BRCA1 Discovery Led to Patent Debate, Genetic Screening

This is part of an occasional series that recalls some of the stories reported 10 years ago in the News section of the Journal.

Although the announcement in 1994 that the BRCA1 gene had been isolated was greeted with much fanfare in the scientific community, it would be the debate about patents on the gene that would capture the spotlight in the following decade. Most recently, the European Patent Office (EPO) announced this May that it has revoked Myriad Genetics’ European patent for their test that detects mutations in the BRCA1 gene. The patent was revoked because of “prior art,” and did not meet the requirements for level of invention, according to the EPO.

In the United States, Myriad Genetics holds the exclusive rights to testing for BRCA1 and BRCA2 mutations, which they market as a combined test called BRACAnalysis. Costs for testing range from $350 for a single-mutation analysis—useful in families where there is a specific known mutation—to $2975 for a full-sequence analysis of both genes. The company also offers a special screen for several mutations commonly found in the Ashkenazi Jewish population for $415.

BRCA1 was not the first cancer gene to be discovered, but BRCA1—along with BRCA2, discovered in 1995—has undoubtedly become one of the most well known. The discovery of the BRCA genes has changed the lives of many of those women who have family histories of breast and ovarian cancers and have decided to undergo testing. Although only 0.1% to 0.2% of the general population are carriers of mutations in either BRCA1 or BRCA2, about 2% of women with breast cancer have one of the BRCA mutations, and about 10% of women with ovarian cancer are carriers.

Conversely, the risk of breast or ovarian cancer among mutation carriers is high. Last year, a study led by University of Washington geneticist Mary-Claire King, Ph.D., suggested that mutation carriers have an 82% risk of developing breast cancer and a 54% risk of developing ovarian cancer by age 80.

Most insurance plans cover genetic testing, but many women decide to pay for the tests themselves, fearful that a positive result will give their employer or insurance company ammunition for discrimination. Some women use aliases, get tested but defer being told of the results, or even refuse testing based on these concerns. “It’s absurd that patients should deny themselves this information out of fear,” said Mark H. Greene, M.D., chief of the Clinical Genetics Branch of the National Cancer Institute.

Women from these families frequently used to assume that they would develop the disease. But now, “women can get off the hook, so to speak, if they’re negative for a mutation that is in their family,” said Henry Lynch, M.D., professor of medicine and professor and chairman of the Department of Preventive Medicine at the Creighton University School of Medicine in Omaha, Neb. Not only does an individual who tests negative know that she is not at increased risk of cancer, but she also knows that her children are not carriers either.

For women who do test positive for BRCA mutations, their options range from increased surveillance to preventative measures that include prophylactic surgery. Among the options Lynch offers to his patients with BRCA mutations is prophylactic mastectomy, which may reduce the risk of breast cancer in mutation carriers by 90%. After patients have finished having children, around age 35 or 40, he offers prophylactic oophorectomy, which may reduce the risk of ovarian cancer by 85% and breast cancer by 25% in mutation carriers, according to a study published in 2002 in the New England Journal of Medicine.

Lynch also teaches mutation carriers how to do breast self-examinations in addition to administering annual mammograms starting at a much earlier age than is recommended for the general population.

There are fewer options for ovarian cancer screening. Transvaginal ultrasound and CA125 have serious limitations, and no screening test for ovarian cancer has been shown to reduce morbidity or mortality. There is a definite need for the development of better screening methods, said Greene.

Although genetic testing now allows many women with family histories of breast and ovarian cancers to make better informed choices, the discovery of these genes has led only to more questions. Only 5% to 10% of the 192,000 women diagnosed with breast cancer in the United States each year have a hereditary form of breast cancer, but as many as 40% of cases of hereditary breast cancer have no known cause.

Even after years of research, scientists still do not know what the BRCA1 protein specifically does or how mutations confer genetic susceptibility at the molecular level. Even the full spectrum of cancers caused by BRCA1 gene mutations—currently known to include breast, ovarian, prostate, and pancreatic cancers—remains unknown.

Furthermore, many of the studies that have established the risk factors for breast and ovarian cancers have not established whether these factors apply to mutation carriers as well. “[You can’t simply assume that they’re going to behave the same way] in mutation carriers as in the general population, said Greene.

These issues are particularly important for cancer patients and their families because “we’re not able to do all these things that people hope for and pray for,” said Lynch.

—Sarah L. Zielinski