First person – Aleena Arakaki

How would you explain the main findings of your paper in lay terms?
The majority of cancer treatment options target rapidly dividing cells in the primary tumor. However, breast cancer patient mortality happens when the cancer spreads to other organs including lung, liver, bone and brain – a process called metastasis. Despite this, we have few therapies against metastasis. Additionally, we have made great strides in targeted treatment options for breast cancer patients whose tumors are driven by estrogen, progesterone and/or HER2 receptors, but we lack targeted therapies for patients whose tumors lack these receptors, termed ‘triple-negative breast cancer’ (TNBC). Our research highlights the important role of and provides mechanistic insight into the role of the tumor suppressor ARRDC3 in regulating cell signaling from the oncogenic G protein-coupled receptor PAR1 to the Hippo pathway. The loss of ARRDC3 in TNBC results in dysregulated signaling through the protein TAZ, which promotes cell migration and invasion and metastasis in mice. This study implicates both PAR1 and TAZ as potential therapeutic targets in TNBC to inhibit metastasis.

When doing the research, did you have a particular result or ‘eureka’ moment that has stuck with you?
In the majority of Hippo pathway studies, YAP and TAZ function has been viewed as redundant, largely due to their structural similarities. When we started this project, we hypothesized that both YAP and TAZ would contribute to PAR1 signaling based on this knowledge. When I did the YAP-specific and TAZ-specific siRNA knockdowns, we were surprised and excited to see a striking effect of TAZ knockdown on PAR1–Hippo signaling that was not observed with the YAP knockdown. This observation moved our research towards uncovering the differences in function of these two proteins and discovering TAZ as the major player in not only PAR1-Hippo signaling but also broadly for GPCR-Hippo signaling, and as the preferential target for ARRDC3 function. Our findings are in line with the growing body of literature implicating TAZ function specifically in breast cancer invasion.

Why did you choose Journal of Cell Science for your paper?
We chose Journal of Cell Science because of their rigorous review process resulting in publications of scientific excellence for a wide audience of cell biologists.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?
My first research mentors were Drs Lenora Loo and Iona Cheng at the University of Hawaii Cancer Center (UHCC). Before I participated in the UHCC summer program, I had no idea of what it meant to have a PhD and didn’t know anything about the process of attaining one. Not only did Drs Loo and Cheng introduce me to the world of cancer research and the possibility of a career in this field, but they also helped guide me on how to get more research experience as an undergraduate and on the process of applying for graduate school. I would not be where I am today without their support and mentorship.

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?
When I was 12, my mom was diagnosed with tongue cancer and given 6 months to live. As I watched her cancer advance, I became determined to learn why this disease had such devastating effects and how we could stop it. My mom passed away 2 years after her mother.
diagnosis and soon after, both of my grandmothers were also diagnosed with cancer. My Obaachan (grandmother, in Japanese) refused treatment due to the late stage of her pancreatic cancer; however, my Tutu (grandmother, in Hawaiian) triumphed through the initial surgery, radiation and chemotherapy of her breast cancer to live for another 7 years until she lost her battle when her cancer metastasized. These personal experiences drive my passion to further our understanding of cancer biology with the hopes to cure more people of this disease.

Who are your role models in science? Why?
The world of academia can be a difficult space to survive and thrive, especially for people from historically excluded groups in science. There are hurdles that people from marginalized groups face in science that can become very discouraging. Every person who has faced this adversity and succeeded is a role model to me. They show me that, as a Native Hawaiian, can also become successful and help others find their way in this system. They also have shown me how to bring my authentic indigenous self to my work as a scientist. These role models demonstrate their resilience and their importance to our society in their contributions to our pursuit of knowledge and medical advances.

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What’s next for you?
I just started my postdoctoral training in the lab of Dr Taran Gujral at the Fred Hutchinson Cancer Research Center. My research project centers on using polypharmacology approaches to identify novel kinase targets in rare cancers in collaboration with Dr Eric Holland and his lab. I hope to apply the new methodology I am learning now towards studying the genetic and molecular basis of cancer health disparities, particularly in Native Hawaiian, Polynesian and Pacific Islander communities.

Tell us something interesting about yourself that wouldn’t be on your CV.
I have been dancing hula since I was 5 years old and started learning Tahitian dance (‘Ori”) about a year and a half ago. During the COVID-19 pandemic, I have had the opportunity to take many virtual Tahitian dance classes and connected with people around the world.

Reference