Genes—to have and to hold

Methodological advances in genomics will benefit research and personalized medicine most if genes are accessible to all.

At present, about 20% of human genes are covered by patents. The question of who is allowed to use genetic information affects both basic and applied research. The much-anticipated translation of genome technology into molecular diagnostics and personalized medicine could hit serious roadblocks unless gene ownership issues are cleared.

A general definition of a product patent on a gene remains elusive. Single mutations are patentable, as are entire genes, and the burden to prove their function is light and often stated in vague terms. A majority of patents cluster around genes linked to disease and, though often discovered and initially patented by universities, are now held by a small number of private companies. According to a study in 2006, 64% of DNA patents are held by the top ten genomics companies.

Patents do not restrict scientific research, say the proponents of gene patenting. Yet the degree to which independent research on patented genes is permissible is a legal gray zone. By definition, a patent is intellectual property that grants a period of ownership to the patent holder. For gene patents this means, in theory, that the holder has the right to prevent anyone from studying a gene. In practice, many researchers ignore patents even though by sequencing a genome or even a panel of genes they are likely to infringe patents left and right. A compliant scientist would need to obtain licenses for every patent—an impossible endeavor.

Even though no infringement lawsuits have yet been brought against academic researchers, the uncertainty nonetheless draws the wrong emotions into the lab. One can see that noncommercial research is not exempt from patent claims, as is evident from the *Madey v. Duke* decision. Physicist John Madey had developed and patented a free-electron laser that Duke University continued to use after Madey's departure. In a patent infringement suit, both a district court and the US Court of Appeals for the Federal Circuit ruled in Madey's favor.

This ruling could have far-reaching consequences if applied to gene patents. According to the judges of the Federal Circuit, "Our precedent does not immunize any conduct that is in keeping with the alleged infringer's legitimate business, regardless of its commercial implications."

We agree that a strong patent system for inventions, such as new drugs, is an essential ingredient in biological and medical research. The alternative is keeping inventions secret for fear of being copied, which would substantially slow progress. What is not clear, however, is whether one needs exclusive rights to the gene itself to make such a drug.

One of the purposes of a patent is to inspire others to think of alternatives to work around the patent. A patent on a diagnostic kit should prompt others to come up with a better one, thus providing the public with choices. A patent on a gene stifles such innovation and works against the original spirit of the patent system.

The question of gene patent legitimacy was raised again recently by the US Court of Appeals for the Federal Circuit's decision to uphold Myriad Genetics' product claim on isolated *BRCA1* and *BRCA2* genes, in which the court ruled that isolated DNA is not a product of nature.

Because the decision was largely based on the definition of the word 'isolated', it would be reasonable to assume that this product claim is not infringed by technologies that do not rely on the isolation of a gene, such as next-generation sequencing.

But in practice, it appears that Myriad's claims on the *BRCA* genes reach far beyond an amplified DNA sequence. Although the company has never sued basic researchers, some are still uneasy. A study conducted by E. Richard Gold at McGill University in 2010 reported that some scientists expressed concerns about contributing their results on *BRCA1* and *BRCA2* to public databases. Legal experts say that even researchers who write software for analysis of mutations in *BRCA* genes, such as Steven Salzberg from the University of Maryland, could be sued for the inducement of infringement.

In recent years, researchers have applied advanced sequencing and other technologies to *BRCA* genes. Yet, unlike in the UK, these techniques have not been translated into a diagnostic test in the USA.

Patents should protect innovation, not hinder research or its translation to the clinic for patients' benefit.