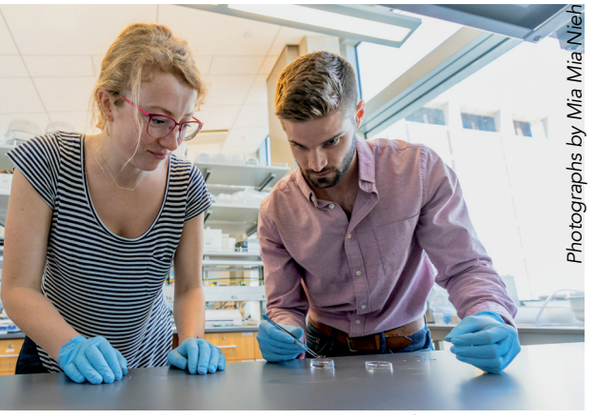
Faculty Q&A

BETH PRUITT

Deep Dive into Heart-Cell Dynamics

Since arriving at UC Santa Barbara from Stanford University in 2018, **Beth Pruitt,** professor in the Mechanical Engineering Department and the Biomolecular Science and Engineering Program, and director of the Center for BioEngineering, has taken a highly collaborative approach while pursuing an ambitious research agenda. Pruitt's lab specializes in designing and making micro-devices used to measure with high precision how cells, and especially those in human heart tissue, respond to changes in their environment. Pruitt was the driving force in establishing the stem cell "biobank" in UCSB's Center for Stem Cell Biology and Engineering, and was recently named a Fellow of the Biomedical Engineering Society. We caught up with her in August.



Photographs by Mia Mia Nieh

PhD students Kerry Lane (left) and Liam Dow at work in the BioEngineering lab.

Postdoctoral scholar Cheavar Blair fills a vial at a hood in Beth Pruitt's lab.

Convergence: *Can you shed some light on the importance of being named a Fellow of the Biomedical Engineering Society (BMES)?*
Beth Pruitt: This is one of the honors I'm proudest of, because BMES is *the* professional society for bioengineers. I was trained as a mechanical engineer, and I was elected a Fellow of the American Society of Mechanical Engineers in 2015. I was very proud of that honor, which was based largely on my group's contributions to microtechnology and measuring systems — tools we have made over the years to measure things that you couldn't measure any other way or couldn't measure as quantitatively as we set out to do. And while those tools have been directed largely at biology, our work was just starting to have an impact in understanding the role of mechanics in biology and the bioengineering of cellular interfaces and environments. Having BMES recognize our work as an important contribution to the field of bioengineering means a lot to me.

C: *One area of your research areas is mechanobiology. What is that exactly?*

BP: When I'm teaching my mechanobiology class, I tell students that they'll find different definitions in different journal papers. So, it's good to think about what the definition is. We start by distinguishing between mechanobiology and biomechanics, two very similar words. If I just want to know the difference between, say, Jell-O and brick, that's biomechanics. I care only about the mechanics of each: how it feels and resists loading, whether it's more like bone or brain. We can use good old mechanical-engineering principles to understand that.

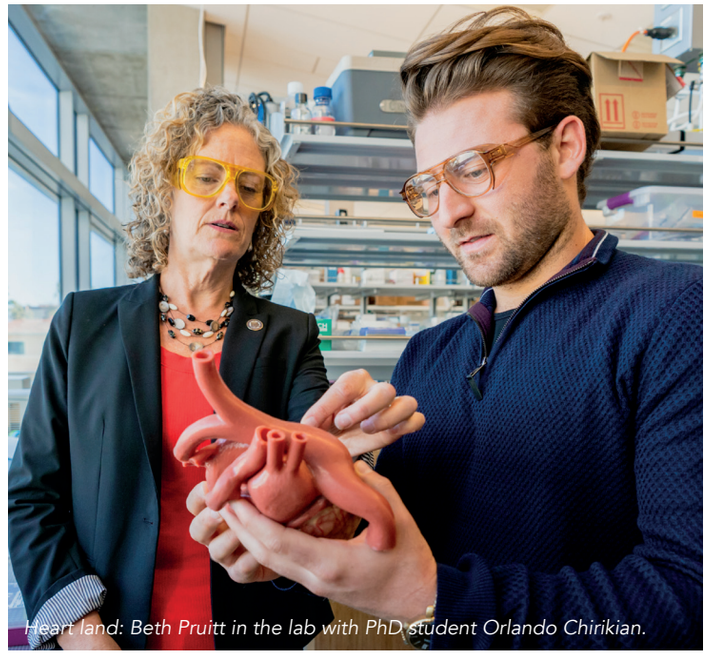
Knowing these properties helps us to design and make a suitable environment or a device to interface with biology. We try to mimic a tissue or the surface of a tissue and then adhere cells to that. We're interested in how the cells' behavior changes depending on whether they are on a soft hydrogel or on a more traditional tissue culture material, like glass or hard plastic.

We know that the cells interface with and respond to their environment by appearing and acting differently, and that's broadly referred to as mechanobiology. We can't treat it like a

static engineered material that has properties that I can measure and that don't change without my intervention. Living materials can remodel themselves to change the mechanical properties of the cells and surrounding matrix material. Living materials also have mechanical sensors and signaling processes to measure and respond to the environment. They can respond through short- and long-range processes, on short and long time scales, by growing or destroying cells or matrix, by changing shape or position, and by changing their cell type and their biomechanics. They are highly dynamic — the ultimate smart material.

Further, mechanotransduction is the process by which cells probe or "feel" their mechanical environment and transform that into these observable cell behaviors or responses by preferentially running different "programs" or biomolecular signaling cascades. And cells have a whole bunch of parallel mechanisms and checkpoints to make sure they do this right every time for reproduction and development to be so successful. A large part of what interests us in our lab right now is not just what happens during normal development and function, but also how it goes wrong in disease progression or injury. We want to know whether mechanical changes act in a feedback loop to mediate biological signaling.

C: *What do you hope comes about as a result of a deeper understanding of the biomechanics of heart-muscle cells?*
BP: We hope that by making finer-scale quantitative measurements of these various cell models, we can start to understand very intricate processes that occur on the molecular level — changing a molecular process on a cell and quantifying the impact it has at the cell level. If we can begin to replicate, for example, some of the hallmarks of heart disease in a human cell model, we can enable a lot of discovery without animals, because we can use these stem cells that were derived, for example, from human skin cells. Importantly, these heart muscle cells, derived from stem cells, are from a human background instead of a mouse genotype or a rat genotype. I always joke that the hearts of mice and men are different, but it's true: not only do they differ greatly in size, but a mouse heart beats about six hundred times a minute, and ours beats sixty. As a result, these two hearts have very different dynamics and mechanics, and very different underlying composition of the proteins that drive a heartbeat. These proteins are also associated with the majority of inherited heart disease mutations that have been documented. So, our goal is to study the role of these mutations in disease processes not only in human cell models but also in the right mechanical environments. In this way, we seek to enable better platforms to test disease mechanisms and potential therapies.


Heart land: Beth Pruitt in the lab with PhD student Orlando Chirikian.

> "In this way, we seek to enable better platforms to test disease mechanisms and potential therapies."

C: *When you arrived at UCSB from Stanford, you became the driving force in establishing the cell bank and the Stem Cell Institute at UCSB. Why was that important — for you and your fellow researchers on campus?*
BP: We had been using three cell lines from the Allen Institute for Cell Science when my lab was at Stanford. These

cells are unique in that different proteins of interest have been labeled, so we can watch protein activity in living cells. They also cost six hundred dollars per vial, so we were really selective at first. We also knew that more lines that would be super-targeted to our research were going to be released soon, and we wanted to buy those, too.

Because these are human-derived cells, there are a lot of controls and protections surrounding their use. We were allowed to proliferate our one vial of cells to hundreds, but only for our own approved research. Gaining the approval to first obtain and then use these cells is a significant undertaking. Through our ongoing collaboration with the Allen Institute, we worked with them and the relevant entities at UC Santa Barbara not only to purchase all of their lines that were available at that time, but also to create a biobank agreement, which greatly increased the access to the cell lines for other labs on campus.

Having the cells available in a biobank eliminates more than half of the paperwork for other labs on campus that would like to use these stem cells. Each lab still needs review by an oversight committee that ensures ethical uses of the cells, but still, it's great to have that kind of "candy store" on campus and be able to say, "I'd really like to see a fluorescent tag on *that* protein." Best of all, when any of us makes improvements or additions to these banked lines, the biobank agreement allows us to "redeposit" and share them with any other lab on campus.

We ended up buying twenty of the lines and then banking multiple vials of them. If you culture the cells in the right way, you can make eighty or a hundred vials from one vial, plenty for my lab, for backup, and for other people who want to use them. This biobank is consistent with UCSB's culture of collaboration and makes it easier for a community of users to share experience, cell lines, and knowledge.

Postdoctoral scholar Anna Kim (left) and Erica Castillo, a Stanford doctoral candidate, image beating heart cells on a microscope in Beth Pruitt's lab at UCSB.

C: *Can you tell us about the graduate program in biological engineering that has been proposed at UCSB?*
BP: The proposal is for a new PhD degree program in biological engineering, and it has gone most of the way through the campus review process now. This interdisciplinary program will draw faculty from both the College of Engineering and the Division of Math, Life and Physical Sciences. The proposal is currently being reviewed by **Executive Vice Chancellor David Marshall** and **Chancellor Henry T. Yang** before moving on to the next stages of UC review. The campus review comments were generally quite positive and the main concerns centered on how to realize the longer-term growth goals of a new program launched during or on the heels of a pandemic. Notably, these same reviewing entities also recognized that campus does already have a strong base of resources in terms of faculty enthusiasm and commitments to teaching, training, and mentoring in the new program. Thus, we believe we can successfully launch the program now, even if faculty hiring and growth toward our goals of launching an undergraduate program may be delayed.

C: *Can you tell us about the process of ramping down and then reopening the lab in response to COVID?*
BP: We went back into the lab on June 15, and people have been making good progress ever since. I'm really impressed. It has highlighted a few places where we need to be more organized, but overall, I'm really proud of my lab for how they have handled this whole situation, how they have made the best use of their time when we were sheltering in place and couldn't enter the lab, and how quickly people got back to their research when they returned.

We've always had a collaborative lab, but this has really fostered a deeper collaboration. If you don't have permission to be in the lab as much as you want to, and someone is going to be there making devices, maybe they make them for their experiments but also for others to use. And someone who is doing the cell manipulation can prepare something for someone else. The pandemic has made us more dependent on each other, and that has really brought out the best in everyone.

We also had some undergrads who were supposed to do research with us this summer, but they're not allowed back in the lab yet, and we don't know when they will be, so we switched all their projects from what they *were* doing to doing video and image analysis. It was a skillset that none of them really had, but we we took a team approach to mentoring them. Each student had a grad-student mentor and would attend a session each week run by one of the mentors or a postdoc to learn about a different mode of analysis. So, they got exposed to all of the things you can do with image data. They became proficient over the summer and are now able to support those who can work in the lab. It's different, but it's working.