Study identifies gene variants to help personalize treatment of eosinophilic esophagitis

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A group of three gene variants, commonly inherited together, may provide clues to more successful treatment of pediatric eosinophilic esophagitis (EoE), a chronic inflammation of the food pipe often confused with gastroesophageal reflux disease (GERD). A new study, led by researchers from Nemours Children's Health System and published in *Clinical Gastroenterology and Hepatology*, identifies genetic variants that help predict which children with EoE may not respond to proton pump inhibitor (PPI) medication therapy as a long-term solution.

"Our goal is to personalize therapy for children with EoE based on their unique genetic profile—finding the right medication, at the right dose for the right child," said James P. Franciosi, MD, senior author and Chief of Gastroenterology, Hepatology and Nutrition at Nemours Children's Hospital. "This novel research study identifies genetic variants that can help us predict which children with EoE will respond to PPI therapy over the course of one year and potentially avoid relapse and additional invasive procedures."

EoE is a chronic immune condition, often caused by reactions to certain foods, that leads to inflammation of the esophagus. Symptoms may include difficulty swallowing, chest pain, heart burn, abdominal pain, nausea, and vomiting. EoE is becoming increasingly more common with both new diagnoses and total number of patients increasing yearly. More than 30 percent of children receiving long-term treatment for EoE experience relapse, but currently it is not possible to predict who is likely to suffer a relapse. Children with this condition are often treated with PPI medications, which are also prescribed for common acid reflux-related conditions.

The research team found that having any of three STAT6 variants that are commonly inherited together increases the odds that PPI therapy will fail children with EoE at some point, either in the initial high-dose therapy phase or the subsequent year of low-dose maintenance therapy.

This prospective, longitudinal cohort study involved 73 children ages 2-16 years old who met the diagnostic criteria for EoE, responded to an initial eight weeks of 2mg/kg daily PPI therapy and were subsequently stepped down to 1 mg/kg daily PPI maintenance therapy for one year. Genomic DNA was isolated, and genotyping conducted. The research team found that patients who initially respond to PPI therapy but carry any of three specific STAT6 variants are at increased risk of relapse after one year of PPI maintenance therapy.

Franciosi noted that a dosage that is too low or too high could lead to treatment failure or PPI-associated side effects including upper respiratory and GI tract infections.

"There is more work to be done before we can say with certainty which children will respond to PPI therapy for this painful condition," said Edward B. Mougey, Ph.D., lead author of the study, and a researcher with Nemours' Center for Pharmacogenomics and Translational Research. "Research is ongoing, and our goal continues to be to personalize, as much as possible, the treatment and care we provide to each child."

"My son is currently in remission and has been responsive to PPIs, but EoE is still a constant condition he is managing—from determining what he can eat, to maintaining his weight and energy levels," said Laura Moore, of Jacksonville, Fla. and mother of a child with EoE. "This research will help improve my son's treatment going forward, but also help other kids will have better experiences in the

future."

More information: Edward B. Mougey et al, STAT6 Variants Associate With Relapse of Eosinophilic Esophagitis in Patients Receiving Long-Term Proton Pump Inhibitor Therapy, *Clinical Gastroenterology and Hepatology* (2020). DOI: 10.1016/j.cgh.2020.08.020