

CRISPR Patents – The story continues

What's going on here?

One might ask: "I thought Broad Institute already '*won*' the patent battle regarding CRISPR?" Now we learn Berkeley will soon be issued a [new CRISPR patent](#) that *predates* the patents previously invented by Feng Zheng and the good folks in Massachusetts.



The first fight

The battle fought previously and arguably '*won*' by Broad Institute relates to what is called in the patent world as an '*interference*'. Berkeley alleges that Broad should *not* be issued a patent because Berkeley's earlier CRISPR filing completely encompasses the subject matter claimed by Broad.

Broad won that fight because Berkeley taught about CRISPR in prokaryotic cells, but did not teach that this activity could be done in eukaryotic cells. Broad is entitled a patent because they included some 'new teaching' and that teaching was deemed 'not obvious'. Thus, they are entitled a patent.

Berkeley's assertion of *interference* was denied because Broad did in fact have something new in their application.

Unfortunately for Berkeley, the community now 'feels' like Broad is dominant in the CRISPR patent battle. But as we will show below, that is certainly not likely to be the end of the story.

Berkeley's earlier patent will soon be granted

A '*Notice of Allowance*' has now been issued for Berkeley's very important early CRISPR patent with a filing date of March 15, 2013. So what does this mean with respect to Broad's already granted patent?

To answer that, one must appreciate that patents often fall within the scope of other patents. Sometimes completely within, and sometimes partly within. Sometimes not at all. The best way to represent this is with a Venn diagram.

Simple Example

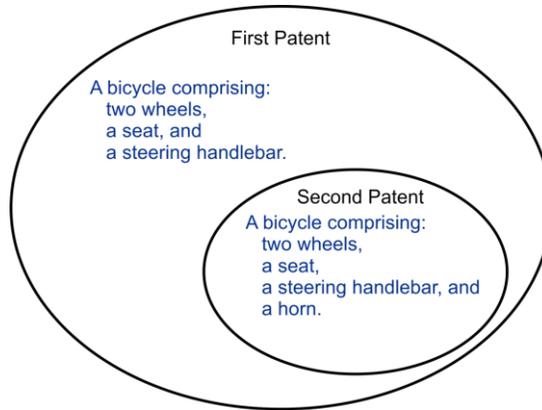
If a first inventor invents and patents a bicycle, the patent having broad claims:

A bicycle comprising:
two wheels,
a seat, and
a steering handlebar.

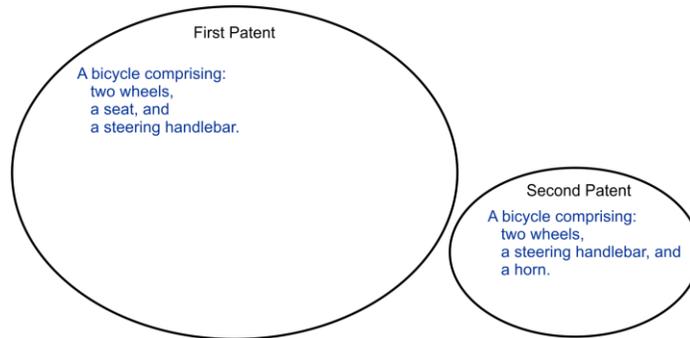
And a second inventor invents and patents an improved bicycle, the patent claiming:

A bicycle comprising:
two wheels,
a seat,
a steering handlebar, and
a horn.

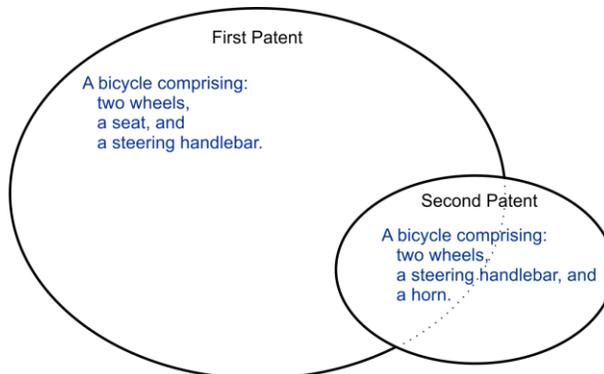
In this instance, the second patent is a complete subset and falls entirely within the scope of the first. It doesn't matter if the second patent issued before the first. It only matter which was filed first. So the Venn diagram is like this:



If the second patent omits an element from the first, say for example the seat, then it lies completely outside the scope of coverage of the first. In this case, the Venn diagram looks like this:



Since the second patent doesn't explicitly denounce the seat, it is more accurate to represent it as a bicycle having two wheels, a steering handlebar, and a horn – and maybe a seat, and maybe not a seat. So the Venn diagram would look like this:



If the second bicycle includes a seat, he must pay a license to the first patent owner. Even though the second inventor has her own patent, she must still pay for a license for all

bicycles she sells that include: two wheels, **a seat**, and a steering handlebar. For bicycles she sells without a seat – no license necessary.

What happens to a third guy (non patentee) who wants to make or use a bicycle having two wheels, a seat, and a steering handlebar, and a horn? Who should he get a license from? The first inventor? The second inventor? Both. Such device infringes both patents. It is not enough to get a license from the second inventor and declare:

"I am in the clear! I've got a license to make these bicycles!"

This person must get a license from BOTH the first inventor AND the second inventor.

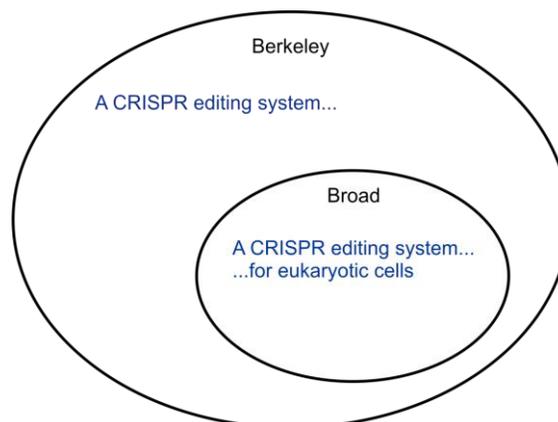
Now that Berkeley has their patent soon to be granted, it is likely that anyone doing CRISPR will require a license from both Broad Institute AND Berkeley. Ouch.

How does the CRISPR Venn look?

Of course, the CRISPR Venn is a bit harder to develop than the bicycle Venn. But if you are reading this then you are likely a pretty sharp person who doesn't mind complex things. So let's try to develop what the CRISPR scenario looks like using Venn diagrams.

Eukaryotic Cells

A first most important distinction of the Broad Institutes patents includes the patentable difference that it applies to eukaryotic cells. Thus, we can draw a first simple Venn diagram like this:



By simply *adding* the distinction of a system that is suitable for eukaryotic cells, Broad is entitled a patent. But they might fall entirely within the scope of the Berkeley patent. If they consider very carefully the claims of the Berkeley patent to find the can omit a claimed element, say for example 'a seat' – then they might possibly lie outside the scope of Berkeley's patent, or perhaps partly outside. One must carefully consider in detail the precise claim of the Berkeley patent.

Berkeley's new CRISPR claim

Here is the first claim of the Berkeley patent:

A method of cleaving a nucleic acid comprising: contacting a target DNA molecule having a target sequence with an engineered and/or nonnaturally-occurring Type II Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-CRISPR associated (Cas) (CRISPR-Cas) system comprising:

- a) a Cas9 protein; and
- b) a single molecule DNA-targeting RNA comprising
 - i) a targeter-RNA that hybridizes with the target sequence, and
 - ii) an activator-RNA that hybridizes with the targeter-RNA to form a doublestranded RNA duplex of a protein-binding segment,wherein the activator-RNA and the targeter-RNA are covalently linked to one another with intervening nucleotides, wherein the single molecule DNA-targeting RNA forms a complex with the Cas9 protein, whereby the single molecule DNA-targeting RNA targets the target sequence, and the Cas9 protein cleaves the target DNA molecule.

Of course, that is not so easy to read. But we'll try to parse it up just a little. To learn whether we lie 'outside' the scope of the claim, we must ask: "Can we *omit* an element – and still remain with a useful system". It is important that we omit something. If we cannot omit some element of the claim, then we infringe the claim.

So, let's look at elements of the claim.

Element 1 – 'contacting a target DNA molecule having a target sequence'.

Can we devise a gene editing system that does not meet this limitation? That is, can we make a gene editing system that *does not* contact a target DNA molecule where the molecule has a target sequence? I have a feeling that is going to be rather hard. It certainly is not a system that relates to today's CRISPR system. Broad Institute does this step of all methods they are doing. Probably everyone does this activity when gene editing. So far, we infringe.

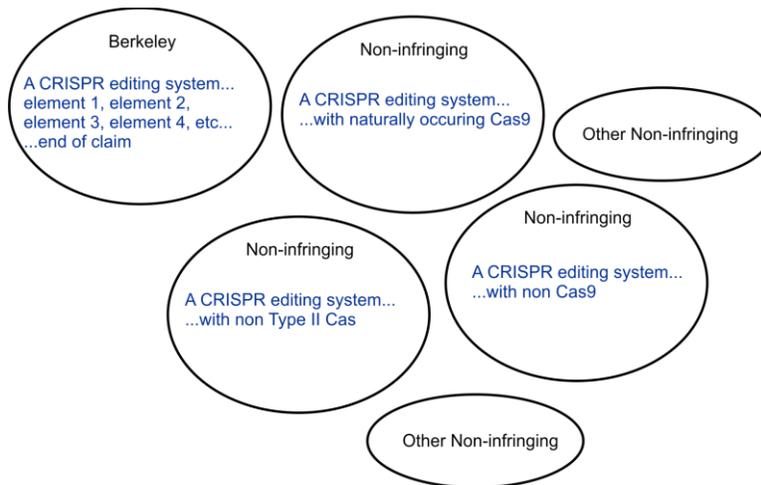
Element 2 – 'engineered and/or nonnaturally-occurring Type II Cas system'

This is interesting. If we use a *non engineered* or *naturally occurring* Cas system, then we do not infringe the claim. Further, if we use a Type I or Type III, IV, ...N Cas system, we do not infringe this claim. There are some possibilities to avoid infringement on this point alone. In order to infringe this claim, one **MUST** use a ***non-natural, engineered Type II Cas system***.

Element 3 – 'a Cas9 protein'

This is another limit. Maybe important. This patent claim does not cover Cas12a, Cas12b, CasX, or any other Cas that is not Cas9. This claim is limited to Cas9. There was probably no need whatever to limit this patent scope to Cas9 – but it is limited to Cas9. If you copy every other aspect identically, but you use Cas12a – then you do not infringe. (except for on very limited consideration called 'doctrine of equivalents' – but Cas12a is certainly not equivalent to Cas9 so it won't apply.)

OK – you get the point. You could continue to proceed through the entire claim element, by element asking whether it can be omitted. In this way, you can learn what type of gene editing systems lie outside the scope of the patent coverage. As one processes along this line of reason, a corresponding Venn diagram can be made for each element. For the first three elements described above, I submit the following Venn diagram:



On a first look, it appears that the new patent while having an early filing date, predating the best Broad Institute CRISPR patent is NOT limited to non-Eukaryotic cells, that is Berkeley's patent does include CRISPR on eukaryotic systems, BUT – it does have other limitations that probably leave lots of room to operate.

While I did only consider the first (usually the broadest) claim of the new Berkeley patent, and there are many additional claims (71) being issued simultaneously. It is necessary to analyze each of these to know whether or not the patent is infringed by various activity.

The important point is that if you already paid the Broad Institute for a license for their CRISPR patents, you did not get a license on the Berkeley patents. Those patents are soon to be issued and you may need a second license from Berkeley to continue your research. The question is whether your activity lies within the scope of the patent or not. I hope you can use the discussion here as a guideline to have a first look at whether or not you will soon be in talks with the Berkeley licensing department.

I invite you to please contact me directly if you would like to learn more about parsing patent claims.