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A massively parallel sequencing solution for clinical diagnosis of genetically diverse metabolic disorders

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For metabolic disorders with similar symptoms and multiple potential genetic origins, definitive diagnosis has relied on sequencing individual candidate genes. Whole-exome sequencing presents an attractive alternative, as demonstrated in a proof-of-concept report by a collaborative group at Baylor College of Medicine and National Taiwan University Hospital. The panel test included 16 genes known to cause either liver or muscle forms of glycogen storage disease (GSD). Obtaining definitive results for 17 patients with clinical, histochemical, and/or enzymatic evidence of a GSD but negative or inconclusive molecular findings, took about eight weeks, including confirmatory Sanger sequencing. The test correctly identified all types of genetic alterations, from single-nucleotide substitutions to large deletions involving more than one exon. By contrast, the current conventional approach is more expensive and much more time-consuming, leaving families in limbo and delaying potentially lifesaving treatment. The authors point out that the technique is well suited for clinical diagnostics and can be scaled up and automated with robotic liquid handling. The technique is likely to be employed in situations such as this example, in which genetically heterogeneous biochemical disorders can be sorted out, but its use in many other clinical contexts will certainly grow. *—Karyn Hede, News Editor*

Gaucher disease patients and *GBA* mutation carriers face little overall increased risk of Parkinson disease

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As the use of comprehensive genomic sequencing accelerates, it becomes imperative to clarify disease risk, particularly for carriers of common mutations with uncertain health consequences. An example is mutations in the β-glucocerebrosidase (*GBA*) gene, which cause Gaucher disease (GD), the most common inherited lysosomal storage disease. Carrier status is relatively common, ranging from about 1 in 100 among the general population to more than 8% among Ashkenazi Jews. Several studies have suggested that carrier status is associated with a greater risk of developing Parkinson disease (PD). However, Rana et al., in a survey of GD patients and their families attending a clinic at Mount Sinai Medical Center, New York City, found a very modest risk of PD. Among nearly 600 patients and families with GD, 11 parents, 5 siblings, and no children had been diagnosed with PD. The researchers estimated the overall PD risk of carriers of *GBA* mutations to be 2.2% by age 65, a figure similar to the risk in the general population, and 10.9% by age 85. This information may reassure individuals who learn that they are carriers, because it suggests that their risk of developing PD is not much higher than that in noncarriers. The study should be of immediate benefit to genetic counselors returning findings to families of Ashkenazi Jewish descent, who are more likely to be screened for *GBA*-mutation carrier status. *—Karyn Hede, News Editor*

NEWS BRIEFS

Genomics and US security: the Committee on Foreign Investment in the United States to weigh in

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The corporate buy-out of California-based Complete Genomics (CG), a DNA-sequencing company, remains in limbo as China-owned giant BGI Shenzhen's offer of $117.6 million is scrutinized for potential national security implications. The merger's fate may hinge on whether the Committee on Foreign Investment in the United States, an interagency group charged with reviewing large financial transactions that could result in control of a US business by foreign individuals, decides whether retaining control of genomic technology in the United States is a matter of economic and national security. CG and its largest competitor, San Diego–based Illumina, were recently close to reaching a merger deal when the former's board suddenly switched allegiance to the Chinese company. The two US companies have been mired in a lengthy court battle over patent rights to proprietary sequencing technology. The case appeared to be going CG's way after a northern California judge granted its motion for partial summary judgment of invalidity of Illumina's claim of patent infringement, but in November 2012 the court said it would reconsider part of its ruling. Now CG's own shareholders are also suing to block the sale. The purchase of CG by BGI Shenzhen would give the Chinese-owned company access to advanced sequencing technology and CG's databases and analytics, along with their client base, which includes the National Cancer Institute and many US universities and research institutes. *—Karyn Hede, News Editor*

Coming this summer: closure on whether genes can be patented


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The long and tortuous saga regarding the legal status of gene patents in the United States will finally come to an end this summer. The US Supreme Court has granted a writ of *certiorari* (that is, they have agreed to hear the appeal) in the now famous legal case orchestrated by the American Civil Liberties Union against Myriad Genetics regarding their patents on *BRCA1* and *BRCA2*.

Significantly, the Court will address only the issue of whether human genes are patent-eligible. This allows a prior decision to stand that invalidated Myriad's broad "methods" claims in

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which they sought to patent the association between mutations in the *BRCA1* and *BRCA2* genes and a high risk for breast and ovarian cancer.

How the Supreme Court will rule is anyone's guess. The fact that it agreed to hear the case simply tells us that at least four justices felt that the Court should weigh in on this issue. I'll personally go out on a (public!) limb and predict that the Court will rule that genes are ineligible for patenting under US law. I'll also predict that, if I'm right, the wheels of scientific progress will keep right on turning, and, indeed, our patients and the field as a whole will be the beneficiaries. *—James P. Evans, Editor-in-Chief*