Joey Garcia
February 7, 2022

Miller School Study of Intricate Cellular Processes Wins Prestigious Early Career Investigator Award

Jacob Rowe, a pharmacology Ph.D. candidate at the University of Miami Miller School of Medicine, has been selected as one of six 2022 recipients of the JBC Herbert Tabor Early Career Investigator Award for his paper “The Evolution and Mechanism of GPCR Proton Sensing.”

Jacob Rowe

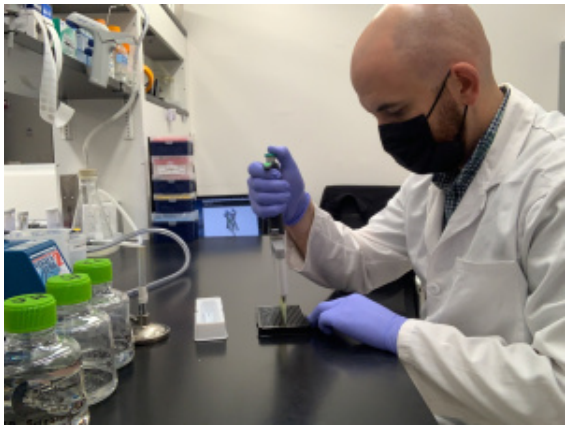
Honoring innovation and excellence in the work of first authors of exceptional research papers published in the *Journal of Biological Chemistry*, the recognition also includes an invitation to a spotlight session at the American Society for Biochemistry and Molecular Biology Annual Meeting.

Rowe’s study was designed to identify the mechanism of proton-sensing G protein-coupled receptors, or GPCRs, a challenge

pursued by researchers for nearly two decades.

Located on the surface of cells, these proteins sense changes in the balance of acidity and alkalinity (pH) in the blood that can be associated with varied medical conditions, including tumor formation.

For example, the low-pH (acidic) environment of pancreatic ductal adenocarcinoma (PDAC) tumors has been shown to activate the proton-sensing receptor GPR68 in cancer-associated fibroblasts (connective tissue cells). This process fosters the expression of proinflammatory cytokines that, in turn, promote the proliferation of PDAC cells.



Jacob Rowe performing functional tests of GPCR variants at acidic and neutral pH.

Rowe's study elucidated this mechanism by identifying three significant components unique to these proteins that are essential for their pH-sensing ability. His findings illuminate the importance of these proton-sensing receptors in other tumor types and low-pH-associated processes such as tissue repair.

“With a complete understanding of how these receptors work at the molecular level, we can genetically control their behavior and thoroughly assess the importance of receptor pH sensing in more physiological settings,” Rowe said. “This will be especially important for biological processes linked to changes in pH, such as ischemia and inflammation.”

While Rowe’s research deepens understanding of the underlying pH-sensing mechanism, only a few drugs that target proton-sensing GPCRs currently exist. Most of these lack selectivity, leading to unintended side effects of ambiguous origin. The next steps in developing more targeted drugs involve identifying candidates from a class of specific protein-based drugs known as nanobodies.

“These findings elucidate the molecular evolution and long-sought mechanism of GPR4, GPR65, and GPR68 pH sensing,” Rowe said. “They also provide pH-insensitive variants that should be valuable for assessing the therapeutic potential and (patho-) physiological importance of GPCR pH sensing.”

Content Type article