RNA-Seq Studies Identify Biomarkers for Early Detection of Pulmonary Diseases

Dr. Avrum Spira explains how the HiSeq® 2000 system and RNA-Seq are enabling new biological insights into pulmonary diseases.

Introduction

Dr. Avrum Spira, a pulmonary and critical care physician at Boston University Medical Center (BUMC), is Chief of the Division of Computational Biomedicine in the Department of Medicine at Boston University. In early 2000, Dr. Spira started a lab with the goal of applying whole-genome gene expression platforms to clinical samples in an effort to develop biomarkers that could lead to potential diagnosis and treatment of pulmonary disorders. Today, Spira's lab uses the Illumina HiSeq 2000 system and RNA-Seq to discover molecular biomarkers that may provide opportunities for early detection of pulmonary diseases.

"I initially focused on lung cancer," says Dr. Spira, "we almost never detect it at an early stage. Using new genomic platforms, we hoped to develop molecular markers that could identify risk, and possibly help diagnose the disease at an early stage." After successful discovery of biomarkers that aid in early detection of lung cancer, Dr. Spira's lab turned their efforts to other smoking-related diseases, specifically chronic obstructive pulmonary disease, also known as emphysema.

"We are expanding our studies to other diseases beyond the lung, pushing into translational areas where genomic technologies can be applied to clinical samples, in clinical settings," explains Dr. Spira. "We're trying to use genomic markers to help predict who might respond to given treatments, and to identify potential new disease treatments and therapeutic targets."

Increased Throughput and Depth of Coverage Drives Discovery

"We chose the HiSeq system for our studies because of its throughput and depth of coverage," states Dr. Spira. "We can run a greater number of samples in a single lane, in a shorter period of time. The HiSeq has outperformed our expectations and is changing the way we use sequencers. The scalability and depth of coverage of the HiSeq is enabling more efficient studies and, ultimately, helping us identify new biomarkers that can potentially impact patient care."

Spira adds, "we believe Illumina's RNA-Seq method offers the best technology for unbiased discovery of disease-related transcript expression. For a number of our projects, we switched from microarrays to primarily a sequencing-based platform because RNA-Seq provides us with a more comprehensive approach to profiling the transcriptome across a broader dynamic range."

"The clear advantage of RNA sequencing is that it allows us to identify transcript alterations and splicing events that may not be detectable on a microarray," says Dr. Spira. In a recent publication, his lab has gone

Avrum Spira, M.D., is an associate professor of medicine, pathology, and bioinformatics at Boston University Medical School and a pulmonologist at Boston Medical Center.

> "We're starting projects that we may not have otherwise taken on...next-generation sequencing with the HiSeq allows an unprecedented view of the transcriptome in lung disease."

back to bronchial airway samples originally analyzed by microarray and re-analyzed gene expression with Illumina sequencing. "The RNA-Seq platform identified many of the changes that the microarray platform found, plus a number of new changes," says Dr. Spira. "There were transcriptomic alterations that the microarray either didn't measure or didn't pick up as changing, that the sequencer does. We can identify additional, potentially valuable biomarkers with the Illumina next-generation sequencing platform."

Illumina Technology is Enabling New Projects

Dr. Spira is starting three new projects for RNA-Seq and the HiSeq 2000. In the first study that is part of the NHLBI's Lung Genomics Research Consortium (LGRC), Dr. Spira's lab will analyze 400 diseased lung tissues using RNA-Seq. "We're starting projects that we may not have otherwise taken on. This study is being done explicitly because next-generation sequencing with the HiSeq allows an unprecedented view of the transcriptome in lung disease," he says. "These tissues have been run on microarrays, so the idea is to find new biologically relevant transcriptomic alterations that reveal more about the pathogenesis of these diseases."

In a second study funded by the NCI's Early Detection Research Network (EDRN), Dr. Spira is using the HiSeq system to develop microRNA-based biomarkers for the early detection of lung cancer. "There are microarrays for measuring human microRNAs, but we don't know how many are in the genome," says Spira. "Sequencing provides a clear advantage, in that you can measure the complete spectrum of small RNAs expressed in the tissue, uncovering novel microRNAs that associate with disease."

In a third study funded by the Department of Defense, Dr. Spira is sequencing premalignant cells from patients at risk for lung cancer. "These are really small, valuable tissue samples," says Dr. Spira. "We elected to pursue sequencing using HiSeq as opposed to an array, because we want to get the most comprehensive profiling of these precious specimens that we can."

Making Sequencing More Accessible

Dr. Spira offered his perspective on the impact that the HiSeq system will have on future projects. "In the last couple of years, sequencing has become far more accessible to the average researcher. The cost of running an RNA-Seq experiment has dropped. We can increase the throughput and run more samples, decreasing the cost per sample," he says. With regard to data analysis, Dr. Spira says, "While the complexity of RNA-Seq data analysis is greater than a microarray, groups like ours and others are developing tools and pipelines for data analysis, making it easier to analyze the data."

Learn more about the HiSeq 2000 system and RNA-Seq Sample Prep Kits at www.illumina.com/hiseq.

Summary

Overview

Avrum Spira, M.D., at Boston University Medical Center is developing biomarkers to help identify and diagnose pulmonary diseases at an early and potentially curable stage.

Challenge

Existing genomic technologies have a narrow dynamic range, limiting their ability to measure low-abundant genes and detect splicing events. This impacts the information needed to make novel discoveries about disease pathogenesis.

Solution

Dr. Spira is using RNA-Seq on the HiSeq 2000 system to identify novel biomarkers for pulmonary diseases.

Benefits

Illumina technology empowers a comprehensive view of RNA expression, with higher throughput and increased dynamic range, enabling new biological studies that can be done quickly and cost effectively.

"While the complexity of RNA-Seq data analysis is greater than a microarray, groups like ours and others are developing tools and pipelines for data analysis, making it easier to analyze the data."

illumına®