Researchers unveil mechanisms to prevent Crohn's disease

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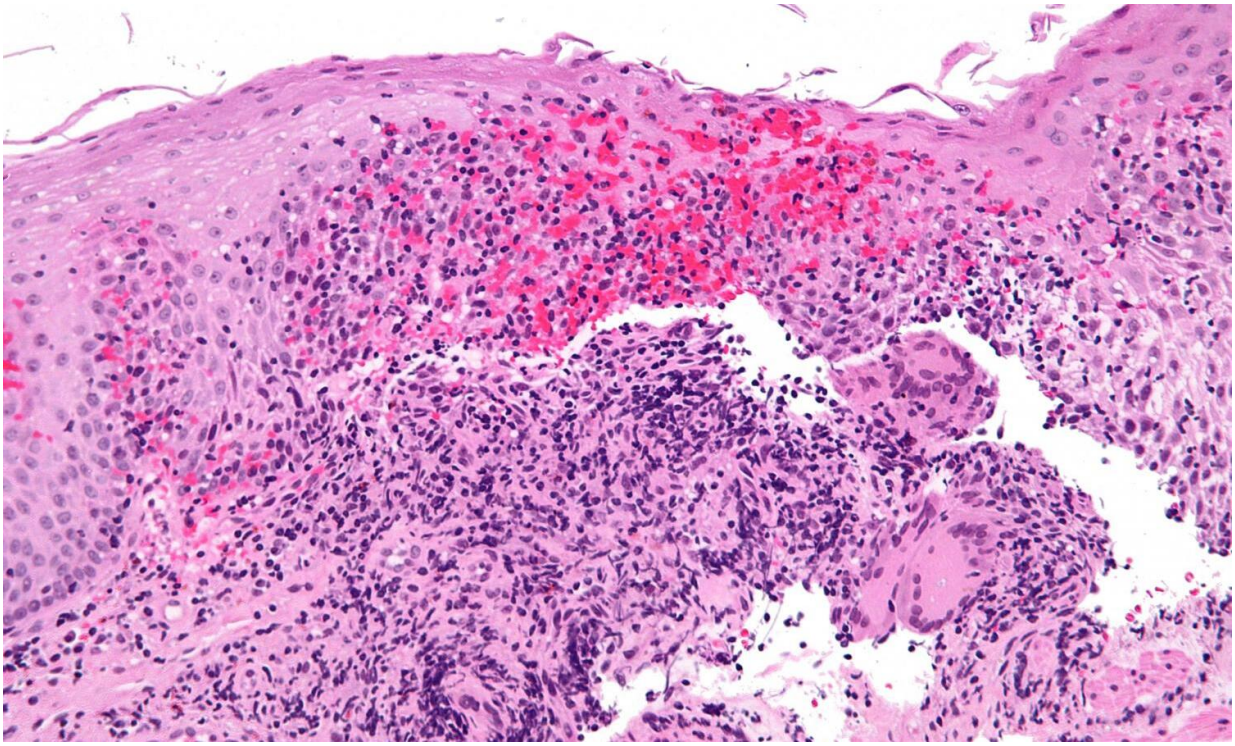

High magnification micrograph of Crohn's disease. Biopsy of esophagus. H&E stain. Credit: Nephron/Wikipedia

In a series of four studies published today in *Gastroenterology*, a journal of the American Gastroenterological Association, Mount Sinai inflammatory bowel disease (IBD) researchers, describe the identification of predictive tools and a new understanding of

environmental factors that trigger IBD.

"Early identification of individuals at high risk for disease development could allow for close monitoring and interventions to delay, attenuate, or even halt disease initiation. This is highly relevant as we seek to predict and prevent IBD, which continues to sharply increase in numbers across the globe," says Jean-Frederic Colombel, MD, Professor of Medicine (Gastroenterology) at the Icahn School of Medicine at Mount Sinai and Co-Director of Mount Sinai's Susan and Leonard Feinstein Inflammatory Bowel Disease Clinical Center. "In the absence of a cure, our clinical strategy will center on aggressive and innovative mechanisms to predict and prevent the disease," says Dr. Colombel.

The series of papers published in *Gastroenterology* provide four unique windows into IBD through the single lens of prevention. "As we approach nearly one hundred years since the discovery of Crohn's by Burrill Crohn at Mount Sinai Hospital in 1932, we see ourselves in a new era where our core scientific innovation will focus on prevention, as a cure continues to elude us. Therefore, our research focus and our team of researchers are aligned as the "Road to Prevention Group," says Dr. Colombel.

Prevention of Progression of Early Crohn's Disease

In a study demonstrating the critical impact of deep remission in recently diagnosed Crohn's disease patients, researchers collected and analyzed long-term follow-up data of 122 Crohn's disease patients in the CALM (The Effect of Tight Control Management on CD) study, a large, 31-site study that evaluated the effect of tight control of early Crohn's. The researchers observed that achieving deep remission early on was significantly associated with an 81 percent decrease in the risk of adverse outcomes over a median of three years. "The data suggests strongly that achieving deep remission early in the course of Crohn's

disease can lead to disease modification with a significant decrease in long-term complications. The implication is that we can play a big role in slowing the disease progression if we catch and treat Crohn's early, highlighting the relevance of prediction and prevention in treating Crohn's," says lead author Ryan Ungaro, MD, MS, Assistant Professor of Medicine (Gastroenterology) at the Icahn School of Medicine at Mount Sinai and a member of Mount Sinai's Feinstein IBD Clinical Center.

Predicting Crohn's Disease Five Years Before First Symptoms

In a study of serum biomarkers of military personnel collected and stored by the U.S. Department of Defense, researchers derived a predictive model for Crohn's disease. In the PREDICTS study (Proteomic Evaluation and Discovery in an IBD Cohort of Tri-service subjects), researchers identified 51 protein biomarkers that were predictive of developing Crohn's disease within five years before diagnosis with a 76 percent accuracy. In total, the researchers evaluated 200 patients with Crohn's disease, 199 with ulcerative colitis, and 200 controls. "The study suggests that biological processes are activated many years before Crohn's, opening the possibility of developing targeted strategies that could work to prevent or delay disease onset. Although we recognize that a preventive strategy may still be many years down the road, studies analyzing samples taken years before diagnosis will likely contribute to a greater knowledge of disease pathogenesis and have the potential to help us improve treatments. When we combine this finding with the knowledge that early intervention can lead to better outcomes for our Crohn's patients, we have a truly relevant headline for a disease that has no cure," says lead author, Joana Torres, Ph.D., MD, Adjunct Assistant Professor of Medicine (Gastroenterology) at the Icahn School of Medicine at Mount Sinai. In contrast to Crohn's disease, no

single marker, alone or in combination, provided good predictive performance for ulcerative colitis.

First Study to Evaluate Association of Metal Exposure and IBD

In a study of metal exposure in the baby teeth of patients who eventually developed IBD later in life, Mount Sinai researchers and colleagues in Portugal collected data from 28 adult Portuguese patients, taking advantage of the country's long tradition of parents storing their children's baby teeth. Baby teeth, like the growth rings in trees, retain information incrementally, storing evidence of environmental exposure from their initial development in the womb until they are shed. Investigators were able to retrieve the baby teeth of 12 IBD patients and 16 unaffected controls, allowing them to study for the first time the association between early-life metal exposures and future risk of IBD. "The data suggests that metal exposure during a critical window in early life may be a risk factor for IBD," says Manish Arora, Ph.D., Professor of Environmental Medicine and Public Health at the Icahn School of Medicine at Mount Sinai. Researchers investigated four metals—lead, copper, zinc, and chromium—and the developmental time periods during which exposure took place going back to the 25th week of pregnancy.

Study of Ashkenazi Jewish Families Suggests Environmental Link

IBD has a long-established familial incidence, and the Ashkenazi Jewish population has an approximately four-fold increased prevalence of IBD. In a study of IBD within Ashkenazi Jewish multiplex families, researchers studied 38 large families with three or more first-degree family members with IBD. The researchers hypothesized that, in a

purely genetically inherited disease, affected siblings would be randomly distributed within the family. The researchers found that affected siblings were significantly more likely to be sequentially affected, with siblings with IBD clustering together within families. "The clustering of affected siblings suggests there are factors beyond genetics that lead to the development of IBD in these multiplex families, likely attributable to a shared environment," says lead author Elizabeth Spencer, MD, Pediatric Advanced IBD Fellow at the Icahn School of Medicine at Mount Sinai. "We are continuing to follow these families in an effort to pinpoint the precise factors. If we can identify these factors, we could alter them as a preventative measure for those at high risk of developing IBD."

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