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Blood test could lead to cystic fibrosis treatment tailored to each patient

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Researchers at Stanley Manne Children's Research Institute at Ann & Robert H. Lurie Children's Hospital of Chicago, and colleagues, used a blood test and microarray technology to identify distinct molecular signatures in children with cystic fibrosis. These patterns of gene expression ultimately could help predict disease severity and treatment response, and lead to therapies tailored to each patient's precise biology. Findings were published in *Physiological Genomics*.

"Our findings pave the way to precision medicine for cystic fibrosis patients, eventually helping us match treatment to each patient's unique genomic pattern of disease," says lead author Hara Levy, MD, MMSc, from Manne Research Institute at Lurie Children's, who is an Associate Professor of Pediatrics at Northwestern University Feinberg School of Medicine. "Our study was the first to identify molecular signatures of cystic fibrosis from a blood test taken during a routine clinic visit, giving us a baseline. Greater understanding of these molecular signatures may lead to unique molecular markers that could help us intervene earlier to changes in a patient's inflammatory response to airway infection or pancreatic function, allowing us to provide more focused treatment. It would be a huge improvement over the one-size-fits-all treatment approach we currently have for patients with cystic fibrosis."

To identify baseline molecular signatures in cystic fibrosis, Dr. Levy's lab obtained genomic information from patients' blood samples using cutting-edge technologies such as Affymetric array and Illumina MiSeq. The team then merged this genomic information with each individual's

clinical history gathered from electronic medical records. They compared this snapshot of patient-specific data with healthy controls. Their study provides strong evidence for distinct molecular signatures in cystic fibrosis patients that correlate with clinical outcomes.

Cystic fibrosis is a progressive genetic disease that damages multiple organs, including the lungs and pancreas. Currently, the average predicted survival is 47 years. Although cystic fibrosis is caused by dysfunction of a single gene (CFTR) and treatment that targets CFTR mutations is available, the relationships between the abnormal gene product, development of inflammation and disease progression are not fully understood. This limits the ability to predict a patient's clinical course, provide individualized treatment and rapidly monitor treatment response.

For example, it is not clear why patients with cystic fibrosis are susceptible to chronic lung infections, since they are considered to have a functional immune system.

"We are now trying to discover why patients with cystic fibrosis become infected so easily," says Dr. Levy. "We are taking a closer look at the immune cells that make up many of the molecular signatures we found in cystic fibrosis."

More study is needed before precision medicine for cystic fibrosis reaches the clinic.

"With more research, a blood test to gather genomic specifics of each patient's disease might be available in the clinic within the next five years," says Dr. Levy. "Precision medicine will revolutionize care for cystic fibrosis patients."

More information: Hara Levy et al, Identification of molecular

signatures of cystic fibrosis disease status using plasma-based functional genomics, *Physiological Genomics* (2018). DOI: 10.1152/physiolgenomics.00109.2018