Richard Westlund
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Collaborative Miller School Study Finds Potential Treatment for Rare Genetic Condition

A collaborative research team at the University of Miami Miller School of Medicine has developed a potential treatment strategy for Alport syndrome, a rare genetic condition characterized by kidney disease, hearing loss, and eye abnormalities.

Top row, from left, Alfonso Sabater, M.D./Ph.D., Bradley Goldstein, M.D./Ph.D., Armando Mendez, Ph.D., and Keyvan Yousefi, Pharm.D. Bottom row, from left, Stefania Goncalves, M.D., Guerline Lambert, M.S., Lina Shehadeh, Ph.D., Wen Ding, PhD., and Amy

Kloosterboer.

“Our team identified high levels of a protein called osteopontin in the renal tubules of laboratory ‘Alport’ mice, causing extensive cholesterol accumulation and other metabolic problems,” said Lina Shehadeh, Ph.D., assistant professor in the Department of Medicine’s Division of Cardiology and the Interdisciplinary Stem Cell Institute (ISCI). “Our prior studies have shown that reducing osteopontin can ameliorate the severity of cardiovascular disease, and this new study aimed to investigate for the first time the role of osteopontin in Alport syndrome.”

Shehadeh is senior author of the study, “Osteopontin Deficiency Ameliorates Alport Pathology by Preventing Tubular Metabolic Deficits,” published in the journal, *JCI Insight*, on March 22. Wen Ding, Ph.D., former doctoral student of pharmacology at Shehadeh’s lab, now doing her postdoctoral training at Yale School of Medicine, is first author, and Keyvan Yousefi, Pharm.D., a current doctoral student of pharmacology in the Shehadeh lab, is second author. Other Miller School co-authors were Alfonso Sabater, M.D., Ph.D., Bradley Goldstein, M.D., Ph.D., Armando Mendez, Ph.D., Stefania Goncalves, M.D., Guerline Lambert, M.S., Portia Ritter, M.S., and Amy Kloosterboer.

Noting that her students did “a phenomenal job” on this study, Shehadeh added, “The rich environment at the Miller School and ISCI enabled this research. Because patients with Alport syndrome have hearing and visual deficits, and also cholesterol abnormalities, we collaborated with faculty from the Department of Otolaryngology, the Department of

Ophthalmology, and the Diabetes Research Institute to assess the impact of reducing osteopontin as a potential therapeutic strategy."

The Miller School researchers found that reducing osteopontin by genetic deletion can prevent kidney, vision, and hearing pathologies in the Alport mouse and could significantly extend its lifespan.

"We now have solid evidence that reducing osteopontin is therapeutic in various disease mouse models," Shehadeh said. "We are now testing several methods of pharmacological inhibition of osteopontin in the Alport mouse, such as using a monoclonal antibody against osteopontin that can be delivered by intravenous injections or small implanted pumps. The goal is to test a pharmacological reagent in mouse and then attempt to transfer this potential treatment to humans."

Shehadeh said she is grateful to the Miami Heart Research Institute for funding and enabling her work.