

# SNP Genotyping: Technologies That Keyed a Revolution in Medicine

By Tricia LeVan, PhD



Dr. LeVan

To realize the promise of genetics in research and medical practice, the Department of Internal Medicine established the CORE "Facility for Mutation and Methylation Analysis." I direct the facility located in the Durham Research Center II to provide services for detection of SNPs (Single Nucleotide Polymorphisms) using a candidate gene approach. Millions of human SNPs have been discovered in recent years — over 6 million from The International HapMap Project alone in its first three years. SNPs are the most common form of genetic variation between individuals and occur once every 1,000 bases or so. This new post-genomic era provides excellent opportunities to identify genes and genetic

changes that will increase our understanding of how such changes cause disease. In the clinical arena, it is becoming possible to utilize the emerging genetic and genomic knowledge to diagnose and treat patients, the path towards personalized medicine. The knowledge of the genetic basis of human disease is also ushering a new era in drug development that is focused on targeted drug development and correlating individuals with their response to specific drugs.

Dr. Ted Mikuls, rheumatologist, leads an investigative team (Karen Gould Fang Yu and Tricia LeVan) studying the effects of polymorphisms in four drug metabolizing genes (GSTM1, NAT1,

NAT2 and EPHX) on rheumatoid arthritis. We found there was a gene by environment interaction of the GSTM1-null genotype, HLA-DRB1 shared epitope and smoking in the pathogenesis of anti-citrullinated protein antibody positive rheumatoid arthritis. A recently-funded grant (PI: Dr. Mikuls; co-Investigator: Dr. LeVan) will investigate the impact of genetic variation in CD14 and Toll-like receptor pathways in rheumatoid arthritis. This grant proposes to determine if variation in these genes will mediate the detrimental effect of tobacco exposure on rheumatoid-specific autoantibody production, disease severity, prevalence of extra-articular disease and pulmonary symptoms.

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## *SNP Genotyping: Technologies That Keyed a Revolution in Medicine—continued*

*Dr. Kathleen Grant, MD, a specialist in addiction medicine, studies the risk and protective factors for methamphetamine dependence. Recently, we have incorporated a genetic element into this study and are collecting DNA samples to generate preliminary data for a R21 application titled “Genetic Basis of Methamphetamine-Induced Psychosis”.*

*In yet another clinical arena, COPD and agriculture exposure, Drs. Susanna von Essen and Debra Romberger, pulmonologists, and I have*

*collaborated since 2001 in a research effort focused on polymorphisms in the CD14 gene and lung function. We found that polymorphisms in the CD14 gene were associated with pulmonary function in farmers. This study formed the basis of a much larger, funded genetic investigation establishing an agricultural cohort with COPD at the Omaha VAMC. This study clearly is relevant to Nebraska because agriculture is vital to the economy of Nebraska and is a risk factor for COPD.*

*In summary, genetic profiling in candidate genes and the subsequent association with disease is a powerful tool in understanding disease susceptibility, which can be applied to all areas of clinical studies.*

*These services are available for academic researchers worldwide. The laboratory operates a Sequenom iPLEX system based on MALDI-TOF mass spectrometry.*

*For additional information or questions call Dr. LeVan at (402) 559-3985.*