WAYNE STATE UNIVERSITY
news release

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NIH-funded study may lead to new screening method and treatment for Cystic Fibrosis

DETROIT – Cystic Fibrosis (CF) is a genetic disorder that causes severe damage to the lungs, intestine, pancreas, liver and kidneys over time. The defective gene changes a protein that regulates the movement of salt in and out of cells, resulting in thick and sticky secretions that plug tubes, ducts and passageways, particularly in the lungs and pancreas.

Symptoms of CF include a persistent cough, wheezing, lung infections and other respiratory issues. It also can cause intestinal blockages, severe constipation and other digestive issues. Currently, there is no known cure for CF. Life expectancy for people with CF is between 42 and 50 years, with lung issues being the primary cause of death in 80 percent of patients.

A team of researchers at Wayne State University has developed an immunoscreening library derived from sarcoidosis tissue that can differentiate CF-specific antigens from healthy controls and lung cancer patients. The team, led by Lobelia Samavati, M.D., associate professor of medicine in the Center for Molecular Medicine and Genetics in WSU's School of Medicine, has published its findings recently in *Scientific Reports*, a journal affiliated with *Nature*.
The article, "Detection of Cystic Fibrosis Serological Biomarkers Using a T7 Phase Display Library," showcases the team's method for the creation of the T7 Phage Library, which may have utility in developing molecular therapy in addition to being useful in diagnostics and forecasting response to therapy.

"Cystic fibrosis is an autosomal recessive disorder affecting the cystic fibrosis transmembrane conductance regulator (CFTR)," said Samavati. "CF is characterized by repeated lung infections leading to respiratory failure and death. While recent advances in medicine have led to increasing the life span of patients with CF by more than 20 years, there is still a tremendous need to develop reliable serum-based biomarkers to detect the infections in CF."

Using a high-throughput method, Samavati and her research team developed a novel platform based on T7 phage library — a cDNA library derived from mRNA isolated from bronchoalveolar lavage (BAL) and leucocytes of sarcoidosis patients. They constructed a microarray platform and immunoscreened with healthy controls, lung cancer and CF subjects. Applying the statistical models, they selected the top 20 frequently significant clones that discriminated CF antigens from healthy controls and LC patients. The performances of the models were validated on an independent validation set. They also identified CF-specific clones that correlate highly with clinical values such as sweat chloride test, BMI and FEV1% predicted values.

The phage display technology and immunoscreening have utilities not only in identification of diagnostic biomarkers, but also may enable Samavati and others to develop a novel targeted therapy utilizing the peptide sequences (mimotopes) as a vehicle to deliver specific drugs.
The results support the hypothesis that recurrent infections lead to immunity and generation of specific antibodies to specific microbial antigens. Antibody detection in sera of patients has a potential value in clinical practice as it is noninvasive and requires minimal bloodwork.
The present study describes a novel approach to identify CF biomarkers. Samavati plans further studies with a larger cohort group of patients and/or longitudinal studies to investigate the role of these antigens in CF, their mechanism of action, and utilities in drug design and monitoring of therapy.

Samavati's research team included Harvinder Talwar, Ph.D., research associate in the Department of Medicine, Wayne State University, who contributed to the study design, sample processing, and conducted analysis; Samer Hanoudi, Department of Computer Science, Wayne State University, who performed preprocessing, the processing of data and statistical analysis; Andreea Geamanu, Department of Medicine, Wayne State University, who handled patient enrollment and data collection; Dana Kissner, Department of Medicine, Wayne State University, who provided access to patients with CF; and Sorin Draghici, the Robert J. Sokol, MD Endowed Chair in Systems Biology in Reproduction and professor of computer science in WSU's College of Engineering, who supervised the data analysis and contributed to the writing of manuscript.

To view the full paper, visit http://rdcu.be/CkPh.

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