Discovery of genetic defect may lead to better treatments for common gut diseases

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Mary Dinauer, M.D., Ph.D. of the Herman B Wells Center for Pediatric Research at the Indiana University School of Medicine and Riley Hospital for Children is an internationally respected researcher, and a practicinghematologist/oncologist. Credit: Indiana University School of Medicine

New findings related to an uncommon genetic disorder may impact the diagnosis and treatment of inflammatory bowel disease (IBD), the most common chronic gastrointestinal illness in children and teens. Two million Americans have IBD which involves inflammation of the gastrointestinal tract.

Researchers from the United States and Canada have identified a genetic defect not previously known to be a cause of chronic granulomatous disease (CGD), an inherited disorder with recurrent bacterial and fungal infections. Some patients also develop gastrointestinal inflammation, as occurred in the patient in whom the new gene defect was discovered. CGD, which occurs in 1 in 200,000, is usually diagnosed in childhood.

In addition to providing insight into CGD, a condition in which an enzyme defect prevents white blood cells in the body from killing invading bacteria, the new findings highlight how abnormal white blood cell function can predispose individuals to IBD, and may help provide insight into why IBD develops. Crohn's disease and ulcerative colitis are the most common forms of IBD.

The research was led by Mary Dinauer, M.D., Ph.D., of the Herman B Wells Center for Pediatric Research at the Indiana University School of Medicine and Riley Hospital for Children, Nicola Wright, M.D., and colleagues at the Alberta Children's Hospital and the University of Calgary, and William Nauseef, M.D., of the University of Iowa.

The new findings are reported in the October 8 print edition of the journal *Blood*.

"We now know that a genetic defect that selectively affects the production of oxidants inside of white blood cells can cause gastrointestinal symptoms of CGD. Exploring the gene defect's role in inflammatory bowel disease and immune processes will be a key priority in the future," said Dr. Dinauer, Nora Letzter Professor of Pediatrics at the IU School of Medicine. An internationally respected researcher, Dr. Dinauer is also a practicing hematologist/oncologist at Riley Hospital and a member of the Indiana University Melvin and Bren Simon Cancer Center.

More information: A new genetic subgroup of chronic granulomatous disease with autosomal recessive mutations in p40phox and selective defects in neutrophil NADPH oxidase activity. Juan D. Matute, Andres A. Arias, Nicola A. M. Wright, Iwona Wrobel, Christopher C. M. Waterhouse, Xing Jun Li, Christophe C. Marchal, Natalie D. Stull, David B. Lewis, MacGregor Steele, James D. Kellner, Weiming Yu, Samy O. Meroueh, William M. Nauseef, and Mary C. Dinauer. *Blood* 2009 114: 3309-3315.

Source: Indiana University School of Medicine