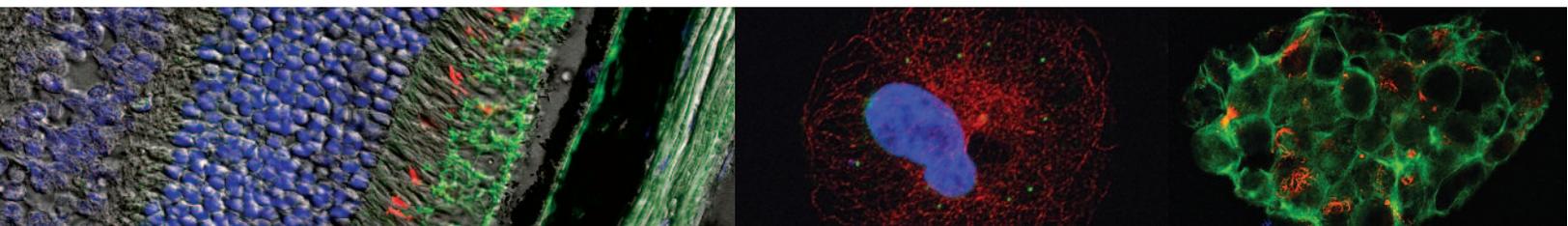


DIFFERENT SCIENTIFIC APPROACHES;
ONE GOAL

*Dr. Kathleen Boesze-Battaglia and Dr. Claire Mitchell Taking a Hard Look at Vision
While Illuminating Studies Across Disciplines*

BY AMY BIEMILLER



Divide and conquer. In scientific research, applying this approach and collaborating on results can yield advances and applications across wide-ranging fields of study. Two Penn Dental Medicine researchers, Dr. Kathleen Boesze-Battaglia and Dr. Claire Mitchell, are doing just that in the fight against blindness. One researcher works predominantly on the question of “why” and the other investigates the “how” of cellular function and eye disease. Together they are producing a body of work focused on addressing genetic conditions like retinitis pigmentosa, the most common form of inherited retinopathy, characterized by progressive vision loss and eventual blindness; age-related macular degeneration, the leading cause of blindness of people over 50; and glaucoma. In the process, they are just as importantly shedding light on disease and cellular behavior and contributing a unique perspective to investigations with applications across disciplines, including the study of periodontal disease.

While it may seem counterintuitive that researchers at Penn Dental Medicine are investigating approaches to treating and curing blindness, scientists like Drs. Boesze-Battaglia and Mitchell are in fact purposefully recruited to the School to build a research enterprise with a depth and breadth that brings together investigators with diverse expertise and experience.

“Today’s research environment is moving at a pace faster than ever before. Effective science means using multiple approaches and technologies. The best research is that which is interdisciplinary and involves multiple investigators with a greater range of expertise,” says Dr. Bruce J. Shenker, Associate Dean for Research at Penn Dental Medicine and Chairman of the Department of Pathology. “These collaborative approaches also enhance overall research productivity and effectiveness as well as significantly contribute to making our entire faculty more competitive for extramural research funding.”

Leveraging Biochemistry. Dr. Boesze-Battaglia is Professor of Biochemistry at Penn Dental Medicine and also holds a secondary appointment as Associate Professor of Biochemistry and Molecular Biophysics in Penn’s School of Medicine. Recruited to the School in 2002, she brought with her a body of research on how the RDS protein, which has over 160 different mutations, leads to retinal degeneration.

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As a biochemist, Dr. Boesze-Battaglia investigates why biological problems within retinal-specific cells occur. She is especially interested in protein structure-function relationships and lysosomes. Proteins often allow a cell to maintain its structure and lysosomes work to break down cell waste and debris. In the eye, these building blocks allow rods and cones to work as photoreceptors, giving us the capacity to not just see, but to perceive color, depth, and intensity. When the chemical process in these cell components goes wrong, eye disease and blindness can be the result.

Working to uncover where in the process things go wrong is key to developing treatment for ocular diseases that, today, have no cure. It is a complex quest that requires much patience.

“Understanding this protein and its contribution to the etiology of retinal degenerative disease is essential in the development of a viable therapeutic approach to slowing the progression of that degeneration,” she says. “Luckily, this work has been continuously funded for almost 20 years.” Dr. Boesze-Battaglia, who holds a Ph.D. in Biochemistry from SUNY at Buffalo, was on the faculty of the University of Medicine and Dentistry of New Jersey for 10 years before coming to Penn Dental Medicine.

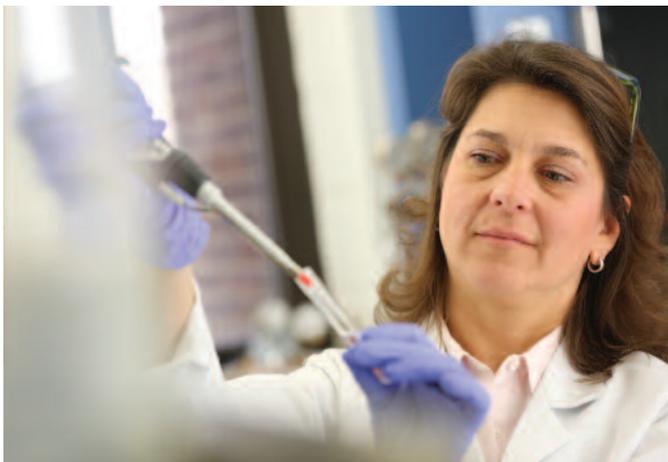
“Our work specifically focuses on understanding why the chemical processes of retinal cells, including lysosome maturation, phagocytosis, and autophagy (a cell’s defensive processes) go awry and contribute to the degenerative phenotype,” she says. “Defects in these pathways not only contribute to retinal degenerative disease, but are also linked to several neurodegenerative phenotypes, an area we are expanding into.”

Different Scientific Approaches; One Goal

Her research holds promise of therapeutic potential; testing is underway to determine if a protein regulator of lysosome maturation can halt the progression of retinal disease by decreasing the accumulation of toxic lipids within the cell.

Applying Physiology. One floor away from the Boesze-Battaglia lab, a newer recruit – Dr. Claire Mitchell, Associate Professor of Anatomy and Cell Biology – is taking a different approach to eye disease and blindness. She investigates how healthy retinal cells carry out their chemical and physical functions and uses these mechanisms to repair the cells in pathological situations.

“As a cell physiologist, the ‘how’ question drives my research forward; how do the processes work in a healthy cell, how are the sequences of pathological events connected,” explains Dr. Mitchell, who joined the School’s Department of Anatomy and Cell Biology in September 2009. Dr. Mitchell, who holds a Ph.D. in physiology from University College London, came from the Physiology Department of Penn’s School of Medicine, where for 11 years she developed her independent lab and where she holds a



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secondary appointment. The cause and effect of cellular strain is of great interest to Dr. Mitchell and here at Penn Dental Medicine she is investigating two areas: the consequences of strain on neurons, and how to acidify lysosomal pH in aging retinal cells.

“We are testing different drugs to determine if we can lessen a cell’s normal inflammatory response to strain, thereby reducing the damage that strain does to neurons. While this work has direct application for glaucoma, we are working on a general level so that the mechanisms we are identifying may apply to cells throughout the whole body,” she says. “In the lysosomal research, we are investigating ways to restore the acidity to lysosomes so that waste material in a cell can be disposed of properly, thus alleviating cell inflammation and improving ocular health.”

Collaborative Infrastructure. Both researchers agree that the collaborative environment at Penn Dental Medicine and throughout the University creates a fertile ground for research.

“Collaborating here at Penn is incredibly easy – we all really want to help each other,” says Dr. Boesze-Battaglia. “I have been able to share my area of study with many other researchers at Penn Dental Medicine and across campus and benefit from their expertise as well. What keeps me here at Penn is the collegiality and intellectual and technical infrastructure of the University. You just can’t find or recreate everything Penn offers anywhere else.”

Through her nine-year tenure with the School, Dr. Boesze-Battaglia has built strong collaborations with fellow investigators that have bolstered the School’s scholarship and led to new projects and funding. “By interacting with my colleagues I have expanded my research interest into understanding how pathogenic bacteria, specifically perio-pathogens, are internalized, persist, and survive,” says Dr. Boesze-Battaglia. Among her collaborative activities are studies with Drs. Edward Lally and Bruce Shenker, both Professors of Pathology, on understanding how toxins released by perio-pathogens lead to disease. “Our collaboration has helped us understand pathogenesis of periodontal infection that we have used to develop a new project in our lab looking at mechanisms of subversion of immune response,” says Dr. Boesze-Battaglia.

Entering on the path of her colleague, Dr. Mitchell notes that she found the strength of the researchers within Penn Dental Medicine especially attractive in deciding to make a move across campus. “I moved here from the School of



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Dr. Claire Mitchell

Medicine because of the wonderful opportunities to work with top-rate researchers and to have the chance to strengthen my understanding of inflammatory processes and biomechanical forces,” she explains. “I really enjoy being one floor away from Kathy with frequent opportunities to bounce ideas off of one another.”

One of Dr. Mitchell’s current collaborative projects is with Dr. Edward Macarak, Chairman of the Department of Anatomy and Cell Biology at Penn Dental Medicine. “Collaborating with Ed has really advanced my work on mechanosensitive processes in neurons,” she says. “As an engineer, he understands these forces at a deep level and has helped us understand how the mechanical strains on cells can activate processes that lead to the release of neurotransmitters and inflammatory signals.”

By working together and with other researchers at Penn Dental Medicine, Drs. Boesze-Battaglia and Mitchell are forming a hypothesis that suggests that early stage macular

degeneration is a dysfunction of lysosomes. “This begins a cascade effect that results in damage down the line,” says Dr. Mitchell. “By targeting the lysosomes, we hope to be able to prevent that damage.”

“Looking at degenerative eye disease and blindness from different angles and working together to find the answers, we leverage the collective knowledge and experience of scientists who all believe that basic science drives mechanisms that drive therapy,” says Dr. Boesze-Battaglia.

“While we are focused on helping prevent the loss of sight encountered in genetic and age-related eye disease, I believe our work has much broader implications,” adds Dr. Mitchell. “Cellular processes are fundamental to all human health. There are many similarities in oral and ocular systems, and the role of inflammation is increasingly recognized as important in both systems. So there is much to be learned and shared that can help advance our understanding across disease applications.”

Encouraging New Researchers. Sharing their work and research perspective with students drives both Drs. Mitchell and Boesze-Battaglia as well. Each serve as preceptors in the School’s Summer Student Research Program, which gives students hands-on experience in basic and clinical science research, and Dr. Boesze-Battaglia oversees the research honors component of a new student honors program she helped to launch this academic year. This competitive opportunity enables students to form mentor relationships and plan, implement, and execute a hypothesis-driven research project over a span of one to two years.

“The real joy of the job is encouraging students to ask their own questions, then see them try their own ideas and look at the outcomes,” says Dr. Mitchell, who also co-coordinates the research seminar series at the School, which is open to students, faculty, and researchers throughout the campus. “One of the best things I can do is inspire students who have an interest in research to pursue that work and develop their sense of intellectual curiosity,” adds Dr. Boesze-Battaglia. “Being a scientist isn’t a job. It’s a way of thinking.” **PDJ**