

Exome Sequencing Improves the Diagnosis of Systemic Lupus Erythematosus

Dr. Graham Wiley comments on how the HiSeq® 2000 system and TruSeq® Exome Enrichment Kits are enabling faster, easier, and more cost-effective research studies.

Introduction

Oklahoma Medical Research Foundation (OMRF) is a non-profit biomedical research institute dedicated to understanding and curing human disease. In the OMRF Arthritis & Clinical Immunology Research Program, world-class autoimmune disease researchers are using genetic information to help answer questions about systemic lupus erythematosus (SLE). In SLE, the immune system attacks the body's own tissues, leading to inflammation, organ failure, and, in some cases, death. With a multitude of symptoms and 11 diagnostic criteria, lupus is one of the hardest diseases to diagnose and even harder to treat. By comparing the genetic information of phenotypically normal individuals with that of people with SLE, scientists such as Graham Wiley, Ph.D., are searching for mutations within genes that might account for the onset of disease.

The Challenge of Linking Genes to Lupus

SLE has a wide range of symptoms and many phenotypes, affecting women more than men by about 90%, and takes a while to properly diagnose. It's been the subject of many genotyping studies and a very large number of single nucleotide polymorphisms (SNPs) and alleles have already been identified as being associated with the disease. Now the field is taking two different approaches. Some are performing GWAS on affected individuals in an attempt to find rare alleles associated with the disease. Others, like Wiley, are moving towards functional sequencing studies to find out why a particular SNP locus is associated with lupus.

Scalable Exome Sequencing as a Solution for Rare Variant Discovery

Dr. Wiley has been using Illumina technology to identify rare mutations in SLE through high-throughput exome sequencing studies. "Exome sequencing provides all of the SNPs in all of the exons across the whole genome. Once you can identify the causal SNP, then you can actually see the SNP and start teasing apart its function and how it affects the genome," he states. "With exome sequencing, you can look at all of the genes, all at the same time."

To prepare his samples, Dr. Wiley has used several exome enrichment products but he prefers the TruSeq Exome Enrichment kits because he can pool samples prior to capture. "With pooling," he says, "it's easier, it's cheaper, and our throughput for captures is much, much faster."



Dr. Graham Wiley, Ph.D., is an Associate Research Scientist in the Arthritis & Clinical Immunology Research Program at the Oklahoma Medical Research Foundation (OMRF).

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For sequencing, Dr. Wiley uses the HiSeq 2000 system because of the level of output, read length, and its ability to accommodate true paired-end reads. This helps with assembly and detection of small indels. “You’re getting 100 bases for each end in a paired-end read and you can run two full flow cells at the same time, load them up, and generate 180, 200 million reads in a lane. HiSeq has been a game changer for us. A project that would have taken us a year, now takes one week.

Enabling Efficient, Cost-Effective Sequencing Studies

Dr. Wiley credits Illumina as enabling his research projects, citing “what would have seemed inconceivable a few years ago is now possible today. Three or four years ago, sequencing the entire exome of 12 or 15 or 24 people would have been an R01 grant project.” Within the community, everybody wants to find the most efficient, cost-effective technology. Right now for resequencing in humans, or basically anything with a reference genome, Dr. Wiley says, “you really can’t beat Illumina,” adding that it is the most flexible technology for answering a variety of questions. “What would have been cost-prohibitive a year ago is affordable now.” Wiley notes, “with the HiSeq, we are getting over 600 Gb of data in a single run. We can produce quality data, in less time, at a better cost.”

According to Dr. Graham Wiley, combining the HiSeq 2000 sequencing system with TruSeq Exome Enrichment offers the most scalable, affordable, easy-to-use solution. Because of advances in Illumina technology, exome sequencing and gene mutation studies can now be done much more quickly and cost-effectively.

Learn more about the HiSeq 2000 system and TruSeq Exome Enrichment Kits at www.illumina.com

Summary

Overview

Oklahoma Medical Research Foundation (OMRF) is a non-profit biomedical research institute dedicated to understanding and curing human disease, including SLE, which is one of the hardest diseases to diagnose.

Challenge

Researchers at OMRF are trying to identify rare gene mutations linked to lupus and tease apart their function.

Solution

OMRF is using the HiSeq 2000 system and TruSeq Exome Enrichment kits to sequence the exomes of dozens of lupus patients.

Benefits

Illumina technology is enabling studies previously not feasible for many researchers due to time, cost, and complexity. Today, exome sequencing studies can be done quickly and cost-effectively.

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