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NHGRI Researcher Provides ClinSeq Update at ASHG Meeting

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PHILADELPHIA (GenomeWeb News) – The National Human Genome Research Institute's ClinSeq initiative is making headway — and appealing to potential volunteers, according to NHGRI genetic disease researcher Leslie Biesecker.

Biesecker described the progress being made on the initiative today at the American Society of Human Genetics meeting here.

NHGRI launched ClinSeq last year as part of an effort to move into translational genomics by bringing together information about human genomes and clinical data using a large number of subjects. Biesecker explained that the study will enable scientists to genomically dissect phenotypes and more — gaining insights into not just rare or common Mendelian variants, but other mutations as well.

The goal of the ClinSeq project is to gather phenotypes for 1,000 unrelated subjects with a range of atherosclerosis conditions. Initially, the team plans to sequence 400 candidate genes for each, sort individuals by their genotypes, and then validate and return appropriate information to participants.

Enrollment for the project began in January 2007. And volunteers have been rolling in since then, Biesecker said. "We cannot keep up with the demand from volunteers who want to participate in a whole-genome sequencing study."

So far, the ClinSeq team has identified thousands of new, non-exon variants. But the large amount of data being generated is presenting new issues for researchers. "Using this data will be a big challenge," Biesecker said.

Even so, the team is working to provide feedback to participants about their research results. Whereas clinical geneticists are used to operating in a rare-variant, single-gene space, Biesecker said, larger studies such as ClinSeq require a different approach.

He and his team are addressing that challenge by looking for genes for which associations are most certain and providing information about these variants to participants. They then move to less certain associations and continue providing feedback until participants tell them they are no longer interested. In so doing, the team also hopes to start defining the line at which participants no longer wish to receive feedback about the research.

"There are a lot of strongly held opinions about where that line is, but there's no data," Biesecker said.

Based on the initial results from the project, Biesecker added, it is clearly possible to consent subjects for whole-genome studies, sift out clinically relevant results, and provide information to participants.

In the future, Biesecker said, ClinSeq intends to move from exome sequencing to whole-genome sequencing. In addition, researchers plan to begin enrolling participants from a variety of different backgrounds (97 percent of the current participants are of European descent) and to incorporate reams of other data on everything from participants; coronary calcium scores to blood pressure scores and clinical chemistry.

"What we will be generating here is a gigantic multiple testing project," he said.