White House Commission to Report on Incidental Findings

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By a GenomeWeb staff reporter

NEW YORK (GenomeWeb News) – The Obama Administration's bioethics advisory panel plans to write a report on how researchers, clinicians, and direct-to-consumer testing firms should handle any incidental but potentially important health-related and genetic information they discover while testing individual patients, customers, and research participants.

In a meeting yesterday in Washington, DC, members of The Presidential Commission for the Study of Bioethical Issues touched on a broad range of issues about what should be done with these incidental findings — and this is a question of particular interest to genomics research.

Physicians deal with the underlying issue of incidental findings on a regular basis, such as when an x-ray taken to evaluate a broken bone reveals an unknown tumor. Genomics researchers and genome-based medical practitioners are far more likely to generate incidental findings, however, because of the sheer volume of genes and variants they come across that are known to be associated with health problems.

The National Human Genome Research Institute has highlighted the importance of this issue by launching the Return of Results Consortium, and the American College of Medical Genetics and Genomics recently issued a set of guidelines for handling incidental findings in genomic research and medicine.

While the bioethics commission report will explore the issues of returning incidental findings in general (MRIs, neuroimaging, etc.), the panel discussion yesterday suggested that genomic findings will be a critical area of focus.

The commission had already tackled this issue in its report last year on whole-genome sequencing, but the tight focus on sequencing in that document left many questions about the return of incidental findings for another day.

"In whole-genome sequencing … it is certain that there are going to be incidental findings, and so we began there," Amy Gutmann, chair of the commission and president of the University of Pennsylvania, said yesterday.

But incidental findings may be encountered much more often in other contexts, she explained. "This new report will consider incidental findings not only resulting from genetic testing, of which whole genome sequencing is a subset, but other modalities, such as imaging, biological specimen testing, and in the context of research, clinical care, and direct-to-consumer offerings."

The few recommendations that the commission's earlier report offered on incidental findings from whole-genome sequencing, which centered on consent and communication efforts, may provide clues about how the commission will approach the issue more broadly in this next effort.

"We recommended that informed consent forms for whole-genome sequencing research should include what data and information, if any, might be returned to the individual," Gutmann said at the top of yesterday's meeting. "We also recommended that individuals be made aware that incidental findings are likely to be discovered in the course of whole-genome sequencing, and that the consent process should convey whether these findings will be communicated, what the scope of the findings are, and to whom the findings will be communicated."

That report also recommended that studies should be done to evaluate different ways to return results to patients and research participants, she noted.

Gutmann explained that a second report was warranted because the commission was "so impressed by the richness and ripeness of this topic for ethical review" that the group decided "that we really needed to delve deeper and more broadly into all the realms in which incidental findings occur."

New findings, new parameters

Yesterday, the commission heard from and engaged in a probing discussion with experts who have different relationships with incidental findings in the research, clinical, and consumer fields. They sought to define the parameters of what is at stake in relation to incidental findings, how the medical value of these findings may be gauged, and what the responsibilities and ethical duties are of clinicians, researchers, and businesses that come across these findings.

As genomic scientists seek greater access to clinical data, as sequencing expands into medicine, and as consumer genomics firms continue to provide analyses of their findings, the barriers between the clinic and the lab are shrinking, raising questions about ethical obligations. Does a researcher have the

same obligation to report findings as a family practitioner, the panel questioned.

The new science has not changed everything, Alex London, a professor of philosophy at Carnegie Mellon University, told the commission.

"There is still a primary duty in each domain that is different: research's duty is to discover new knowledge, the company's duty is to its shareholders, and the clinician's duty is to patients," he said.

Robert Green, an associate professor at Brigham and Women's Hospital's Division of Genetics and co-chair of the incidental findings group that wrote the ACMG's incidental findings report, explained how individuals might use genetic information that is discovered incidentally.

He told the group about a study in which he was involved that disclosed research participants' status for APOE-4, which indicates an increased risk for Alzheimer's disease.

"When we started this, in the year 2000, this was a very scary proposition," said Green. "We were really lambasted on all sides for actually disclosing this kind of information to individuals."

However, he said that "it turned out that people really wanted this information," and he noted that they acted on this information. "They tried to exercise, [and took] vitamins and medications to reduce their risk. … And, as you might imagine, people who learned they were E4 positive… were five times more likely to purchase long-term care insurance, a very rational response, but one that scares the pants off of the insurance industry."

Green also said that more empirical data on how people will respond to receiving such genetic information is on the way, particularly through the MedSeq program that he is directing, and which received a $9.6 million NHRGI grant late last year.

Considering guidance and context

It is plausible that the commission will look to ACMG's recommendations on incidental findings for guidance as the group goes forward developing this report.

Those guidelines proposed broadly that labs conducting exome and genome sequencing for clinical purposes should notify physicians about their patients' status for about two dozen conditions, genes, and variants that are very serious and for which there are some interventions. The expectation is that this list will be amended "at least annually," Green said, as more genes and variants are more directly related to specific medical issues.

The panel also discussed how these conditions and variants might be chosen, suggesting that they will entertain the idea that some findings are much more important than others either because of their links to diseases or because they are actionable.

For ACMG, the thinking was to create "a minimum list" of variants and genes — the ones that "you really wouldn't be able to sleep at night" if you knew about and did not return, Green said.

The ACMG recommendations were tightly focused on situations in which a clinician orders whole-genome or whole-exome sequencing, but they did not address incidental findings in genomics research in general or direct-to-consumer testing services, two areas that the commission is likely to consider.

The panel discussion did not provide much to signal how the commission may differentiate incidental findings from research groups compared to direct-to-consumer firms.

If the commission veers toward drafting a regulatory approach to how DTCs should handle incidental findings, they might be adding more layers to a field that already has a very fuzzy regulatory structure, Gail Javitt, a research scholar at Johns Hopkins University's Berman Institute of Bioethics and a counsel at the law firm Sidley Austin, explained to the panel.

She pointed out that the Centers for Medicare and Medicaid Services handles lab testing quality through CLIA, that the Food and Drug Administration regulates medical devices, and that the federal government and individual states already have some regulations for DTCs.

Also, in relation to DTC genomics firms, there is a question about whether the term 'incidental findings' is applicable, because there is the assumption that consumers have ordered the service to explore their genomes, Joanna Mountain, senior director of research at 23andMe, told the commission.

Because 23andMe states on its website that its purpose is to help "individuals learn about and explore their DNA," and because "anything we can tell you about your DNA is part of the package," Mountain said, all of the information could be seen as pertinent and not incidental.

Mountain also explained that private firms like hers can use terms of service agreements to clarify their relationships with their customers, and that 23andMe states in its agreement that not all of the information that the firm will provide to customers will be welcome or positive.

"We've been blunt from the beginning," she said, noting that customers may find that they have blood-clotting propensities, or that "your father is not your father."

She also said that certain genetic information that is deemed particularly sensitive, such as BRCA status, is blocked unless the consumer chooses to find out about it. The intentional selection on the part of a willing consumer of certain highly meaningful, disease-related information creates a different context from the clinic or the lab, which is why 23andMe avoids the 'incidental findings' term.

The commission did not say when it plans to release its report, though Gutmann noted that the group's work has only just begun.