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LAB & CLINIC

THE CROSSOVER CAREER OF MIRA EDGERTON

BY JIM BISCO

SALIVARY RESEARCH was pioneered in UB's Department of Oral Biology by its first chair, Solon (Art) Ellison, and then propelled into the modern technological era by Michael Levine, '71, whose work influenced a generation of young researchers, among them Mira Edgerton.

"So many of us here now have been trained by Mike. He stressed the importance of getting involved in research in a substantial way," she says today about her work with him in the 1980s. "At the time, salivary research was in its infancy, and it was exciting to be a part of that. For a dentist, it was very interesting because it was such a new area and people didn't really appreciate the importance of saliva to oral health."

Edgerton, a research professor in both oral biology and restorative dentistry, has been mining the rich potential of salivary research for more than 20 years. (She earned a DDS at Case Western Reserve University in 1979; and a certificate in removable prosthodontics in 1981, an MS in oral science in 1984 and a PhD in oral biology in 1994, all at UB.)

She has seen patients in the clinic who have lost saliva due to medications, chemotherapies and various other reasons. She has seen patients in her prosthodontics practice with Sjögren's syndrome, an inflammatory disease that destroys salivary function.

"When you see what a severe problem it is to their oral health and sometimes even to their eating and swallowing and functioning, you appreciate the importance of saliva," she says.

Edgerton says that her clinical practice gives her unique insights into patients with particular problems and the clinical issues that can be addressed in basic research. "In my research component here, I look at specific aspects of basic science and salivary research that could potentially benefit these patients at some point," she says.

Edgerton recalls that during her specialty training in the 1980s, the search for an effective salivary substitute was underway to help people afflicted with dry mouths. While the search continues for that elusive goal, the research focus, according to Edgerton, has narrowed.

"We didn't really understand what the multitude of components were in saliva," she says. "Saliva has hundreds of proteins and most of them have their own distinct function—and there are families of proteins with interrelated functions. I think where the field has evolved is to a better understanding of individual components and proteins in saliva and how we can enhance them."

Edgerton began to explore salivary antimicrobial agents, specifically the histatin and defensin proteins that keep bacteria and yeast from overgrowing. Such overgrowth leads to oral candidiasis, an opportunistic disease found in patients receiving cancer chemotherapy, AIDS patients, diabetics and in many elderly groups, especially those using oral prostheses.

"Histatin is sort of the innate immune in saliva," she explains. "Then there is the host immune. These two branches of immunity that we're studying prevent oral candidiasis. Sjögren's patients have a lot of oral candidiasis because they lack the innate immune of the histatins and salivary components, whereas the HIV patients are missing another immune component."

HIV-positive patients have been a particular focus—they often develop a high level of this disease. For a long time the search was on for the missing immune component that predisposes these patients to the disease, lowering their CD4 cell levels.

Edgerton collaborated with Sarah Gaffen, a former member of the oral biology department who is now at the University of Pittsburgh, in research that revealed why these patients are so susceptible to candidiasis: they lack a Th cell known as Th17, a principal defense component required for immunity.

"We're trying to develop the immune components for HIV patients who are Th17 deficient," she says. "If we understand the immune basis for the defect, then we can look at ways to modulate or replace or enhance what they're missing in their immune system."

Edgerton's hope is that salivary proteins can be used as therapeutics. "There still is not any good drug on the market now to treat oral candidiasis. It's actually a very large problem. So we're hoping that natural proteins will be therapeutic agents. Our ultimate goal for this research is to come to a clinical chair-side application."

This goal reflects the new focus of the National Institutes of Health (NIH) on bringing basic research findings more quickly to clinical applications, according to Edgerton. "I think we're seeing things on the horizon that will translate to clinic," she says. "There's an awfully big patient population that has bacterial yeast infections for which targeted peptide therapies will be very, very helpful. We're getting close."

Edgerton has received NIH funding for her research for the past 20 years. She recently received a $115,000 grant through a provision of the American Recovery and Reinvestment Act of 2009 that provides funding to explore areas beyond the focus of one's research.

"Often when you're doing research, you find really cool and interesting things that you'd like to pursue but that are not directly the main thrust of your work," she says. "The stimulus money funds that for you. In one of the fungal proteins that we looked at, we discovered that if the yeast are missing this protein, they can't colonize in mice and they don't have any infection properties. We never expected to find that. It was something we found in the course of looking at our histatin targets. So we submitted to the NIDCR (National Institute of Dental and Craniofacial Research) that we would like to see why it is essential for the yeast to colonize and become variable in this protein. It was a neat opportunity to go beyond what we initially planned with our various findings."

Edgerton, who is director of the doctoral program in oral biology, appreciates working with a wide variety of students, from undergraduates to postgraduates. "The really fun thing about being at a university dental school is to get students excited and involved with research—to look beyond what they see in the clinic," she says.

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Edgerton has played an integral role in helping to build an internationally recognized oral biology department. "We've recruited a lot of younger, new people in the department that have great careers ahead of them," she says. "Oral biology is a great place to be as a researcher. It's a really collegial department with lots of exchange of ideas."

Edgerton was a violinist when she was an undergraduate at Ohio State. "I decided that was probably going to be too tough a lifestyle and career, so I went back to the sciences," she recalls. "Dentistry just seemed to be an interesting area that combined science, research and medicine. It's a terrific career."