Insights on How an Experienced CCO Delivers Novel Ideas to the World of Genomics

An Interview with Joanne M. Hackett

Value & Outcomes Spotlight was fortunate enough to sit down with Joanne M. Hackett, Chief Commercial Officer at Genomics England, to talk about the impact the field of genomics is having on personalized medicine. Joanne began her career as a clinical scientist, before coming to the United Kingdom to be one of the main driving forces in the commercialization of precision medicine. In her current role at Genomics England, Joanne focuses on developing and managing strategic relationships with industry. With an international career in and out of the lab, across start-ups and Fortune 500 companies, Joanne has accumulated keen insights on personalized medicine.

VOS: Can you present for our readers some of the likely applications of genome sequencing for the realization of personalized medicine? What are the public health implications?

Joanne M. Hackett: The development of next-generation sequencing (NGS) has drastically reduced the time and cost of sequencing a genome. This has had 2 important knock-on effects: first, it is now relatively simple to convert biological information into digital data; and second, the scale at which we can sequence whole genomes has turned this into a big data field. This is significant for understanding why there is so much hype around genomics. Because we are so data rich, there are several technology fields converging—meaning the potential applications are limited only by our own imaginations.

Before we talk about applications, it's important to understand the science. Being able to sequence a genome is not the same as understanding a genome. A tremendous amount of research goes into identifying not only gene variants, but also the traits they are associated with and the molecular pathways they influence. That is the research that underpins everything else that follows. There is still much we don't know when it comes to understanding the genome.

In a healthcare context, gene variants are proving to be useful biomarkers for predicting disease susceptibility and diagnosis, drug response, and adverse drug reactions. This is helping to transform the ways we deliver healthcare through faster and more cost-effective disease diagnoses and also make better-informed treatment decisions. Getting the right drug to the right patient is central to personalized medicine. Identifying those genetic biomarkers is at the heart of what we do here at Genomics England—we sequence a patient's DNA, analyze it for known clinically actionable variants, and return the results back to the clinicians who can then decide on the best course of treatment.

And that leads us nicely to the application area that excites me the most—the treatment. Diagnosing patients is only part of the mission. We can find the right patients, but we still need to have the right drugs available to treat them.

There's an argument as to whether the cost of personalized medicine is justifiable in relation to the positive impact that same funding could have on broader public health initiatives. It's hard to argue against when you consider how many hospital admissions are brought on by smoking or alcohol consumption. But personalized medicine is just an application of research. That same research can be applied to public health initiatives by giving greater insights into the genetic predispositions of a population. Identifying high-risk subsets of a population can give you a better chance of understanding behaviors and drivers that could be addressed to improve population health and reduce the strain on healthcare systems. In that regard, we should not treat this as an "either/or" scenario. The important thing is to encourage the research that will continue to present more opportunities to improve health wherever there is need.

We now have 16 years from the first full sequence of human genome publication. What is the research bringing over the next 5 years?

I think we'll see the biggest changes in pharma. I'm sure you have heard a lot of people talk about the need to "fail earlier" in drug development. I think we'll see that mindset shift to "succeed earlier." It's a subtle difference. The focus on failing earlier is looking at the way science is evaluated in a commercial pipeline and placing the emphasis on scientific rigor. In 5 years' time we'll know a lot more about the molecular mechanisms of disease progression and how to target them. This is where the relationship between genomic and real-world data will start to shine through reverse translation. This should make it easier to find the "winners" in a drug development pipeline and to run powerful, precision clinical studies designed around the principle of getting the right drug to the right patient. ›

In 5 years' time we'll also be talking about new classes of drugs on the horizon. Cell and gene therapies are starting to change things already, and we know that gene editing will come sooner or later. These techniques will continue to develop alongside our increased understanding of our molecular biology. Of course, this will need to be supported by strong legal and ethical frameworks to make sure they are regulated responsibly.

Can you provide examples of how personalized medicine is helping patients with the diagnosis and treatment of rare diseases?

Through the 100,000 Genomes Project we've been fortunate enough to witness firsthand the strength and determination of families affected by rare diseases. Patients with rare diseases are often subjected to a seemingly never-ending rotation of specialists, tests, and a devastating lack of answers. By analyzing the whole genome, we are now able to start providing some answers. The diagnosis alone can be a tremendous relief to patients and their families, helping to narrow down the focus and bringing a sense of much-needed closure.

Again, this all goes back to the research that helps us understand the mechanisms underpinning conditions. For example, one of our participants in the 100,000 Genomes Project is a young girl named Jessica. She was enrolled in the project with her parents, due to the frequent epileptic fits she was suffering. As you can imagine, this was extremely distressing for the family, especially not knowing what was causing the fits. Jessica's genome was analyzed and compared with those of her parents. This produced a few potential variants of interest, one of which was identified by our open-source PanelApp. This tool has information on thousands of genes that may be linked to rare diseases, as reported by doctors and researchers. The variant was identified in a gene called SLC2A1. Without the fully functioning gene, a particular type of sugar wasn't being transported to her brain, resulting in the fits. We were able to diagnose this as Glut1 deficiency syndrome. Fortunately for Jessica and her parents, adjusting to a low-carbohydrate, ketogenic diet is able to provide an alternative energy source to her brain and significantly reduce the number of seizures she experiences.

While this isn't the case for every patient with a rare disease, it does show the value a diagnosis can have. For others it may be a case of being able to recommend a particular treatment or referring them to a relevant clinical trial.

For readers of *Value & Outcomes Spotlight,* there is particular interest in health technology assessment (HTA)—how are NICE and other HTA agencies responsible for population-wide decision making coming to grips with personalized medicine applications?

In first instances, it's understanding the technology. We're fortunate in the United Kingdom that notified bodies and regulators are very proactive in facilitating the responsible adoption of new technologies. The key is in understanding what new technologies can do, how they do it, what the need is, and what the risk is.

If we look at something like whole genome sequencing (WGS), this raises some interesting questions around the clinical and cost-effectiveness and broader impact of healthcare treatments and tests. As much as NGS has made WGS cheaper, it is still relatively expensive. A lot of work is going into demonstrating clinical utility, health economics, and understanding the risks and ethical considerations. Organizations like NIHR, NICE, and MHRA all enable new technologies and protect the interest of the population. It's that last bit that people tend to forget sometimes. The population are the main stakeholders and the taxpayers for all of this.

At Genomics England, we involve participants of the 100,000 Genomes Project actively in our decision making. This is extremely useful for us, as it grounds us in real-world needs of patients and helps build trust around emerging technologies.

ADDITIONAL INFORMATION

To learn more about personalized medicine, go to ISPOR Personalized/ Precision Medicine Special Interest Group at www.ispor.org/specialinterestgroups.