



**HIGHLIGHTS:**

A recent study has shown that immune signals given by variations of a single gene can trigger different immune responses and, when combined, are associated with increased severity of Crohn's Disease, particularly in Ashkenazi Jews. The study is being presented at the annual meeting of the American Gastroenterological Association May 20-25 in Los Angeles.

**IMMUNE SIGNALS GIVEN BY VARIATIONS OF A SINGLE GENE ARE ASSOCIATED WITH INCREASED SEVERITY OF CROHN'S DISEASE, PARTICULARLY IN ASHKENAZI JEWS**

**LOS ANGELES (May 22, 2006)** – Building on previous evidence supporting the theory that the pathophysiology of Crohn's Disease is altered by genetic variation, recent studies have found that the combination of immune signals given by three variants of a single candidate gene affects the severity of the disease, particularly among Ashkenazi Jews. The findings, presented at the annual meeting of the American Gastroenterological Association, were reported by researchers from Cedars-Sinai Medical Center, the University of Washington and Mount Sinai School of Medicine.

Crohn's Disease is an inflammatory bowel disease that causes inflammation or ulceration of the gastrointestinal tract and can sometimes run in families. While the cause is unknown, many professionals believe that the body's immune system may overreact to normal intestinal bacteria or that disease-causing bacteria and viruses may play a role in triggering the condition.

The recent study, funded by the National Institutes of Health, shows the effect of one particular gene – a Crohn's Disease candidate gene named TLR 5 – on both Jews and non-Jews with the disease.

It is estimated that American Jews are three times more likely to develop Crohn's Disease than the population as a whole. Approximately 80 percent of the six million Jews in the United States are Ashkenazi Jews, an ethnic group whose ancestors are from eastern and central Europe,

As Jerome I. Rotter, M.D., first author of the study, director of research and co-director of the Medical Genetics Institute at Cedars-Sinai Medical Center explained, the innate immune system senses microorganisms and pathogens using a family of proteins known as the Toll-Like Receptors (TLRs). This recognition activates both the innate and adaptive immune system, with each TLR recognizing a specific pattern of microbial components.

The aim of the study was to investigate three TLR5 gene variants and their relationship to Crohn's Disease, the response to two types of bacterial antigens (OmpC porin and CBir1 flagellin) and their relationship to ethnicity. There were 889 Crohn's Disease patients in the study and 236 controls (persons without Crohn's Disease).

“An important part of the study was its approach. By subdividing the subjects by ethnicity and antibody response we were able to show that the candidate gene TLR5 has an effect in both Jews and non-Jews, but its effects are particularly noteworthy in the Jewish population,” Rotter said.

While the treatment of Crohn's Disease is improving, it is still associated with a high morbidity and a large number of hospitalizations and surgeries, Rotter said. "This study demonstrates that it will be important to include ethnicity, clinical phenotypes and quantitative physiologic traits in future investigations that may eventually lead to new and better therapies for Crohn's Disease's different sub-forms."

Researchers from Cedars-Sinai's Inflammatory Bowel Disease Center and Medical Genetics Institute authored 23 other studies that will be presented at the association's annual meeting.

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The first of eight hospitals in California whose nurses have been honored with the prestigious Magnet designation, Cedars-Sinai Medical Center is one of the largest nonprofit academic medical centers in the Western United States. For 18 consecutive years, it has been named Los Angeles' most preferred hospital for all health needs in an independent survey of area residents. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. It ranks among the top 10 non-university hospitals in the nation for its research activities, and since 2004 has been fully accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP). Additional information is available at [www.cedars-sinai.edu](http://www.cedars-sinai.edu).

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