Next-generation sequencing tests to become routine

Cancer patients in the US and UK will soon access next-generation sequencing (NGS) as part of routine clinical care. In the US, the Centers for Medicare and Medicaid Services (CMS) finalized a plan to cover diagnostic laboratory tests using NGS for patients with advanced cancer, a move designed to increase the use of approved gene-targeted therapies, increase access to clinical trials and help oncologists and patients make informed treatment decisions. In the UK, the National Health Service will launch a new service in October 2018 to provide access to the latest in genomic testing and management for the whole country. The NHS England Board will establish a national NHS Genomic Medicine Service “making the NHS the first healthcare system in the world to systematically introduce whole genome sequencing into healthcare,” says NHS chief scientific officer for England, Sue Hill. This rollout to all patients follows from the success achieved by Genomics England’s 100,000 Genomes Project, which will wind down at the end of 2018. Analyst Puneet Souda of Leerink Partners wrote in a note to investors that a boost to NGS testing is a positive for instrumentation makers which include Illumina and Thermo Fisher Scientific, and in the US it will help shape regulatory and reimbursement pathways for NGS tests for advanced cancers. Companion diagnostics should similarly benefit from having a well-defined commercialization path. When CMS first proposed its plan to cover NGS tests, some concerns were expressed by traditional laboratory test developers that under these new rules, their business would be eroded. Voices were raised, in particular, after the FoundationOne CDx, a companion diagnostic from Foundation Medicine, was approved last November to direct use of more than a dozen targeted cancer therapies (*Nat. Biotechnol.* **36**, 124–125, 2018). But NGS coverage applies only to somatic testing for advanced cancers and therefore does not impinge on traditional tests for hereditary testing, screening and other non-advanced cancer conditions.

Mark Ratner

“With all the recent privacy scares, it’s kind of an odd time to be asking a million people to voluntarily hand over decades of health records and DNA samples—but that’s exactly what the NIH is doing today.” A tweet on NIH’s genomics program. (@WIRED, 7 May 2018)

“If you only have 80% of the genome, you wonder what’s in the 20% you’re missing. The completeness is a big deal,” said Todd Mockler, of the Donald Danforth Plant Science Center in St. Louis. With the whole genome of the rose in hand, researchers will seek to restore scent to roses, which have lost it due to generations of breeding for size. (*The New York Times*, 30 April 2018)

ing with time, according to the World Health Organization. Worldwide, around 50 million people have dementia, with close to 10 million new cases annually. And with an aging population, the total number of patients suffering from dementia, about 60% of whom have Alzheimer’s, is projected to reach 82 million in 2030 and 152 million in 2050. Only a handful of drugs are approved to treat Alzheimer’s, and they only alleviate symptoms without stopping or reversing the disease.

Many hope the guidelines may reenergize the field. “There is a new enthusiasm that the authorities want to work with us, they don’t want to see drug development come to a stop,” says Gary Romano, who heads the development of drugs to treat Alzheimer’s at Johnson & Johnson.

The guidelines may open up funding and clinical trials for companies not focused on β -amyloid or tau. “You see an increase in the targets advancing in clinical trials and a diversification,” says Heather Snyder, senior director of medical and scientific relations at the Alzheimer’s Association. Of 23 new programs funded by the association, only one is in an amyloid-targeting drug, according to Snyder.

“Microglial function and inflammation are going to be the leading edge,” says Tetsu Maruyama, CSO of the London-based Dementia Discovery Fund, a venture capital fund focused on dementia treatments. Normally, microglia police the central nervous system, and remove toxic molecules like β -amyloid and tau tangles. However, in AD-induced inflammation, they fail to clear aggregated amyloid, and may themselves produce toxic cytokines. Some companies are starting to test drugs that might restore microglia to their normal function.

One such program is Denali Therapeutics’ DNL747, a molecule that inhibits kinase RIPK1, an enzyme highly expressed in AD patients in response to inflammation. Denali struck a development deal with Takeda earlier this year, to start an early-stage clinical trial of healthy volunteers with DNL747.

“While ICER has no medical nor governmental authority, there is significant concern that this report will be used to deny access to life-saving care [for cystic fibrosis patients].” Sentiments of the charity Cystic Fibrosis Research on the call by the Institute for Clinical and Economic Review for a 70% reduction in the price charged for Vertex’s suite of cystic fibrosis therapies. (*thepharmaletter*, 4 May 2018)

“The ruling has some very interesting language about patents being a public franchise. This is not the first time the court has said this, but this is the loudest.” Jacob Sherkow of New York Law School opines on the US Supreme Court ruling

Annexon Biosciences has under development a program focused on complement-mediated neurodegeneration, betting that blocking C1q in the complement cascading pathway will forestall loss of neuroconnections that accompanies inflammation of nervous tissue. Alektor, which signed a \$205-million deal with AbbVie, is also focused on immune deficiencies as the basis for neurodegeneration. NeuroTherapia is looking at cannabinoid receptors in the brain to tame microglia. Their lead product, NTRX-07, a selective cannabinoid type 2 receptor agonist, reduced the expression of inflammatory agents, resulting in neuronal survival and proliferation in preclinical studies. GliaCure is developing a molecule, GC021109, that binds PsY6 receptors on microglia, inducing phagocytosis, and perhaps restoring the function to microglia.

But these programs may face problems down the road. The FDA does not indicate what kind of biomarker they would be willing to accept, and researchers don’t really know how the disease progresses, and what a biomarker would need to show.

Still, many hope the guidelines will have a large impact on the field. “FDA guidelines are always very powerful,” Corinne Lasmezas, a neuroscientist at The Scripps Research Institute, says. “I think the effect it will have is very large.”

Approval based on biomarkers requires follow-up after the drugs are on the market, according to the guideline. But as recent experience shows, the follow-up may be lacking. Of 24 therapies granted accelerated approval by the FDA from 2009 through 2013—mostly in oncology—fewer than half went through a round of trials after approval to demonstrate that they were, in fact, effective for a minimum of three years after approval.

In the long run, it is not important which of the pathways is successful, Maruyama says. “If amyloid works in the long run, we will need complementary medicines, and if it doesn’t, we will need other approaches.”

Eva von Schaper Munich

that the controversial *inter partes* review process is constitutional, countering drug companies’ argument that such matters should go to trial. (*STAT News*, 24 April 2018)

“We have nothing against CRISPR. We love it and use it all the time. But we’re talking about changes that are just massive. It’s like if you’re editing a short story: if you’re changing so much of it, you might as well just rewrite the whole damn thing.”

Jef Boeke, director of the Institute for Systems Genetics at NYU Langone Medical Center on the program’s ambition to recode the human genome to make it resistant to all viruses. (*STAT News*, 1 May 2018)