ACMG Recommends Labs Return Some Incidental Genetic Findings to Doctors, Patients

March 21, 2013

By a GenomeWeb staff reporter

NEW YORK (GenomeWeb News) – The American College of Medical Genetics and Genomics is recommending that labs conducting exome and genome sequencing for clinical use should notify physicians about their patients' status for a number of conditions, genes, and variants that are found during the sequencing.

Incidental genetic findings that are unrelated to the conditions that patients are being tested for generally are not returned to them or their doctors, but that practice should change, at least for a small number of conditions, the group said in a report released today.

The report, "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing," was released at the ACMG Annual Clinical Genetics Meeting in Phoenix, and the recommendations were approved by the ACMG board of directors.

Now that exome and genome sequencing are beginning to become more commonly used in medical care, more physicians will be using these technologies to test for genes and variants related to certain conditions in patients. ACMG said today that it believes that incidental findings unrelated to the primary reason for ordering such tests should be returned to the physician, who could then discuss the findings with the patient and manage the information in the context of that patient's clinical presentation and family history.

A working group took over a year to develop the ACMG recommendations. It created a list of over two dozen conditions, genes, and variants that are well understood and for which there is the possibility that medical and other interventions could be helpful to patients, if the conditions are detected before symptoms arise.

If a physician orders a genome or exome sequence to help diagnose a cardiac condition, for example, it is possible that the sequencing will reveal a gene that predisposes the patient for cancer. In such a case, the early discovery of the oncogene could empower the patients and physicians to step up their surveillance plans or make lifestyle choices that could their lower risk or reduce mortality.

ACMG's list includes conditions with strong connections to genes and mutations, such as hereditary breast and ovarian cancer; Lynch Syndrome; Marfan Syndrome; hypertrophic and dilated cardiomyopathy; familial hypercholesterolemia; retinoblastoma; tuberous sclerosis complex; and others.

The group acknowledged in the report that this list "should, and will, evolve, as further empirical data are collected on the actual penetrance of these variants, and on the health benefits and costs that might follow from their disclosure as incidental findings."

The working group noted that there is "an active debate" about whether human genomics researchers also should return incidental findings, but pointed out that these recommendations solely focused on sequencing that was carried out at the request of a clinician, and are not policy proposals designed to cover genomics and disease research.

By recommending that incidental genetic findings be provided to physicians and patients, but only for a limited number of relatively well-characterized disorders and genes, the working group recognized that clinical sequencing is a growing field that is still very much in its infancy.

"The genome has an extraordinary potential for providing health-related information about both rare and common conditions, but it has been difficult to draw a line and suggest that one set of findings should be part of the medical report and another set should not," Robert Green, a medical geneticist at Brigham and Women's Hospital and Harvard Medical School and co-chair of the ACMG working group, said in a statement today.

"In these recommendations, despite a scarcity of clear scientific evidence, we have identified a small number of conditions, genes, and variants through consensus that are likely to have a positive impact upon the health of patients and their families if identified incidentally," he said.

Leslie Biesecker, who is chief of the National Human Genome Research Institute's Genetic Disease Research Branch and the working group's other co-chair, noted that the recommendations will only affect a small number of people

who have their genomes sequenced in the course of clinical care, but for them these test results could be invaluable.

The recommendations mean that "a small a small percentage of families that are sequenced, perhaps not more than [one to two percent], will learn unexpected but potentially life-saving information about an illness they may have never suspected they were at risk for," Biesecker said. "Thus, these recommendations are an innovative approach to addressing one of the most difficult problems in genomic medicine and help transition us toward new models of delivering genomic information."