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Arthritis News

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GENETIC PROFILES MAY PLAY ROLE IN DETERMINING RISKS OF COMMON INFECTIONS FOR RHEUMATOID ARTHRITIS PATIENTS

SAN ANTONIO, TEXAS—Identifiable genetic factors may predispose rheumatoid arthritis patients to common infections, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

In the largest reported analysis of associations between genetic variations and risks of common infection, researchers studied data on 632 patients with early rheumatoid arthritis who were taking part in a clinical trial of methotrexate versus the TNF inhibitor etanercept. Serious infections were found to be rare, but 62 percent of patients reported at least one common infection during the year-long study. Analysis of the 457 patients who consented to genotyping revealed that upper respiratory infections and urinary tract infections occurred more often in those patients with particular variants in genes known to be important for immune function.

Rheumatoid arthritis, which causes inflammation in joints and other organs of the body, is an autoimmune disease that leaves patients more prone to common infections than the general population. This study demonstrates that genetics may play an important role in defining this susceptibility to common infections in patients with early rheumatoid arthritis. While researchers did not compare the frequency of infections in subjects taking disease modifying anti-rheumatic drugs (DMARDs) to participants not on DMARD therapy, upper respiratory infections were found to be more common in those being treated with methotrexate than in those treated with etanercept.

"This study is the first to use data on a large number of patients with early rheumatoid arthritis and demonstrates that a combination of genotypes predispose those patients to common infections such as upper respiratory and urinary tract infections," said S. Louis Bridges, Jr., MD, PhD, University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, Alabama, and an investigator in the study. "These findings are preliminary and need to be corroborated in additional studies to assess the clinical utility of this genetic information in rheumatoid arthritis and other inflammatory diseases."

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR's annual meeting, see www.rheumatology.org/annual.

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Editor's Notes: Dr. Bridges will present this research during a scientific session at the ACR Annual Scientific Meeting from 2:30–2:45 PM (3:30–3:45 PM) on Monday, October 18, in Ballroom B of the Henry B. González Convention Center. He will be available for media questions during a briefing at 8:30 AM CT (9:30 AM ET) on Tuesday, October 19, in the on-site Press Conference Room, Room 218.

Presentation Number: 532

Genetic Risk Factors for Infection in Patients with Early Rheumatoid Arthritis taking Etanercept or Methotrexate

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PURPOSE: Patients with rheumatoid arthritis (RA) have increased susceptibility to infections compared to the general population and are frequently treated with immunosuppressive drugs. We analyzed the impact of single nucleotide polymorphisms (SNPs) in genes encoding tumor necrosis factor-α (TNF), lymphotoxin-α (LTA), and Fc gamma receptors on susceptibility to infection in subjects with early RA treated with methotrexate or etanercept.

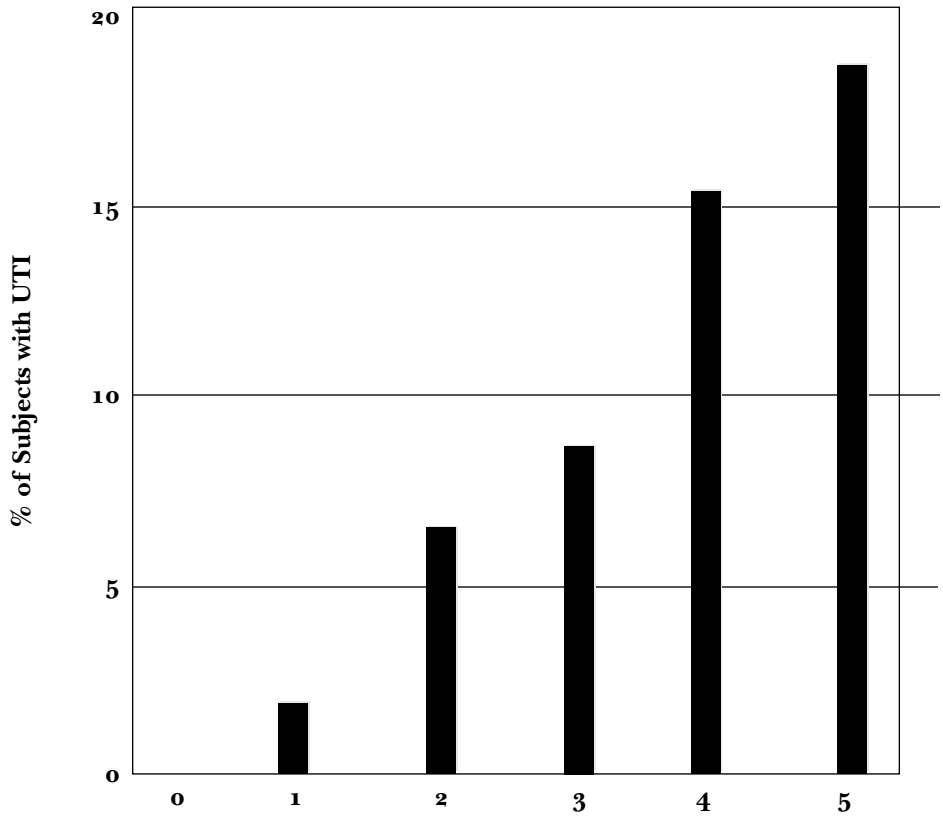
METHODS: We utilized detailed clinical data and genomic DNA from subjects enrolled in a prospective, one year clinical trial comparing the efficacy and safety of methotrexate (MTX) and the TNF inhibitor etanercept. Of the 632 subjects in the trial, 457 consented to genetic studies and were genotyped at the following polymorphisms: TNF -308, -238, and +488; LTA +249, +365, and +720; FCGR2A 131 H/R; FCGR3A 176 F/V; and FCGR3B NA 1/2. Over the 1 year study period 62% of the subjects reported at least one infection. We examined the association between SNP alleles and haplotypes and infections using multivariate logistic regression and an ANOVA model, adjusting for prednisone dose.

RESULTS: The neutrophil-specific FCGR3B NA2 allele was associated with an increased risk of upper respiratory infections (URI). At least one URI was noted in 52% of subjects (99/191) with the FCGR3B NA2/NA2 genotype compared to 42% (77/181) of those with the NA1/NA2 genotype and 39% (23/59) of those with the NA1/NA1 genotype (P=0.037; Table 1). Urinary tract infections (UTI) were significantly associated with the TNF -238 A (P=0.038), LTA +365 C (P=0.024), and FCGR3A F (P=0.052) alleles. The likelihood of having a UTI during the study period increased according to the number of risk alleles defined by these three SNPs (P=0.001; Figure 1).

CONCLUSIONS: This is the largest reported analysis of the impact of genetic polymorphisms and risk for prospectively identified common infections. We have identified several polymorphisms in genes with important roles in inflammation and host defense that are associated with susceptibility to URI and UTI in RA patients receiving MTX or etanercept. These findings have important implications for the role of genetics in susceptibility to infection.

Table 1. Association between URI and FCGR3B genotype.

	NA1/NA1	NA1/NA2	NA2/NA2	Total
No URI	61% (36/59)	58% (104/181)	48% (92/191)	232
1 URI	20% (12/59)	24% (44/181)	23% (44/191)	100
≥2 URIs	19% (11/59)	18% (33/181)	29% (55/191)	99
Total	59	181	191	431



Percentage of subjects with given number of risk alleles who had at least one UTI during the study period.

Disclosure: L.B. Hughes, None; L.A. Criswell, None; T.M. Beasley, None; J.C. Edberg, None; R.P. Kimberly, None; L.W. Moreland, None; M.F. Seldin, None; S.L. Bridges, None.