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UAMS Receives \$3 Million NIH Grant for Novel Pituitary Gland Research

LITTLE ROCK — A University of Arkansas for Medical Sciences (UAMS) research team has been awarded a \$3 million grant from the National Institutes of Health (NIH) to test promising findings that could lead to better treatments for hormone loss caused by a malfunctioning pituitary gland.

The five-year R01grant from the NIH National Institute of Diabetes and Digestive and Kidney Diseases is focusing on the pituitary's hormone-producing cells, with a particular focus on manipulating a protein that the team found controls how the cells behave.

"Understanding how pituitary cells shift their functions to respond to changing needs could help us not only treat hormone deficiencies but also potentially control cancer cells that similarly 'switch fates' to resist treatments," said Angus MacNicol, Ph.D., coprincipal investigator and a professor and vice chair for the College of Medicine Department of Neuroscience.

MacNicol, an expert in molecular biology, is joined on the study by two other coprincipal investigators: Gwen Childs, Ph.D., an expert in pituitary physiology and a distinguished professor, and Melanie MacNicol, Ph.D., an expert in cell biology and an associate professor. Both are in the Department of Neuroscience.

Angela Odle, Ph.D., an assistant professor in the Department of Neuroscience, and Stephanie Byrum, Ph.D., an associate professor in the College of Medicine Department of Biochemistry and Molecular Biology, are co-investigators on the project.

The three co-principal investigators joined forces more than 10 years ago, and Angus MacNicol hopes the team science approach will continue to advance their work.

"We have complementary expertise, and none of us could have moved our previous projects forward to the point we are now if we had all been working independently," he said. "We have a synergy where the sum is greater than the parts." UAMS Receives \$3 Million NIH Grant for Novel Pituitary Gland Research Page 2

Current hormone replacement therapies cannot fully replicate the body's natural hormonal cycles, highlighting the need for innovative approaches. The pituitary gland, located at the base of the brain and no larger than a pea, produces hormones that regulate critical bodily processes, including growth, metabolism and stress response.

Cells within the gland have unique flexibility — called plasticity — to adjust which hormones are produced in response to changing conditions. A protein called Musashi plays a critical role in how the cells function in hormone production, MacNicol said. Further understanding of Musashi's regulatory mechanisms could potentially lead to the design of small molecules that would force Musashi to help cells work more effectively, or even less effectively, to correct defective hormone production.

"Ultimately, the hope is that we could control pituitary function to compensate for hormone loss as we age," MacNicol said. "This could lead to new ways to restore hormone balance. An ability to control Musashi activity could be applicable to inhibit cancer cells from becoming resistant to treatments."

The team is using state-of-the-art mRNA (messenger RNA) and miRNA (micro RNA) sequencing alongside mass spectrometry to provide a comprehensive analysis of the gene expression and protein synthesis that govern pituitary cell function. Unlike traditional research that centers on gene transcription, the study is exploring how the cells behave after the genetic instructions are copied from the DNA into the mRNA.

"The techniques we're applying are cutting-edge," MacNicol said. "They haven't been applied to the pituitary before. That's why people are excited about the project."

UAMS is the state's only health sciences university, with colleges of Medicine, Nursing, Pharmacy, Health Professions and Public Health; a graduate school; a hospital; a main campus in Little Rock; a Northwest Arkansas regional campus in Fayetteville; a statewide network of regional campuses; and eight institutes: the Winthrop P. Rockefeller Cancer Institute, Jackson T. Stephens Spine & Neurosciences Institute, Harvey & Bernice Jones Eye Institute, Psychiatric Research Institute, Donald W. Reynolds Institute on Aging, Translational Research Institute, Institute for Digital Health & Innovation and the Institute for Community Health Innovation. UAMS includes UAMS Health, a statewide health system that encompasses all of UAMS' clinical enterprise. UAMS is the only adult Level 1 trauma center in the state. UAMS has 3,485 students, 915 medical residents and fellows, and seven dental residents. It is the state's largest public employer with more than 11,000 employees, including 1,200 physicians who provide care to patients at UAMS, its regional campuses, Arkansas Children's, the VA Medical Center and Baptist Health. Visit www.uams.edu or www.uamshealth.com. Find us on Facebook, X (formerly Twitter), YouTube or Instagram.

