Gene variations linked to intestinal blockage in newborns with cystic fibrosis

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University of North Carolina at Chapel Hill researchers working as part of the International Cystic Fibrosis Consortium have discovered several regions of the genome that may predispose cystic fibrosis (CF) patients to develop an intestinal blockage while still in the uterus.

A report of this international study appears online April 1, 2012 in the journal *Nature Genetics*. It was the work of the North America CF Gene Modifier Consortium, which brought together dozens of investigators from the United States, Canada, and from France, to identify genetic variations that could be linked with meconium ileus (MI), an intestinal obstruction that usually requires emergency surgery for treatment, and can result in a substantially increased rate of serious health problems.

MI affects roughly 15-20 percent of all patients with CF, a genetic condition that causes scarring throughout the body, especially the lungs and pancreas. Though every CF patient carries mutations in both copies of the same gene - coding for a protein called cystic fibrosis transmembrane conductance regulator, or CFTR - symptoms can vary widely from patient to patient.

The genome-wide association study (GWAS) of more than 3,700 CF patients identified non-CFTR genetic variants in the cell membrane that separates the interior of cells from the outside environment. More specifically, the variants involved genes responsible for ion transport in the lower end of the small intestine.

"These variants involve cells in the small intestine that predispose CF patients to develop MI while still in the womb," said one of the senior study authors Michael Knowles, MD, professor of pulmonary and critical care medicine at UNC and a member of UNC's Cystic Fibrosis-Pulmonary Research and Treatment Center.

"The discovery provides new understanding of the pathogenic mechanisms underlying MI. In addition, it offers the possibility of developing therapies to intervene in utero," Knowles said. "Further, it provides molecular insight into the role of genetic variation in ion transporters in CF, which may be applicable to more commonly, and severely, involved organs such as the lungs."

Provided by University of North Carolina School of Medicine