The nascent CRISPR-Cas9 patent landscape in Canada

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CRISPR-Cas9 is a technology with the potential for an unimaginable impact on society. CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) allows scientists to edit genomes in living organisms at the cellular level by guiding a “scissor-like” protein to targeted sections of DNA within a cell, and then prompting it to alter or “edit" the DNA in some way. Potential uses already in the pipeline include improving immunity to cancer, curing AIDS by extracting HIV from human immune cells, building muscle in muscular dystrophy patients and replacing antibiotics as a strategy to combat bacterial infections. These applications just scratch the surface of already-explored medical uses. The possibilities, both inside and outside medicine, are truly endless.

As with prior transformative technologies that came before it, from the sewing machine to the smartphone, there are bound to be explosive fights over who owns CRISPR-Cas9. The spoils to the owner, or owners, are sure to be in the billions. And indeed, two academic groups – one at the University of California-Berkeley (UC) and the other at the Broad Institute (affiliated with Harvard and MIT) – have been engaged in a high-stakes war for several years over who invented CRISPR-Cas9.

On September 10, 2018, the U.S. Federal Circuit Court of Appeals rendered an important decision finding that UC’s earlier-filed patent application did not disentitle the Broad Institute (Broad) from its own foundational CRISPR-Cas9 patent in the United States. The Court affirmed that Broad’s contribution was patentably distinct from UC’s earlier CRISPR-Cas9 discovery. This decision led us to consider how the CRISPR patent war will affect research and commercialization of CRISPR-based inventions in Canada.

The CRISPR patent war

CRISPR-Cas9 is a genome editing technology that edits sections of DNA in cells by inserting, deleting or replacing DNA at targeted sites. Medical use of this technology has moved beyond the hypothetical. Last year, researchers in the U.S. successfully used CRISPR-Cas9 to correct a disease-causing mutation — the leading cause of sudden death in young athletes — in viable human embryos.

UC and Broad are the key players in the discovery and first uses of CRISPR-Cas9. The two are battling each other to determine which has priority to the claimed invention. The main issue is whether UC’s patent for the use of CRISPR-Cas9 in any cellular environment renders obvious (and therefore invalidates) Broad’s later-filed patent for the use of CRISPR-Cas9 specifically in eukaryotic cells (cells with a nucleus, including animal and human cells).

The main patent battlegrounds have been in Europe and the United States. In Europe, UC is the victor to date. UC was awarded an EU-wide foundational CRISPR patent having broad application in a wide variety of cell types. Conversely, Broad’s foundational CRISPR patent

was revoked due to a procedural error that left Broad with a later filing date, and the patent was found invalid based on intervening prior art. Broad indicated that it will appeal the decision.

In the U.S., Broad has had greater success. In response to a challenge by UC, the U.S. Patent Trial and Appeal Board (PTAB) found that Broad's patents cover distinct subject-matter such that no interference exists between UC and Broad's patents. UC appealed the decision, arguing that too much weight was given to the Broad inventors' statement that using CRISPR-Cas9 in eukaryotic cells had an unpredictable likelihood of success and that, in fact, UC's work created a reasonable expectation of success in eukaryotic cells.

In its September 10 decision, the Federal Circuit affirmed the PTAB's decision, deferring to its findings of fact. The Court pointed specifically to statements by the UC inventors that they were unsure if CRISPR-Cas9 would work in eukaryotic cells and that they had many frustrations in getting CRISPR-Cas9 to work in human cells. The evidence also indicated that the UC team recognized that the Broad team's contributions were significant.

The battles in the U.S. and EU are far from over, and uncertainty over ownership of CRISPR technology will make it more difficult for UC, Broad and others to ensure they have freedom to develop and make available CRISPR applications free from downstream patent infringement.

Possible path to peace

The uncertainty about the CRISPR patent landscape presents a barrier to innovation. CRISPR patents can inhibit future innovation premised upon this technology, both where access to the patents is not made available or terms of use are restrictive. Users of CRISPR technology may need to obtain patent licenses from UC, Broad and others as the price of admission for operating in the space. Fortunately, while the parties have been battling, they have generally been making their technologies available to researchers for widespread academic research uses.

One way to facilitate easier access to technology created by multiple groups is to create a patent pool from which multi-party licenses can be obtained. Amid the uncertainty over CRISPR-Cas9, on April 25, 2017, MPEG LA, LLC announced its creation of a global CRISPR-Cas9 patent pool, "pooling the foundational CRISPR/Cas9 patent rights under a single nonexclusive, cost-effective, transparent license." However, for the pool to be successful, many, if not all, patents deemed to be essential must be submitted. Broad has taken steps to join the CRISPR-Cas9 patent pool, but UC has not. Without UC joining, the patent pool does not resolve the present issue. We and others are watching closely to see if UC entertains the possibility of joining the patent pool following the Federal Circuit's recent ruling.

CRISPR air in Canada?

In Canada, the CRISPR patent dispute has yet to begin. Both UC and Broad have active patent applications yet to be reviewed by the Patent Office. Precedent in the U.S. and EU provides guidance on the battle lines. We expect that the parties will see their U.S. and EU disputes through, with the outcomes influencing their decisions and the views of the Canadian Patent Office examiners that will be reviewing the pending applications.

A search of Canadian Patent Office records reveals 210 published patents and pending patent applications referring to CRISPR and Cas9. These patents and applications are owned by numerous geographically dispersed entities in a variety of technological fields. To

commercialize these technologies in Canada, licenses to CRISPR's foundational patents and particular applications may be needed. As CRISPR-based technologies move from the lab to the market, licensing patents from a variety of sources may prove more difficult.

For Canadian researchers and companies, clarity of ownership and terms of use will be paramount. We are hopeful that the prospect of never-ending litigation and stifled innovation will cause UC and Broad to resolve their dispute and create a pathway for broad and clear access to CRISPR patents. This is precisely what happened with the sewing machine in the mid-1800s, though it took years of acrimonious litigation before a deal could be reached. Given the potential commercial applications for CRISPR and also the serious ethical concerns arising from its use, integration of patent access into broader CRISPR standard-setting cannot come soon enough.

We will be tracking the developments of the CRISPR-Cas9 patent war with great interest. If you need advice on the use of CRISPR-Cas9 technology in Canada, please contact Nathaniel Lipkus at nlipkus@osler.com or 416.862.6787.

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