Trainees in the Spotlight

Christina Theodoris
Scientific Artist

Pam Goldberg Smith

Christina Theodoris earned her BS in Biology at the California Institute of Technology and is currently pursuing her MD/PhD at the University of California, San Francisco, in Developmental and Stem Cell Biology. She is a student researcher at the Deepak Srivastava laboratory at Gladstone Institutes, focusing on gene regulatory networks and their disruption in cardiac disease to identify targets for network-correcting therapies. As an artist and a scientist, Christina endeavors to strike a balance between her 2 passions, using her experiences in art to move forward through the setbacks and missteps that are an accepted part of the scientific process as, after all, “there are no mistakes in art.”

Tell Us a Bit About Your Background

I was born and raised in Atlanta, where my parents immigrated from Greece. My parents initially came to the United States for graduate school—my father in electrical engineering and my mother in physical therapy. Growing up in Georgia, I always loved playing with my sister in the forest and really enjoyed nature and art. My sister and I were always excited for the daily math puzzle my dad would give us to figure out on the drive to school, and I was inspired by my mother’s compassion for her patients. For high school, I went to a public magnet school for art and science. Thanks to the mentorship of my extraordinary teachers, I was fortunate to be selected for the national Marie Walsh Sharpe art program, where I studied with artists Susanna Coffey and Chuck Forsman, and the national Earthwatch Institute program, where I researched signal detection theory with whiptail lizards in the Arizona desert. Experiences like these set me on the trajectory to pursue my passions in art and science.

What Influenced Your Career Choice?

When I went to college, I knew I wanted to pursue a career in medicine; I loved pediatrics and working with kids. At Caltech, I worked with Eric Davidson, who is considered a grandfather of gene regulatory networks and developmental biology and, unfortunately, has since passed away. He always had an open door for students to talk with him about anything from their current research to theorizing about the Doushantuo fossils in China. He taught me how to think about networks of genes rather than isolated pathways, and I wanted to apply these concepts of gene regulatory networks to human disease to find therapies for patients as a physician scientist.

What Led You to Study Cardiovascular Science in Particular?

As an undergraduate, I worked on gene regulatory networks in early development in sea urchin, which is a basic organism. I wanted to apply these concepts to human disease to identify important regulatory nodes that could be targeted therapeutically, and I was fortunate to be able to realize this goal in Deepak Srivastava’s laboratory at Gladstone Institutes at University of California, San Francisco. Dr Srivastava has been a perfect role model of how clinical work can direct your research to focus on questions relevant to patients—the genetic cause of the cardiac valve disease I studied during my PhD was initially identified in patients he saw in clinic as a pediatric cardiologist. I was also closely mentored by Katherine Pollard and Benoit Bruneau for the bioinformatics and epigenetic aspects of my research, and they all have been great inspirations to me to continue studying gene networks in congenital heart disease.

What Can You Say About Your Current Project and What Excites You About It?

My research in the Srivastava laboratory harnessed human-induced pluripotent stem cell–based disease modeling to reveal the transcriptional and epigenetic mechanisms of NOTCH1 haploinsufficiency in calcific aortic valve disease (CAVD). After mapping the gene networks disrupted by NOTCH1 haploinsufficiency in calcific aortic valve disease (CAVD). After mapping the gene networks disrupted by NOTCH1 haploinsufficiency in calcific aortic valve disease (CAVD).
haploinsufficiency, we developed a network-based small molecule screen that identified promising network-correcting molecules for CAVD in our human-induced pluripotent stem cell–based disease model. In parallel, we determined that long telomeres protect against age-dependent cardiac disease caused by NOTCH1 haploinsufficiency and that telomere shortening in NOTCH1-haploinsufficient mice is sufficient to elicit age-dependent CAVD that closely mimics the human disease, thereby providing an in vivo model to discover molecules that prevent CAVD.\(^3\) Finally, we resolved that telomere shortening dysregulates genes that physically interact with telomeres, suggesting a potential mechanism for telomere-dependent regulation of homeostatic gene expression. It is really exciting that we have advanced our understanding of the gene regulatory networks governing CAVD to identify potential promising therapies.

What Have Been Your Main Challenges and How Have You Overcome Them?

Any time you have research projects, you will run into technical issues. I think it is important to think creatively, outside the box, to solve these issues. For example, when we needed to expose a huge number of cells to shear stress to model blood flow in the aortic valve, and only impractically tiny chambers were commercially available, I turned to my background from other scientific fields—in this case physics—to develop our own large flow chamber that reproduced the fluid dynamics of the valve. I also think it is super important to let the data itself lead you and make conclusions from the results you see rather than the results you might have expected. I have been fortunate to have supportive and diverse colleagues to turn to for advice. Collaborating with people who think in diverse ways across laboratories and institutions ultimately moves science forward because we pool together our knowledge and expertise to develop therapies for patients.

How Do You Spend Your Time Outside of the Laboratory?

Visual art has always been a major part of my life. My art\(^4\) focuses on distinct concentrations, such as the values instilled in youth through toys, and has been influenced by many amazing mentors, including my high school instructor, artist Kevin Cole, and comic/design artist, Bernard Chang. Bernard taught me at Art Center College of Design and opened my eyes to the beauty and comic illustration. I also love playing classical and jazz piano. My favorite composer is Mikhail Glinka, who wrote a beautiful piece called “Razluka” through which my instructor, Angela Oyzboyd, showed me the musicality within piano, how music can be a form of expression. I also enjoy hiking and playing volleyball with my husband and friends.

Between Your Scientific and Artistic Pursuits, How Hard Do You Work?

Art and science have been my passions throughout my life. I guess a lot of times people feel they are different, but for me they are interconnected. There is a lot of problem solving in art. With each brush stroke in a painting, for instance, you have to think ahead and be creative about how you are going to express the image or emotion from your imagination onto the canvas. When you encounter a block in science, you also have to think creatively to solve the problem. Art, both visual and musical, has always been a positive outlet to express myself.

What Would You Do to Improve Training in Research?

I would incorporate computational biology into the core curriculum. With biology involving more and more large-scale data sets, it is becoming more important for biologists to have a strong understanding of computation and statistical inference, both so that they can better analyze their own data and to better communicate with collaborators.

What Do You Like and Dislike About Research?

Research is exciting because it is about innovation and the pursuit of truth, understanding the basic mechanisms of biology and disease to develop therapies for patients. Working with patients is rewarding because of the difference you make on the individual level, and research is rewarding because developing therapies can have wide-reaching effects. Although research can be challenging, it is not really something I dislike. You need to be persistent and creative, but I enjoy that it is challenging.

What Has Been the Most Exciting Moment in Your Career Thus Far?

I cannot pinpoint an exact moment. Any day where I am working with patients and have meaningful interactions helping kids is exciting. Or in the laboratory when we get results showing something completely new that we did not understand before and it opens a new door for therapy for those kids.

What Can You Say About Working in Pediatrics?

I love working with children. I will always carry with me the profound influence of my first experience leading a therapeutic art program as a volunteer for Free Arts for Abused Children, where I worked at a residential facility with children who had been removed from their homes because of abuse. Despite my training and previous experience with children, for weeks the group did not seem to have trust in me, their peers, or even themselves. In their past, many had been hurt by their own caretakers; how could I convince them to trust me to help them heal? But, I returned week after week with new approaches to dispel the kids’ fear of drawing something “wrong.” I remember when I finally saw their lines begin to transform from rigid, introverted marks to bold, expressive strokes, and I will never forget the last day of the program when one of the girls told me that she had learned “there are no mistakes in art.” Despite its challenges, pediatric medicine is the most fulfilling of callings, and I am devoted to helping children heal through both art and science.

What Worries You Most About Your Future and What Do You Hope for Your Future?

Research is a long-term investment. It can be easier to take more short-term approaches, but I think it is important that
as a society we continue to invest in basic science as a path to innovation and discovery of therapies for human disease. In my future, I would like to pursue a career as a physician scientist treating patients in pediatric cardiovascular genetics and continuing research determining the gene regulatory networks governing cardiac disease to identify promising targets for network-correcting therapies.

Disclosures
None.

References
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