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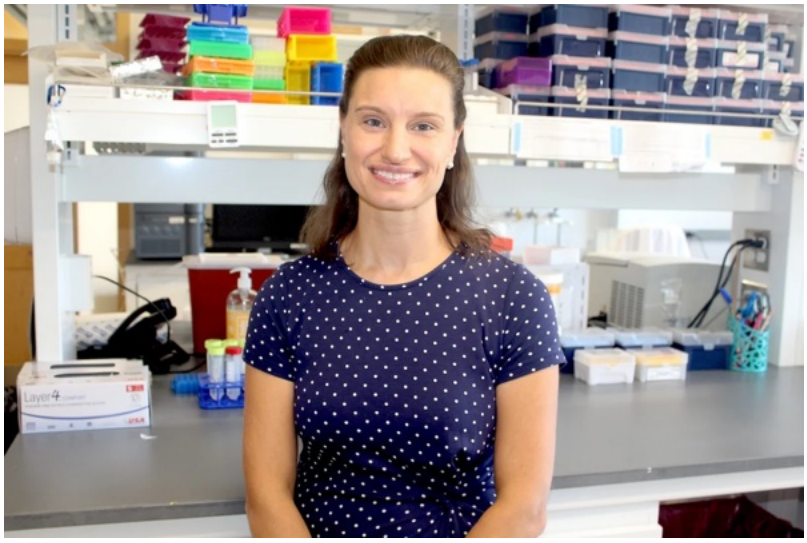
URI professor wins national grant to study rare diseasethat can lead to cirrhosis, liver failure

Pharmacy Professor Nisanne Ghonem's American Liver Foundation award will help fund probe into novel medications to treat primary sclerosing cholangitis



URI College of Pharmacy Associate Professor Nisanne Ghonem recently received a research award from the American Liver Foundation for her study of medications to treat primary sclerosing cholangitis, a rare autoimmune disease that can lead to cirrhosis and liver failure.

KINGSTON, R.I. — Nov. 18, 2024 — University of Rhode Island College of Pharmacy Associate Professor Nisanne Ghonem is among eight recipients in the country of a pilot research award from the American Liver Foundation, which will help advance her research into a rare liver disease that can lead to cirrhosis, liver failure and ultimately, premature death.

Primary sclerosing cholangitis (PSC) is a chronic autoimmune disease characterized by the accumulation of harmful bile acids and liver inflammation. The condition causes bile ducts inside and outside the liver to become inflamed and scarred, and eventually narrowed or blocked, according to the National Institutes of Health. When this happens, bile builds up in the liver and causes further damage, leading to pain in the abdomen, itchy skin, diarrhea, and jaundice, potentially leading to cirrhosis. As cirrhosis progresses and the amount of scar tissue in the liver increases, the liver slowly loses its ability to function, eventually leading to failure.

There is no effective therapy for PSC, which is often caused by an immune system reaction to an infection or toxin, especially in people who are genetically predisposed to it and may also have inflammatory bowel disease, including ulcerative colitis and Crohn's disease. Ghonem's study, partially funded by the American Liver Foundation, investigates new medications to treat cholestasis (a failure of bile flow) in those with PSC.

The study will measure the presence of mutations in UGT genes, which are involved in the elimination of harmful bile acid molecules, and metabolizing medications. Ghonem and her team will test the effects of drugs called peroxisome proliferator-activated receptor (PPAR) activators on UGTs, mutations that may dampen the effectiveness of the drugs in treating PSC.

"Our earlier research found that patients with PSC who were treated with fenofibrate, a PPAR alpha activator, have improved UGT processing of bile acids," Ghonem wrote in a project description. "We also found that fenofibrate can reduce the inflammatory

response of immune cells to bile acids. However, to date, no studies have directly compared the newer candidate PPAR drugs to understand which medication performs best, and the role of the UGT gene mutations in influencing the treatment response to these drugs in PSC is unknown."

Therefore, Ghonem's study will compare the PPAR activators and their impact on UGT mutations, UGT enzymes, immune cells called T-cells, and liver cell inflammation. The study will help address the unmet need in treating PSC by seeking new mechanisms for PPAR drugs to improve symptoms, and provide a rational basis for selecting current PPAR drugs to treat the disease.

Ghonem's award is one of eight ALF 2024 Pilot Research Awards distributed across the country, which will help fund innovative projects seeking to address important questions related to PSC, Autoimmune Hepatitis, or Biliary Atresia. The goal of the program is to provide funding during the pilot phase of research projects focused on new areas of investigation, innovative ideas, or "high-risk, high-reward" projects that have the potential to generate breakthrough findings and significantly advance the field.

"There are more than 100 different types of liver diseases. We need innovative research into these rare diseases that might not be funded elsewhere," said Emmanuel Thomas, ALF board chair and associate professor at the University of Miami School of Medicine. "It's essential for us to understand how to treat these diseases, and how we can explore solutions that could help young patients living with liver disease."