



From Postdocs to PI's: Training Scientists For Success

Faculty members Mathew Blurton-Jones, PhD, Kim Green, PhD, and Masashi Kitazawa, PhD, are principal investigators (PI) of productive, independent laboratories at UCI MIND all aiming to target the underlying cause of and develop effective treatments for Alzheimer's disease (AD) and related disorders.

How did they get to where they are now? After graduate school in 2003, they came together from different backgrounds to train with renowned scientist, Frank LaFerla, PhD, who continues to run a successful laboratory of his own at UCI MIND.

Blurton-Jones, Green, and Kitazawa reflect on their training experience and what they believe to be their most important contributions to the field thus far:

Why did you choose LaFerla's lab at UCI MIND for your postdoctoral training?



Blurton-Jones: *As a graduate student at UC San Diego, I had been studying the effects of estrogen on neuroplasticity to try to understand why women are more likely to develop AD than men. Around the same time, my grandfather*

developed the disease, which naturally reinforced my desire to continue AD research. I knew that UCI MIND had several leading scientists – Carl Cotman, Andrea Tenner, and Charlie Glabe to name a few. I was initially drawn to Carl's lab because he was using exciting new gene analysis and bioengineering approaches to study AD. While in Carl's lab, Frank published his first paper on the triple transgenic mouse model. The excitement surrounding this innovative new model led me to begin collaborating with his team and, soon thereafter, to pursue a second postdoc to explore some of my own ideas with this new model. For example, I started to think about how stem cells could

potentially be used to model or perhaps even treat AD, and Frank gave me the freedom to pursue this relatively wild new idea.



Green: *After my doctoral training at University of Leeds, I decided to spend a year backpacking around the world. As my last two weeks approached, I started thinking about what I wanted to do next and remembered meeting Frank*

at a conference the year before. He was known in the late 90's for his work on calcium in AD, which was the focus for my PhD. His team was doing great work. So, during my last stop in LA, I had the opportunity to interview for a postdoc position and got it. And then when I got to UCI, Frank had just made the triple transgenic mice, and my research focus changed at that point.



Kitazawa: *I was very interested in how chemical agents affect the nervous system. So, I pursued my PhD in environmental toxicology where my research focused on using cell cultures to examine environmental chemicals, including*

pesticides in Parkinson's disease. Then, I wanted to expand my knowledge in toxicology to other neurological diseases, so my mentor recommended AD and mentioned a rising hot shot at UCI, Frank LaFerla. Frank was known for his triple transgenic mice and I wanted to expand my techniques, skills, and knowledge to working with mouse models for my postdoc training. Fortunately, he offered me a position to join his lab.

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From the Director

Joshua D. Grill, PhD



Dear UCI MIND friends and supporters,

Another year has passed and it is time to take stock and plan for 2020. 2019 was eventful, marked by important discoveries and progress. Though there were visible setbacks, at the time of writing we are eagerly awaiting more information about Biogen's candidate drug aducanumab. Biogen recently announced intent to submit to the FDA for approval of aducanumab, a treatment previously declared "futile" in large registration clinical trials (www.mind.uci.edu/biogens-about-face). If this effort is successful, aducanumab may be the first ever disease-modifying therapy for Alzheimer's disease. You can expect to hear more from us on this important development in the New Year. Nonetheless, it is clear that while our progress remains rapid, there is still much work to be done to rid the world of Alzheimer's disease and related disorders.

The work that lies ahead necessitates a critical aspect of UCI MIND's mission—to train the next generation of clinicians and scientists. UCI MIND has an incredible track record of training productive independent researchers. In this issue of *MIND Matters*, we highlight three faculty members who trained with former director, Frank LaFerla, and now lead highly productive laboratories of their own at UCI MIND (pp. 1, 3-4). Our faculty and staff's long-term commitment to UCI MIND is a source of great pride. In this issue, we also highlight four staff members who have a combined 90 years of service to Alzheimer's disease research (p. 5). These leaders in our organization are testament to the personal commitment of each member to our mission.

We know we cannot achieve a world without Alzheimer's disease alone. Philanthropic partners, such as the Naeves (p. 6) and all those acknowledged in this special issue of *MIND Matters* (pp. 9-11), are equal stakeholders in our efforts and successes – so are research participants and advocates like Paula Gann and her daughter Kyle Scrivner (pp. 7-8). Paula and Kyle were recently invited to serve on California's Governor's Task Force on Alzheimer's Prevention and Preparedness, organized by our friend Maria Shriver. UCI MIND will host a meeting of this important Task Force in 2020.

We hope you continue to follow these and other developments at UCI MIND in 2020, and we wish you and your families a Happy Holiday Season and prosperous New Year.

Global Recognition for Leading-Edge Research



Faculty member, Vivek Swarup, PhD (left) and his team were highlighted by the Society for Neuroscience (SfN) at an international conference in October.

Dr. Swarup's research, which focuses on identifying biological processes at the core of Alzheimer's disease, was selected among 14,000 projects to be discussed at SfN's press conference and featured in its "Hot Topics" publication that calls attention to the most promising research trends in neuroscience worldwide.

Dr. Swarup's project used big data analytics to examine networks of genes in over 1,000 brains donated by research participants. The study identified key biological changes unique to Alzheimer's disease that are not altered during normal brain aging, pointing to the potential for new therapeutic targets.

From Postdocs to PI's

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LaFerla
THEN



LaFerla
NOW

What were your most important accomplishments as a postdoctoral trainee?

Blurton-Jones: *Of course there's those scientific moments where you see for the first time a really exciting result. When we first got the result that our stem cell transplant was improving behavior and memory impairment in AD mice, that was super exciting.*

Green: *We were fortunate – we all had a string of discoveries. One of mine, for example, was that nicotinamide (high doses of vitamin B3) restores cognition in mice with AD, which has led to a current clinical trial in people. I view that as good translational science that worked here at UCI MIND. It feels good to have made a discovery that led to a clinical trial that might help people with the disease.*

Kitazawa: *I was probably the first in the lab to explore the link between inflammation and AD in mice. Obviously there were other investigators in the field studying that, but at the time it wasn't the main topic. Right now, it is! Another one is the link between muscle disease and AD. Degenerating muscles, like in inclusion body myositis, accumulate amyloid beta just like in the brain, but those people somehow don't develop AD. I continued to investigate this and published some work on the topic.*

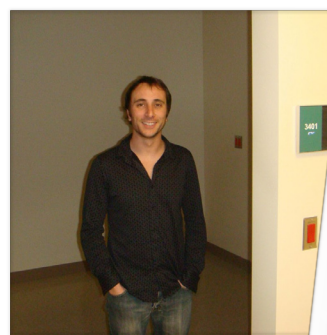
What is the focus of your independent lab?

Blurton-Jones: *When I started my own lab in 2011, I began to investigate whether we can use induced pluripotent stem cells (iPSCs) to better understand AD. Most recently, we have used iPSCs to generate and study microglia, the immune cells of the brain. Part of what has encouraged us to study microglia are new findings in the field that have shown that many AD risk genes are primarily expressed in microglia. So those are the cells we need to be studying to better understand the disease and develop promising new therapies.*

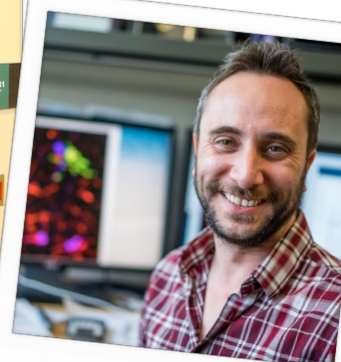
Green: *Microglia. When I started my lab in 2011, we looked at a lot of different things, including microglia which people weren't really interested in at the time. And somewhat through luck, we found a way to get rid of microglia completely, which was unheard of. We published this finding in 2014 and there was originally a lot of disbelief. No one believed we could eliminate an entire tissue from the brain and that the mice would be fine. But now, it's a widely used, reproduced, and very popular approach.*

Kitazawa: *After a few years at UC Merced, I came back to UCI in 2016 and launched my lab focusing on environmental risk factors for AD using cell cultures and animal models. Right now, we're looking at the potential effects of chronic copper exposure in drinking water as well as particulate matter, or air pollution. There is emerging epidemiological evidence that these environmental factors may be associated with cognitive decline, so now the question is, what is the mechanism?*

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Green
THEN



Green
NOW

From Postdocs to PI's



Blurton-Jones
THEN



Blurton-Jones
NOW

What have been your most important contributions to the field thus far?

Blurton-Jones: Probably two-fold. The first is developing an approach to differentiate iPSCs into human microglia, and now a lot of researchers and biomedical companies are using our approach. This allowed us to ask the next set of questions, which is our second big achievement. We are now using iPSC-derived microglia combined with gene editing tools to try to understand what exactly AD risk genes do to microglial function. Most recently, we've taken this to the next step by transplanting those human cells back into mice with AD pathology to see how the genetic mutations change microglial responses to pathology.

Green: Our method to completely eliminate microglia in mice is the most important contribution that I will ever make. It has been a highly influential finding that is now used by more than 200 groups across the world and has led to many important discoveries. It's hopefully inspiring clinical trials in Europe and the U.S. Because we figured out how to get rid of microglia, it allows us to explore what these cells do in the disease, which was just not possible before.

Kitazawa: We've published some important findings on the link between copper and inflammation, as well as the vascular damage caused by copper.

Is there anything you took from LaFerla's mentorship that you use with your own trainees?

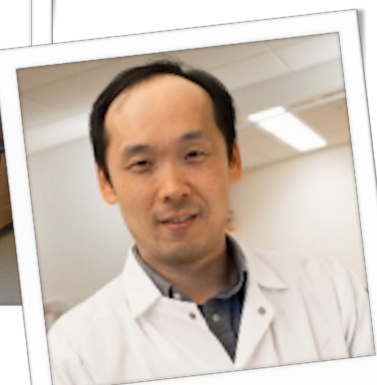
Blurton-Jones: To give my graduate students and postdocs the freedom to pursue what they're passionate about in their research, with some guidance and advice of course! It's not an easy career, so I think having that freedom to embrace our intellectual curiosity is critical. Frank also taught me the importance of interpersonal relationships – how to talk confidently about our research and engage people in what we're doing at both the scientific and lay levels. Frank is an expert at that.

Green: Everything. Frank had a big lab with lots of people, allowing me to take on mentorship roles for other trainees, which gave me the experience and perspective needed to start my own lab. With Frank, we also learned the importance of branding, which you can see in his contributions to UCI MIND and the School of Biological Sciences.

Kitazawa: I appreciate how Frank gave us freedom to research within the capacity of his lab. I feel that works very well for my lab as well. I think it's good for young postdocs who have lots of ambitions and some crazy ideas (that we may not have anymore) to try to test them. If it works, that's great. If it doesn't, we move on to the next idea. It may be a little risky, but it can lead to some surprising results. Especially for the AD field, where we may need to look at the problem from a different point of view to see what we've missed. Those ideas are probably going to come from fresh postdocs bringing in new ideas.



Kitazawa
THEN



Kitazawa
NOW

Happy Anniversary! Staff Spotlight



ANDREA WASSERMAN
Chief Administrative Officer
30 YEARS

Andrea was first introduced to UCI MIND as an undergraduate researcher in the lab of founding director, Carl Cotman, PhD. Upon graduating in 1988, Andrea joined the staff excited to begin a fulfilling career. Her tenure with UCI MIND has included many different roles from lab technician to brain bank staff to lab manager to brain bank supervisor and ultimately, to her role as Chief Administrative Officer. In her leadership position, Andrea maintains a productive research organization and facilitates collaboration among the hundreds of campus-wide faculty, staff, and students who comprise the Institute. What she enjoys most about her job are the daily interactions with her colleagues and community supporters, "To work with a group of individuals that all have the same goal, integrity, work ethic and drive is a great honor. As the nation faces an epidemic of Alzheimer's disease, it is very important for all of us to have a better understanding of the nature of the disease, how to diagnose it, and a clear perspective about the research that is on-going nationally and internationally with the ultimate goal of identifying a therapeutic or, better yet, a cure for the disease. I am excited to play a small part in that process."



SHIRLEY SIRIVONG
Manager of Clinical Research Operations
20 YEARS

Shirley is professionally and personally invested in the mission of UCI MIND due to her family history of dementia. Her professional career began as a student assistant. Upon graduating from UCI, she was hired as a patient care coordinator. Soon after, Shirley was promoted to the dual role of managing clinical research operations for the Alzheimer's Disease Research Center, as well as organizing community outreach activities.

As UCI MIND has grown over the years, so has Shirley's critical role in managing the clinical research program and personnel. Shirley reflects on her time with UCI MIND, "I never thought I would work with the same department so long, but it has been easy to do so. I love what I do and work with a fantastic group of colleagues who share the same mission. Whether helping families through their journeys or conducting research visits to improve our knowledge in this field, I find my work to be rewarding on so many levels. I am proud to be part of the UCI MIND team and grateful every day to be part of the effort to make a difference."



DAN HOANG
Data Manager
20 YEARS

Dan joined UCI MIND upon graduating from UCI with a double major in Biological Sciences and English and a minor in Asian-American Studies. During a time with no Internet access, Dan was hired to help file papers and organize journal articles for founding director, Carl Cotman, PhD. Though his initial trajectory was not computer programming, Dan's unique skillset was recognized earning him promotions toward his current position as Data Manager.

Dan's substantial knowledge of computer operations is essential to UCI MIND. He oversees the data informatics infrastructure that allows investigators to perform research projects. He is responsible for data sharing within the NIH/NIA Alzheimer's Disease Research Center network. And he is a critical member of the team that operates the UCI Consent-to-Contact Registry (c2c.uci.edu). Dan enjoys problem solving daily and shares, "When I see that a UCI MIND researcher published a paper that I helped with, it feels good to know that I've contributed a little to the fight."



DANA GREENIA, RN, MS
Clinical Research Administrator
20 YEARS

Prior to joining UCI MIND, Dana served as Chief Administrative Officer for the Department of Neurology where she met Claudia Kawas, MD, Principal Investigator for *The 90+ Study*. With encouragement from Dr. Kawas and an interest in learning about aging and dementia research, Dana brought her experience in administration and clinical care to the 90+ team in 2009. Dana has served as Clinical Research Administrator for *The 90+ Study* for over a decade, managing multiple groundbreaking research projects such as a clinical trial to test a now FDA-approved radioactive tracer for brain PET imaging. In addition to participating on research projects, Dana mentors students, presents community and professional lectures, and serves as point-person for all things related to *The 90+ Study*.

What Dana enjoys most about her job are the research participants, staff, and faculty with whom she works, "I work with the most brilliant scientists and the most committed participants. I learn from them, and honestly, there is never a dull moment! They really are just as excited as I am to contribute to research."

Philanthropy Spotlight: The Naeves

In 2007 everything changed for Virginia Naeve and her family. Her beloved mother, Helen, was diagnosed with Alzheimer's disease. Virginia and her siblings began reading everything they could find about Alzheimer's and dementia. They consulted experts, communicated regularly as a family, and learned everything they could.

"When my kids were growing up, I used to say that the key to motherhood was flexibility. I later learned that when caring for someone with Alzheimer's disease, flexibility not only comes in very handy, it's essential."

Among other things, Virginia learned by experience how to ease her mother's transition into assisted living, how to cope with taking her mother's keys away, and how to navigate the complexities of holidays (see Virginia's blog: anewpathformom.com).

Virginia and her husband Bob have brought that same level of flexibility, learning, and strategy to their support of UCI MIND. For the past six years, they have hosted the annual *Wine for the MIND* event in their home, which generates donations of wine for the silent auction at the annual *A December to Remember* Gala.

Virginia is also an active member of the Gala Planning Committee and UCI MIND Leadership Council. Their dedication and passion is matched by their generous philanthropic support.

Ever the planners, Virginia and Bob began talking a few years ago about retirement and how that eventual reality will impact their ability to give. Concerned that a change in cash flow after retirement would limit their ability to support UCI MIND, the Naeves met with their financial planner to discuss options.

Their advisor suggested they give appreciated stock, instead of cash, to maximize their giving and minimize their taxes. Gifts of stock serve a dual purpose of avoiding capital gains tax and achieving philanthropic goals. When gifted to UCI MIND, gifts of appreciated assets like stock generate the full fair market value.



Bob and Virginia Naeve at their home with UCI MIND Director Joshua Grill (right) for the annual *Wine for the MIND* event

These types of strategic gifts are the cornerstone of planned giving techniques that allow passionate individuals to support Alzheimer's disease research in ways that make the most sense for their personal financial situation. The UCI Office of Planned Giving works closely with donors like the Naeves to strategize and be creative.

"My own mother had no idea that I was her daughter," says Virginia. "That fact alone keeps me interested and focused on supporting Alzheimer's research at UCI MIND until a cure is found."

Now, with their planned gift, Virginia and Bob are doing just that.

Research Advocate Making a Statewide Impact

California is home to more people with Alzheimer's dementia than any other state, with an estimated 660,000 people afflicted in 2019. The prevalence is projected to increase 30% by 2025 and 127% by 2040, unless researchers discover effective preventions.

In an effort to build an infrastructure to combat Alzheimer's disease and related dementias, California Governor Gavin Newsom established a Task Force, chaired by former California first lady Maria Shriver, to develop recommendations on how local communities, private organizations, businesses, government, and families can prevent and prepare for this health crisis. A complete list of Task Force members can be found at chhs.ca.gov.

Here, we had the opportunity to interview appointed Task Force member Paula Gann, who also serves as a research study partner with her daughter Kyle Scrivner, a participant in the UCI MIND Down Syndrome Program led by Ira Lott, MD.

What was your reaction when you were asked to join the Task Force?

Gann: *I was shocked but also very pleased to be asked. Maria Shriver, the chair of the Task Force, felt that people with intellectual and developmental disabilities should be represented because she's aware of the link between Down syndrome (DS) and Alzheimer's disease (AD) and understands the impact and need in this population. So, the committee in Sacramento contacted the National Task Group on Intellectual Disabilities and Dementia Practices (NTG), who recommended me because I've been very involved in advocacy since Kyle's diagnosis.*



Paula Gann with her daughter Kyle Scrivner

What was your experience when Kyle was diagnosed with Alzheimer's disease?

Gann: *It was a real blow for me because I didn't know anything about the co-occurrence of DS and AD at the time. I think there is this attempt to protect parents of people with DS from having to think about it and also a general lack of knowledge among those providing care and support for people with DS. So, I did a deep dive into the Internet, and in my endeavor to learn everything I could, I found the NTG, a coalition that advocates for the needs of families facing intellectual and developmental disabilities and dementia. Through my involvement with the NTG, I learned about the DS research program at UCI MIND and called the program manager, Eric Doran.*

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Invest in Discovery

Are you 70 ½ or older and do you have an individual retirement account?

Did you know that you can fulfill your required distribution from your IRA through a charitable rollover? It can reduce your taxable income and support Alzheimer's disease research at UCI MIND.

For more information about IRA rollovers, please call **949.824.6233**.

Research Advocate Making a Statewide Impact

Why did you and Kyle decide to get involved in the UCI MIND Down Syndrome Program?

Gann: *It was a no-brainer for me. I just really believe in research. What we're doing now might not benefit Kyle, but it's going to benefit the people coming after Kyle, and that's important. At the same time, we don't want to get to the point where people with DS become guinea pigs for everything. But, in AD research there's a real potential to learn from people with DS.*

"People with DS are at higher risk for AD than any other population."

When you think about it, every middle-aged adult with DS has plaques and tangles in their brain, but not all of them develop dementia. What is the protective factor keeping that from happening? If we can figure that out, we can not only help people with DS but also the whole population.

What do you hope to accomplish on the Task Force?

Gann: *I plan to represent the entire intellectual and developmental disabilities population. Also, I live in a very rural area and want to be a voice for people with AD in those types of areas where there is a dearth of resources. The current state plan for AD doesn't mention these issues at all, so I want there to be consideration for this population in the next plan. There are two main recommendations I'm working on for the Task Force.*

"One is to develop housing with adequately trained and paid staff for people with intellectual and developmental disabilities and dementia."

People with DS are oftentimes born to women who are older, and it's very difficult for aging parents to care for a child with AD. So, care often falls to siblings in the midst of balancing their own careers and families. Help is needed. I think having programs that allow people to live a good quality of life until the end is really important. People with DS used to be placed in institutions, and we don't do that anymore. So, we shouldn't be doing that at the end of their life either.

"My second recommendation is for all California Alzheimer's Disease Centers to have access to specialists who are knowledgeable about aging and DS."

We have "Teledoc" now, which is a technology that can be used to make these kind of doctors more accessible so that parents have a place to get an accurate diagnosis and appropriate care.

How might your experience with research contribute to the Task Force?

Gann: *I want to communicate what I've learned from research with the Task Force. People with DS are at higher risk for AD than any other population, and we need to pay attention to that. Though they are more vulnerable, they do not all develop dementia. We've got something to learn here and need to look at the research being done to help the general population. I'm really grateful that I found the research program with Dr. Lott and Eric. I think Kyle is contributing, but we've also gotten a lot back and I've learned a lot. At our first visit in 2017, I felt like for the first time I had people who were knowledgeable, educated, and could really speak to me about what was going on with Kyle. I hadn't had that before.*



Ira Lott, MD (left) and Eric Doran, MS (right) lead the UCI MIND Down Syndrome Program.

For more information, please visit mind.uci.edu or contact Eric Doran: 714.456.8443 or edoran@uci.edu

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