

# Patenting CRISPR-Cas9: The legal battle

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## Who am I ?

- Doctorate in Chemistry (Oxford University)
- I am a European Patent Attorney, and was a partner in the British patent attorney firm Dehns for many years
- Together with my wife, Prof Sigrid Sterckx (UGent), I have written a book and many articles about patents on medicine-related subjects
- No conflicts of interest in relation to the subject matter of this talk

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## Scientific background (1)

- In **bacteria (prokaryotes)**, the DNA is essentially freely floating in the cell.
- In **plants and animals** (the things we might want to modify to prevent a disease) the DNA is tightly wrapped up in the nucleus. Such cells are **eukaryotes**.

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## Scientific background (2)

- If we want to genetically modify cells, then ideally we must ensure that the modification occurs **at the desired location** – otherwise we may get undesired, off-target, events.
- **CRISPR-Cas9** seems to offer us the ability to make the DNA change we want at the very place we want it to be made.
- For **humans**, this opens the prospect of avoiding genetic disease.
- For **plants and farmed animals** it offers the chance of making billions of dollars.

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### Scientific background (3)

- **CRISPR is an antiviral “immune system” found in bacteria** (prokaryotes).
- The bacterial DNA contains short viral DNA sequences flanked by palindromic sequences as well as DNA coding for a protein “**scissor**”. The viral sequences reflect previous viral infection of the bacteria (or its ancestors).
- When a virus injects its DNA into a **bacterium**, the system swings into action, drawing the scissors to remembered sections of the viral DNA and chopping it up, thereby **disabling the viral attack**.

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### Scientific background (4)

- **Jennifer Doudna's group** at University of California, Berkeley (**UCB**) showed that a CRISPR-Cas system could be programmed to **home in on any desired short DNA sequence, not just viral sequences**.
- They did this with **free (i.e. unpackaged) target DNA** and published this in a seminal article in 2012. They also filed a **patent application**.
- **Neither** the paper **nor** the patent application contained any suggestion that the CRISPR system could work if the target DNA was packaged, i.e. as in the nucleus of a plant or animal (eukaryotes).
- Documents on file suggest that they did **not** believe CRISPR would work on eukaryotes.

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### Scientific background (5)

- But the potential financial rewards (and the Nobel Prize) that might come from showing that **eukaryotes** could be CRISPR'ed were such that **others** of course did try it out.
- **Feng Zhang** and his group of the **Broad Institute/MIT** showed that it could. In late 2012 they filed a **patent application** and published results in a paper.
- **This time**, both the paper and the patent application mentioned **eukaryotes**.

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### Legal background (1)

- At the relevant time, **US law** provided that the first person to make an invention can get a patent even if someone else filed their patent application for the same invention earlier. **The question of who invented first is sorted out in an “Interference”**.
- In **Europe**, what matters is **who filed first**, BUT the application must contain words that fully support the definition of the invention in the patent's “claims” (the sentences defining the scope of the monopoly that the patent gives to its owner).

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## Legal background (2)

- ▶ Since the late 1800s, we have had an **international treaty to simplify the patent application procedure**.
- ▶ If X files a patent application for invention Y on date A in country B, then X (or others to whom she has assigned the right to claim priority from that first patent application) can file a **further application Z** in country C and have it **treated as if it was filed on date A, as long as Z is filed within a year of date A**.
- ▶ But the **assignment of the right to claim priority** must, according to the European Patent Office, have taken place **before Z was filed**.

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## Licensing of the patents

- ▶ Both **Broad and UCB** have set up operations to license their CRISPR patents to others. **Many licences have been granted**.
- ▶ However, using CRISPR on plants or animals might be covered by **both** the Broad and the UCB patents, and higher licence fees can of course be charged if Broad can knock out the UCB patents and vice versa.
- ▶ Alternatively, they could **pool** their patents for licensing purposes.
- ▶ However, the **Nobel Prize can only be granted to a maximum of three people**, and more than three are involved.

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## The patent battles

- ▶ **Patent battles** are rarely fought in lots of countries – the **US** is the most important, closely followed by “the rest of the world”, typically represented by Europe. If one party wins the US and the other the rest of the world, then it is time to **negotiate a revenue-sharing deal**.
- ▶ The “**nuclear option**” (proving that all the patents are **invalid**) is NOT attractive to the parties. Here, the key question is **obviousness** – if the subject matter of a patent is obvious, then the patent is invalid.

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## Obviousness

- ▶ **Was it obvious that CRISPR would work on free-floating non-viral DNA** (the experiment that formed the basis for **UCB's** publication and patent application)?
- ▶ To my mind **yes**.
- ▶ Knowing CRISPR worked on free-floating DNA, was it **obvious to use it on eukaryotic DNA**? The **question** is “was it obvious to try with a reasonable expectation of success?”
- ▶ **It clearly was obvious to try**. The expectation was poor, but the potential reward was huge. Millions of Belgians buy lottery tickets. The potential reward makes the outlay a reasonable bet.

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## The US and EU battles

- ▶ These are based on entirely different grounds.
- ▶ The EU one is more formalistic, so I will start with that.

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## The EU battle

- ▶ US patent applications are filed by the inventors so it is they who have the right to claim priority when filing elsewhere.
- ▶ **Broad did not have the rights assigned by all the US inventors when they filed for the EU.** If they don't have the right to claim priority then their EU patents are invalid because their work was published before the application for EU was filed – **the claims lack novelty.**
- ▶ At the **opposition** stage, the **European Patent Office has revoked Broad's patent.** Broad appealed and the Technical Board of Appeal **hearing** will take place in **January 2020.**
- ▶ If Broad is lucky, the point will be passed to the highest instance (Enlarged Board of Appeal) and **we might see a decision in 2021.**
- ▶ Personally, I believe that Broad will lose.

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## The US battle (part 1)

- ▶ **An interference was declared between Broad and UCB.** The interference would be denied if CRISPR on eukaryotes was inventive over CRISPR on free-floating DNA.
- ▶ The **US Patent Office decided that CRISPR on eukaryotes was indeed inventive over CRISPR on free-floating DNA.**
- ▶ UCB appealed, but lost.

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## The US battle (part 2)

- ▶ **A few months ago,** the US Patent Office declared a **second interference.**
- ▶ **The question this time is who was first to invent CRISPR on eukaryotes, UCB or Broad.**
- ▶ The fight is getting personal with not-so-polite language.
- ▶ We might see the outcome (before appeal) next year.
- ▶ Personally, I think Broad will win.
- ▶ However, **Broad is urging UCB to pool their patents (and share the royalties),** perhaps to avoid UCB pulling the "nuclear trigger" (having all of the patents declared invalid).

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## The more fundamental question

- Should it be the patentees who decide whether or not others have access to use a foundational technology like CRISPR which could be life-saving ???

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## The End

Thank you for your attention

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