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ANALYSIS

Wrangle over rights to *BRCA1*

Many observers were surprised at the beginning of August when the US Patent Office (PTO; Washington, DC) granted OncorMed (Gaithersburg, MD) patent no. 5,654,155 (the '155 patent) covering a full-length DNA "consensus" sequence for the tumor suppressor gene *BRCA1*. They had expected that Myriad Genetics (Salt Lake City, UT) would win the race. Back in October 1994, Myriad and its collaborators revealed that they had isolated *BRCA1*, and the company has at least eight US patents pending that cover the wild-type gene, several mutations and neutral polymorphisms, and diagnostic methods. The earliest patent was filed on August 12, 1994, yet none has issued.

A further complication in determining who owns what around *BRCA1* is that, earlier this year, the PTO granted the University of California (UC; Oakland, CA) patent US 5,622,829 (the '829 patent). This covers 12 mutations in the *BRCA1* gene that predispose women to breast and ovarian cancer and diagnostic methods involving those mutations.

Over 200,000 women will be diagnosed with breast or ovarian cancer this year in the United States alone. While only an estimated 5–10% of these cases will be due to mutations in the *BRCA1* gene, diagnostic rights could be worth a conservative \$100 million a year. Nearly 200 mutations in *BRCA1* have been published and another 1000 have been identified. Most, if not all, will be patented.

Given the number of patents filed on *BRCA1*, who will own the diagnostic rights? Assuming Myriad is granted a patent on the wild-type gene, it should have the upper hand—Myriad will have the right to exclude others from using the gene for diagnostic testing. In order to screen patients, however, Myriad may require licenses to the numerous patents covering mutations, like UC's '829 patent—or risk a patent infringement suit.

UC's first set of claims, their "composition claims," cover all uses for 12 claimed *BRCA1* allele compositions, including diagnostic testing. Isolating and sequencing a claimed allele may, therefore, trigger patent infringement. The fact that Myriad will not know before screening what mutation patients have is irrelevant; patent infringement does not turn on what the potential infringer thought.

UC's second set of claims covers methods of screening patients by "detecting the pres-

ence or absence of specific hybridization" between an oligonucleotide spanning the mutation and a patient's *BRCA1* gene. These claims pose less of a problem. Given the number of mutations identified, most diagnostic testing will involve end-to-end sequence of patients' genes and avoid patent infringement. OncorMed has already obtained a nonexclusive license to UC's '829 patent.

OncorMed is similarly filing patents, presumably in the hope of forcing Myriad to the negotiating table. OncorMed's '155 patent claims "an isolated consensus DNA sequence of the *BRCA1* coding sequence." OncorMed sequenced the entire *BRCA1* genes of five individuals with no history of hereditary cancer. Based on the neutral polymorphisms' frequency of occurrence, OncorMed arrived at a "consensus" sequence that it claims is required to properly interpret diagnostic results.

OncorMed's strategy is questionable. First, OncorMed's consensus sequence differs from Myriad's published wild-type *BRCA1* sequence. So long as Myriad uses its wild-type sequence as a baseline, it should avoid patent infringement. Second, the validity of OncorMed's patent is a concern. OncorMed conceded that the seven polymorphisms in its claimed consensus sequence had been published more than a year before the patent's US filing date in February 1996; the filing, therefore, falls outside the normal 12 month "grace period." The polymorphisms are also disclosed in one of Myriad's European patent applications. OncorMed defended its patent by stating that the patent examiner was aware of all of the prior publications.

Myriad may have an opportunity to draft claims in the US (or to file a continuation with claims) that specifically cover the consensus sequence claimed in OncorMed's '155 patent or that invoke an interference to determine priority of invention. Alternatively, Myriad may do nothing and rely on the fact that its patent—when it issues—is likely to cover the wild-type *BRCA1* gene and oligonucleotides capable of amplifying and sequencing the gene. Without the right to amplify patients' genes, OncorMed will not be able to perform diagnostic testing.

Nevertheless, OncorMed currently holds the only issued patent for a full-length sequence of *BRCA1*. Moreover, the patent enjoys a legal presumption of validity, which is not easily overcome. Until Myriad is granted a patent, OncorMed is free to use the wild-type *BRCA1* gene for diagnostic testing.

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