TELLURIDE SCIENCE
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ELEVATING SCIENCE AND DISCOVERY

Dr. Aylin Rodan's Reflections on How Telluride Science Impacted Her Career

In 2016, I moved to the University of Utah as an Assistant Professor. A senior colleague, Don Kohan, suggested that I attend the Telluride Epithelial Physiology and Cell Biology meeting. I wrote to one of the organizers, Tom Kleyman (whom I had never met) and received… no response. Later that fall, I gave a talk at the American Society of Nephrology Kidney Week meeting. Afterwards, Tom came up to me and invited me to the Telluride meeting. So, in 2017 I attended my first Telluride meeting. One of my memories from that first meeting is going for beers with Tom, David Pearce, and David Ellison. These are three of the most accomplished and highly respected people in my field. Like me, they are all nephrologist physician-scientists. They have also all served as chiefs of their divisions (a role Tom remains in). We talked about a controversial paper that had recently been published, and we talked about Tom's favorite ion channel, the epithelial sodium channel (ENaC); I remember telling Tom that I learned more about ENaC in 20 minutes talking about it that evening as I had up to that point. Another memorable experience for me was giving the Town Talk a few years later, which Tom also nominated me for. Although I've given a lot of talks, I was nervous, and didn't sleep much the night before. The talk went well though, and stands out in my mind as a unique experience; it also taught me about going beyond my comfort zone and communicating with different types of audiences.

A couple years later, Arohan (Ro) Subramanya was giving a talk about a kinase we are both passionate about, the WNK (With No Lysine (K)) kinase. Cary Boyd-Shiwarski in his lab, together with her husband, Dan Shiwarski (also Telluride attendees), did an experiment in which they were looking at fluorescent protein-tagged WNK expressed in cultured cells. Cary is interested in potassium, which is regulated by WNKs, so she threw 50 mM potassium on the cells. What they saw surprised them: the fluorescent WNK proteins coalesced into what looked like droplets. This was the first indication that WNKs undergo a process called liquid-liquid phase separation to form biomolecular condensates, a phenomenon that was being observed for other proteins, but the role of which was still somewhat unclear. In his talk, Ro talked about how this protein behavior was being driven by the intrinsically disordered region in the C-terminus of the protein. Some years before, I had cloned Drosophila WNK, and spent a lot of time staring at its sequence in the process. I had noticed early on that the C-terminus of Drosophila WNK was rich in glutamine residues,but had no idea why. Listening to Ro's talk, I realized that the glutamine-rich C-terminus of Drosophila WNK could be driving similar phase separation and condensate

formation behavior. So, I talked to Ro about it, and we started a collaboration that resulted in this paper being published in *Cell,* "WNK kinases sense molecular crowding and rescue cell volume via phase separation":

https://www.sciencedirect.com/science/article/pii/S0092867422012612

We demonstrated that not only do both mammalian and Drosophila WNKs undergo this phase separation behavior in response to hypertonic stress and the resultant macromolecular crowding that occurs, but Ro's lab did a series of experiments showing that condensate formation is required for the cell to recover its cell volume after it shrinks in the face of hypertonicity. This paper gets to the heart of how a cell senses and regulates its volume, a fundamental and tightly regulated property.

Following the publication of this paper, we submitted a grant that is now funded by the National Institutes of Health, "Control of the Renal WNK Signaling Pathway by Phase Transitions":

https://reporter.nih.gov/search/qjzRRfySBEOXC5cKZRIF8w/project-details/10753772

We are now carrying this work forward to understand more about WNK biomolecular condensate formation and its role in physiology. As part of the project, Ro's lab recently visited my lab in Utah, and we had a great couple days of talking science as well as a Telluride-style joint lab snowshoeing outing in Big Cottonwood Canyon. This gets to my final point about why I love Telluride so much: it brings together two of my favorite things, mountains and science.

Telluride Science has introduced me to important role models and mentors and sparked ongoing collaborations which have resulted in a high impact paper and NIH funding. It has further reinforced the value of the people and the relationships that drive science by bringing together different ideas and viewpoints in a synergistic way. This is also fundamental to how I am thinking about leading my division, and I think was part of the message that made me an attractive candidate for the position.