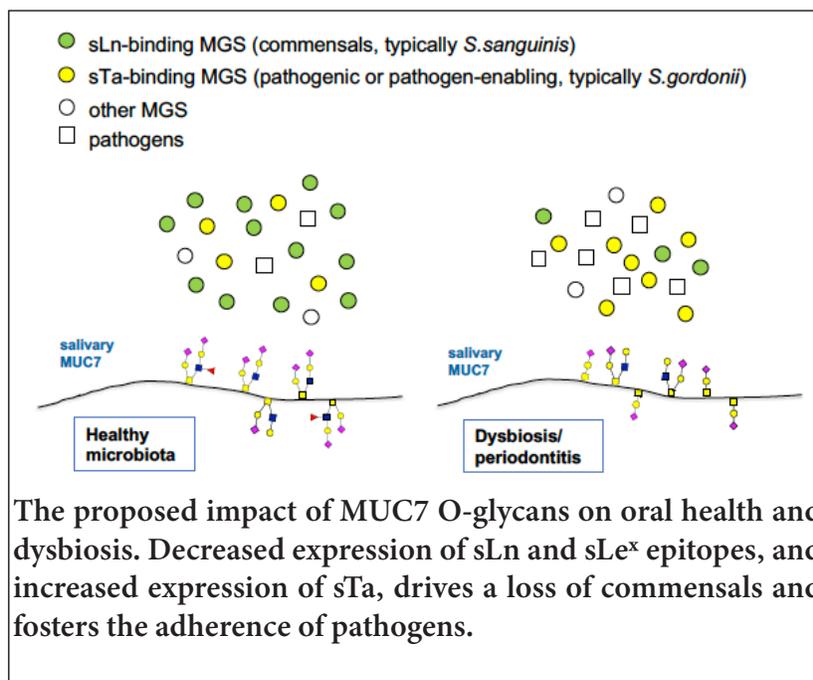
While her studies are focused on how certain MUC7 O-glycan structures play a role in harboring or promoting oral pathogens, the benefits of her investigative work reach far beyond oral health.

### Adhesins are useful tools

Bensing has been instrumental in developing an affordable and convenient toolkit for analyzing glycoproteins. The toolkit includes “glycan-binding probes,” based on streptococcal adhesins identified by Bensing, Sullam, and a team of collaborators.

Scientists who study a wide range of diseases, including cancer and arthritis, may use the tool kit to probe changes in glycoprotein structures in various human tissues, and microbial habitats such as the gut.

The world of microbes and bacteria is daunting, mysterious and forever-evolving, and basic scientists like Dr. Barbara Bensing are finding ways to delve into the inner workings for answers about disease and health.



## Q and A: An Interview with Dr. Jialing Liu



*Jialing Liu, PhD*

*Professor of Neurological Surgery, UCSF  
Principal Investigator, Brain and  
Spinal Injury Center (BASIC) and the  
Cerebrovascular Research Program,  
UCSF Weill Institute for Neuroscience  
Staff Scientist, SFVAHCS*

**Q: Your basic research looks at how the brain responds to ischemic stroke, hypoglycemia, and traumatic brain injury. How/why did you decide to study these issues?**

**A:** I began my research career studying how the brain responded to drugs and addiction. Although that was fascinating, I decided later to concentrate on neurological diseases and injuries, which are highly prevalent. My father died of traumatic brain injury (TBI), but I think my choice was driven more by interest rather than emotion. My research tilts a little more towards stroke and other neurological diseases than brain trauma. In fact – apart from stroke or cerebrovascular diseases – neurodegenerative diseases, such as Alzheimer’s and Parkinson’s, or depression would be equally

fascinating to me with respect to their etiologies.

**Q: How may your research eventually benefit Veterans health and the public in general?**

**A:** Stroke is a leading cause of death and disability worldwide. Risk factors for stroke, like diabetes and hypertension, affect our Veterans in rates similar to the general public. Hypoglycemic brain injury, linked to poor management of diabetes, is a big problem among Veterans, as it is in the general population. Brain trauma (other than accidents) uniquely affects war Veterans. Insight into the pathophysiology of stroke and brain injuries could lead to therapeutic interventions. Currently, there are only less than a handful of options to treat stroke, which are based on a collective effort of basic and clinical research.

**Q: Some 15 years ago, you made a key discovery that opened some new neuroscience research paths. What path did you take?**

**A:** In 1997-98, when I was still a postdoc here at the San Francisco VA Health Care System (SFVAHCS), I made a serendipitous finding that showed great therapeutic potential and have since opened many new areas for discovery. For a very long time, the dogma in neuroscience was that the brain could not regenerate, unlike many other organs. However, evidence of new neurons from neuroprogenitor cells – those cells

in the central nervous system that generate many neural cell types (including neurons, astroglia and oligodendrocytes) – began to pop up during the 1990s, mostly in research in rodents and birds.

While searching for evidence of stroke-induced DNA repair in the brain, I injected animals with an analog of thymidine, one of the four nucleotides of DNA. I detected an increase in cell proliferation at special locations of the brain after brain ischemia, which I later proved and characterized as neurogenesis.

Since our report in 1998, the field has blossomed into many important and exciting directions. I chose to remain focused on understanding the functional significance of endogenous neural regeneration after stroke or brain injury and how to augment this innate ability for repair and recovery.

**Q: What is your lab researching now?**

**A:** To effectively study the functional aspect of neurogenesis, my research group has invested resources in developing neurobehavioral tests to determine both motor and cognitive function of rodents with various brain injury models. Our expertise led to the establishment of the Neurobehavioral Core Facility at the SFVAHCS, which provides support for this type of neuroscience research.

*continued on page 4*

Recently, there have been new studies showing that the endogenous neurogenesis in humans occurs at a lower frequency and slows down at an earlier stage compared to rodents, suggesting that rodent and human brains develop on a very different time scale. The exact function of neurogenesis in adults remains unclear; however, at least in the rodents, it correlates with brain health and metabolic state.

**Q: You've homed in on one small region of the hippocampus. How does such a tiny area impact so many brain functions?**

**A:** Brain regions are interconnected and made up of so many networks. Anatomically separate brain regions work together, or network, when the brain performs a certain function, as revealed by shared neuronal activation patterns detected by functional MRI (fMRI).

For a long time, we have been searching for the mechanism through which the function of the hippocampus – a brain region crucial for memory formation but remote from the stroke epicenter – is affected by a stroke insult in the cerebral cortex. In mice models, we induced stroke injury in the cortex, while leaving the hippocampus intact, at least structurally. However, the animals suffered memory impairment when they underwent behavioral tests and showed signs of hippocampal hypoactivation when they explored a novel environment. They also exhibit changes in electrophysiology recordings, including a type of brain oscillation specific to the

hippocampus, called sharp wave associated ripples (SPW-R).

To our knowledge, our study was the first to report SPW-R changes after stroke. In collaboration with a German research group, we have mapped out the connectivity between the cortex and hippocampus and continue to use this connectome-based neuroinformatics (complete map of neural connections in the brain) to predict functional impairment in various stroke models based on neural networks and functional connectivity.

To that end, we are also establishing a white matter connectome (neural maps) based on diffusion tensor imaging (DTI), to be used in addition to the tract tracing connectome, which will provide further insight into the role of white matter damage in mediating cognitive function.

**Q: How do you “see” all of this? What technological tools are you developing to “see” even more?**

**A:** Over the years, I have ventured into technologies that can better determine the neurophysiology aspect of the brain. During the last decade, I have developed interest in vascular remodeling because I gradually began to appreciate the importance of “good plumbing” in brain health.

I decided to develop tools to measure blood flow in the realm of optical imaging because MRI does not offer sufficient spatial resolution for rodents.

Since 2012, we have collaborated with a group of engineers in Seattle to develop blood flow imaging modalities to determine how blood flow changes during the stroke. This collaboration resulted in novel discoveries made by my group that Type 2 diabetic mice exhibited impaired collateral flow after ischemic stroke, similarly to patients with metabolic syndrome. Our follow-up studies continue to develop imaging modalities to quantify penetrating arteriole blood flow and capillary transit time.

This will help us to better understand the role of vascular remodeling in vascular risk factors and the impact on functional recovery. Through years of planning and fund gathering, we have also developed imaging method and analysis algorithms using multiphoton microscopy with Dr. Michael Stryker at UCSF. Our research goal is to determine pial and capillary flow, as well as leukocyte-platelets aggregates, which may potentiate clot formation.

As the Scientific Director of Neurobehavioral Core at the SFVAHCS since the early 2000s, my group has pioneered in validating a number of behavioral tests, including the gait analysis and pasta consumption test; and we have refined the Barnes maze test to compare search strategy. Because of the limitation of behavioral tests, we have been searching for a functional test that is more specific to brain regions and lately have resorted to electrophysiology.

Our recent endeavor in in-vivo multichannel extracellular recording detected for the first time that ischemic stroke affected sharp-wave associated ripples, a brain oscillation specific to a region of the hippocampus, serving as an anatomic substrate for stroke induced hippocampal dysfunction. Compared to stroke with more focal injuries, we found that mice with Type 2 diabetes displayed

more diffused abnormality in neural synchrony and network communication in addition to impaired hippocampal network.

**Q: What would most people be surprised to know about you?**

**A:** Probably a few things. I was a competitive rifle shooter in my youth, winning medals for my accomplishments. I also rescued

six German shepherds in the last couple of years, since I like big/wild intelligent beasts. I am also fascinated by lions, and I sponsored Kevin Richardson's Foundation by purchasing habitat and raising awareness to create safe, natural spaces where lions and other native species can flourish. I also hope to someday work in Antarctica.

## In the Helix



Juanita Kalif

NCIRE Contracts & Grants Specialist III

**Q: What's your hidden talent?**

**A:** I spend many hours doing word and number puzzles such as Wordle and nonograms.

**Q: What's the first career you dreamed of having as a kid?**

**A:** As a kid, I dreamt of being an Avon Lady. I remember when the Avon Representative would come to my house and open her suitcase full of makeup samples for my mother to try out. It seemed to be a fun job, looking classy and going door-to-door to play with makeup. Hats off to all the Avon Representatives; I am a regular customer.

**Q: Have you ever completed anything on your "bucket list"?**

**A:** While I don't have a bucket list, I've done something that I've always wanted to do. In July, I went on my fourth whale watching boat tour and for the first time saw Orca whales. While traveling through the Salish Sea, near the San Juan Islands in Washington state, the T37 pod gave us a show. It was pretty spectacular.



Pamela Thropp

NCIRE Project Manager/Science Writer

**Q: What's your hidden talent?**

**A:** I can whip up scrumptious pies and cookies (so they tell me) on the fly. Our house was always the gathering place for our twin boys and all their friends. As they grew up, more and more would stay in the kitchen and "help."

**Q: What's the first career you dreamed of having as a kid?**

**A:** When I was a young girl, I dreamt of being a nurse, mainly because I enjoy helping others. My mom and her best friend grew up in small towns in Maine. And when they were old enough (in 1959), they got nursing jobs in California, drove out and never looked back. I thought that being a nurse could be helpful and adventurous.

**Q: Have you ever completed anything on your "bucket list"?**

**A:** Yes! I have gone scuba diving in some wild places!: I have descended into the Blue Hole, experienced night diving, and unintentionally swam with hammerheads.



Kasey Campos

NCIRE Staff Research Associate I

**Q: What's your hidden talent?**

**A:** My hidden talent is how fast I read! I usually read anywhere from 2-4 books a week! My favorite genre is Romance.

**Q: What's the first career you dreamed of having as a kid?**

**A:** Aside from wanting to be a princess, I've always wanted to be a doctor; and I am still planning on pursuing that dream in the coming years.

**Q: Have you ever completed anything on your "bucket list"?**

**A:** Yes! A few years ago, I went skydiving. I can't say that I'll ever do it again, but it was exhilarating!

If you or someone you know is an NCIRE employee and would like to be an In the Helix participant, please feel free to contact us at [dna@ncire.org](mailto:dna@ncire.org).

We'd love to hear from you!

# New Funding Awards

**Congratulations to the following Principal Investigators for your recent funding awards!**

**Rebecca Sudore, MD**

Project Title: Notice of Special Interest: Alzheimer's-Focused Administrative Supplements for NIH

Sponsor: NIH

Project Start Date: 6/15/2022

**Carolyn Gibson, PhD**

Project Title: Does the Co-use of Tobacco and Cannabis Increase the Risk of Earlier Age at Menopause?

Sponsor: University of California Office of the President

Project Start Date: 7/1/2022

**Michelle Estrella, MD**

Project Title: Kidney Biomarkers in Treatment for Acute Decompensated Heart Failure

Sponsor: NIH

Project Start Date: 7/1/2022

**Raymond Swanson, MD**

Project Title: Integrating Pathogenic Mechanisms in Parkinson's Disease - Supplement

Sponsor: NIH

Project Start Date: 7/1/2022

**Bruce Ovbiagele, MD, MSc, MAS, MBA, MLS**

Project Title: Stroke Minimization Through Additive Anti-atherosclerotic Agents in Routing Treatment II Study

Sponsor: NIH

Project Start Date: 9/1/2022

**Kristine Yaffe, MD**

Project Title: Military Risk Factors and Dementia in Veterans: The Impact of Race & Social Determinants of Health

Sponsor: DoD

Project Start Date: 9/1/2022

**Michael Weiner, MD**

Project Title: Alzheimer's Disease Neuroimaging Initiative (ADNI4)

Sponsor: NIH

Project Start Date: 9/14/2022

## Grant Funding Opportunities

### Industry Opportunities (as of 8/16/2022)

Please contact Newton Ong, [newton.ong@ncire.org](mailto:newton.ong@ncire.org) or at x23892, for further information on the following Industry Opportunities.

**PPD**

A new opportunity a study in patients with both COPD and alpha-1 antitrypsin deficiency (AATD)

*continued on page 7*

## Shanghai Henlius Biotech, Inc.

A Randomized, Double-Blind, International Multicenter, Phase III Study to Evaluate the Anti-Tumor Efficacy and Safety of HLX10 (Recombinant Humanized Anti-PD-1 Monoclonal Antibody Injection) or Placebo in Combination with Chemotherapy (Carboplatin/Cisplatin-Etoposide) and Concurrent Radiotherapy in Patients with Limited-Stage Small Cell Lung Cancer (LS-SCLC)

## Abbvie

Protocol Title: A Phase 2, Open-Label Trial to Evaluate Safety of Epcoritamab monotherapy in Subjects with Relapsed or Refractory B-cell Non-Hodgkin Lymphoma when Administered in the Outpatient Setting Study M23-362

## PPD

Pleural Effusions; the patient pathway and standard of care for treatment of these patient

[Please visit this link for the full list of Industry Opportunities.](#)

## NCIRE Federal Funding Opportunities (as of 8/16/2022)

Please contact Azarah Wong, [azarah.wong@ncire.org](mailto:azarah.wong@ncire.org) or at x23891, for further information on the following Federal Funding Opportunities.

### NIH funding opportunities specific to COVID-19 Research:

<https://grants.nih.gov/grants/guide/COVID-Related.cfm>

**CDMRP: FY22 Traumatic Brain Injury and Psychological Health Research Program (TBIPHRP)** is currently accepting applications for various mechanisms. <https://cdmrp.army.mil/funding/tbiphrrp>

- Pre-Application: Various Due Dates August 24 – September 1, 2022
- Full Application: Various Due Dates September 14 – December 8, 2022 (some by invitation only)

**NIH: NIDA, NIMH, and NINDS Research Opportunities for New and “At-Risk” Investigators to Promote Workforce Diversity (R01 Clinical Trial Optional)** <https://grants.nih.gov/grants/guide/pa-files/PAR-22-181.html>

- Due Dates for New Applications: September 08, 2022; January 06, 2023; May 05, 2023; September 06, 2023; January 09, 2024; May 06, 2024; September 06, 2024; January 08, 2025; May 05, 2025
- Due Dates for Resubmission Applications: October 06, 2022; February 07, 2023; June 06, 2023; October 06, 2023; February 06, 2024; June 06, 2024; October 08, 2024; February 06, 2025; June 06, 2025
- Additional info: <https://www.ninds.nih.gov/funding/about-funding/diversity-r01-new-and-risk-investigators>

[Please visit this link for the full list of Fderal Funding Opportunities.](#)

## NCIRE Contracts & Grants Promotion

It is with great pride that NCIRE announces the promotion of Azarah Wong, CRA, to Associate Director, Sponsored Research, effective September 1, 2022!

Azarah joined NCIRE as an Executive Assistant to the Chairman of the Board in 2003. She has been a Certified Research Administrator since 2006 and has led the Grants and Contracts Team as their Manager since 2017. As Associate Director, she will work with me to shape and execute the institution's grants policy and sponsored programs vision while continuing to manage all federal pre and post-award activities.

Please join us in congratulating Azarah on this well-earned promotion!

# Message from the Chief Executive Officer

This first week of September brought elevated temperatures and a lot of sunshine. I hope you were able to keep cool and safely enjoy the outdoors! A big thanks to the featured investigators, Barbara Bensing, PhD and Jialing Liu, PhD, for their time. We appreciate the opportunity to share their research.

Over the past three months we have moved in phases. At the end of August, NCIRE completed the physical move from building 14 to buildings 210 and 3 at SFVAHCS. Human Resources, Accounting and Executive Leadership are in building 210, ground and first floor. Contracts and Grants, IT, and Procurement are located in building 3. The central NCIRE entrance point is the first floor of building 210, and can be found within the hallway heading towards the Auditorium.

As we approach the end of the fiscal year, our finance team is working on budgets for FY2023. Please review and respond to inquiries to ensure our spending plan for FY2023 is accurate.

Save the date for NCIRE's annual virtual employee benefits faire to be held October 31 – November 4, 2022. Staff are invited to meet with representatives from various health plans to learn the current benefit details. Any changes to annual choices must be made between October 31 - November 11, 2022 using the UltiPro UKG portal.

In 2021, we initiated the process to transition from the Cayuse system, which currently provides pre-award functions for grant applications, to iMedRIS. Over the past year, NCIRE has worked to test the system. Once implemented, iMedRIS will provide both pre- and post-award management infrastructure. The full implementation is planned for December 2022.

Our newsletter committee is a small group of dedicated hardworking volunteers. If you are interested in learning more about the committee or participating at any level, please contact [dna@ncire.org](mailto:dna@ncire.org).

Our next issue will be published early December 2022.



Rebecca Rosales, MBA, CRA  
Chief Executive Officer

## About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support over 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

NCIRE is a 501(c)3 nonprofit. (Tax ID #94-3084159). Visit NCIRE at [www.ncire.org](http://www.ncire.org)



Follow us on LinkedIn:  
<https://www.linkedin.com/company/ncire>

Like us on Facebook:  
<https://www.facebook.com/NCIREVeterans>

Follow us on Twitter:  
<https://twitter.com/NCIRE-Veterans>

The DNA Newsletter is an NCIRE Publication.  
Editor-in-Chief: Rebecca Rosales, Chief Executive Officer  
Staff Contributors: Tai Arceneaux, Lydia Blednyh, Azarah Wong, Andy Evangelista, Theresa Gio, Newton Ong

Please send comments to [dna@ncire.org](mailto:dna@ncire.org)