Cancer biology graduate student travels 'ROCKy' road toward a cure for post-radiation dry mouth

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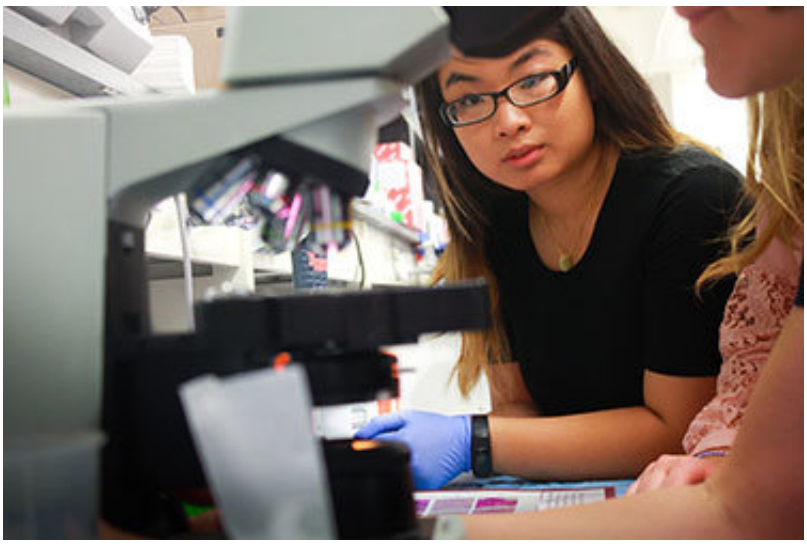

Wen Yu "Amy" Wong. Credit: Gaius J. Augustus

The United States is in the midst of a head-and-neck cancer epidemic. Although survival rates are relatively high—after treatment with chemotherapy and radiation—survivors can suffer permanent loss of salivary function, potentially leading to decades of health problems and difficulties eating.

It is unknown why the salivary gland sometimes cannot heal after radiation damage, but Wen Yu "Amy" Wong, BS, a University of

Arizona cancer biology graduate student, may have taken a step toward solving that riddle.

Radiation often comes with long-term or even permanent side effects. With a head-and-neck tumor in radiation's crosshairs, the salivary gland might suffer collateral damage.

"When you get radiation therapy, you end up targeting your salivary glands as well," Wong said. Losing the ability to salivate predisposes patients to oral complications and an overall decrease in their quality of life. "Salivary glands help you digest food, lubricate your mouth and fight against bacteria. After radiation, patients could choke on their food because they can't swallow. They wake up in the middle of the night because their mouth is so dry. They often get cavities."

Favorite foods may lose their flavor. "Saliva produces certain ions that help you taste," she said. "Patients lose the ability to enjoy food. The best steak is very bland to them."

The quest to restore salivary function in post-radiation head-and-neck cancer patients starts with learning why the salivary gland is unable to heal itself after radiation damage.

Wong's study may have helped to unravel this mystery. Her team looked closely at two proteins, E-cadherin and β-catenin, which allow communication between cells. Normally, these proteins bind cells together, but after radiation damage, these connections are severed. "Think of them as telephone wires," Wong said. "Radiation is like lightening hitting a telephone pole. That breaks the ability of one friend to talk to another on the other side of the city."

Just as a maintenance crew can repair downed telephone poles after a storm, the body is able to heal itself after injury. Unfortunately, in post-

radiation dry mouth, salivary glands' ability to regenerate might be blocked.

In the lab, Wong was able to artificially force the regeneration of salivary glands, allowing her to learn where there are obstructions in the regeneration process. Wong particularly was interested in something called the ROCK pathway, which might go awry in the wake of radiation, blocking E-cadherin and β-catenin from reuniting.

"If I use an inhibitor to prevent this ROCK signaling pathway, these two proteins come back together," Wong said.

The next step is to learn more about how a defective ROCK pathway blocks salivary glands' natural ability to regenerate following radiation damage. Unlocking this secret could uncover novel ways to treat or cure post-radiation dry mouth.

Earlier this month, Wong and her co-authors were recognized by the American Physiological Society for their investigation, which was published in June by the *American Journal of Physiology—Regulatory, Integrative and Comparative Physiology*. Wong, along with Maricela Pier, BS, a research specialist with the UA College of Medicine—Tucson Department of Cellular and Molecular Medicine, and Kirsten Limesand, Ph.D., of the UA Cancer Center and professor of nutritional sciences with the UA College of Agriculture and Life Sciences, was selected for the APSselect award, given to the best articles in physiological research.

Wong selected Dr. Limesand's lab as her "home base" throughout her graduate studies because "I wanted to connect with a woman in science who understands the difficulties. She was very easy to talk to, and the people in the lab provide a very nurturing environment. She is a great mentor."

Dr. Limesand takes her role as a mentor seriously, and finds it deeply satisfying.

"Hands down, the most rewarding aspect of my career is training students," Dr. Limesand said. "They're our next generation of scientists, tackling the big questions that need to be solved."

Dr. Limesand is a professor with the UA Cancer Biology Graduate Interdisciplinary Program, which emphasizes translational research to address significant problems relating to cancer development and treatment. Students are prepared for careers in cancer research through an interdisciplinary approach involving faculty members from a wide range of disciplines.

"I have students from cancer biology and physiological sciences, and I've been on committees of genetics students and immunobiology students," said Dr. Limesand. "These diverse perspectives add to the research we're doing."

More information: Wen Yu Wong et al, Persistent disruption of lateral junctional complexes and actin cytoskeleton in parotid salivary glands following radiation treatment, *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* (2018). DOI: 10.1152/ajpregu.00388.2017

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