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Study finds genetic analysis can aid treatment of eosinophilic Esophagitis

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Personalized medicine—where the proper medicine and proper dose are used for the individual patient—moved a step closer to reality for children suffering from eosinophilic esophagitis (EoE), an inflammation of the food pipe often caused by an allergic reaction to certain foods. The study, led by researchers from Nemours Children's Health System and published today in the *Journal of Pediatric Gastroenterology & Nutrition*, suggests that a simple genetic test from a saliva sample may greatly boost response rates in children with eosinophilic esophagitis who are treated with a class of medications called proton pump inhibitors (PPIs), which are commonly prescribed to treat acid-related conditions.

"Currently only 30 to 60 percent of children respond when treated with proton pump inhibitors to reduce inflammation from eosinophilic esophagitis," said senior author James P. Franciosi, MD, Chief of Gastroenterology, Hepatology and Nutrition for Nemours Children's Hospital. "Our study found that treatment response is strongly influenced by common genetic variants that affect how the body metabolizes or responds to PPIs. These findings could lead to individualized therapy based on a person's genetics."

Eosinophilic esophagitis (EoE) is a chronic immune condition that leads to inflammation of the esophagus. Symptoms include difficulty swallowing, abdominal pain, nausea, and vomiting. EoE is considered rare, but new diagnoses are increasing, along with the total number of patients. PPIs, which are often prescribed for a more common

condition—gastroesophageal reflux disease, or GERD—are one treatment for EoE.

The research team analyzed DNA from esophageal tissue biopsies of 92 patients, from 2 to 16 years old. In children who received PPI therapy for EoE, the study found patients with a combination of certain common gene variants were nearly nine times more likely to fail to respond to PPI treatment. They also found that based on the genetic analysis, some patients were less likely to respond to certain dose levels, and genotyping may allow for more accurate customization of doses.

"Without considering information about a patient's genetics, clinicians may be prescribing a lower or higher PPI dose than is necessary, which could lead to treatment failure or PPI-associated side effects including upper respiratory and GI tract infections," said lead author Edward B. Mougey, Ph.D., of Nemours' Center for Pharmacogenomics and Translational Research. "The general strategy of dose adjustment to compensate for genetic variants of drug-metabolizing enzymes carried by an individual is the cornerstone of precision medicine."

Dr. Franciosi notes that the next step for this research is to conduct clinical trials for EoE and acid-related disorders such as GERD to determine exactly how to adjust PPI dose based on an individual's genetics. He said, "Using genetics to personalize PPI drug therapy to the individual patient may ultimately improve efficacy and reduce side effects, resulting in significant benefits for many children."

More information: Edward B. Mougey et al, CYP2C19 and STAT6 Variants Influence the Outcome of Proton Pump Inhibitor Therapy in Pediatric Eosinophilic Esophagitis, *Journal of Pediatric Gastroenterology and Nutrition* (2019). DOI: 10.1097/MPG.0000000000002480

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