

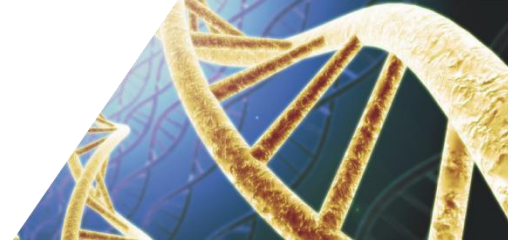


CRISPR/Cas9 technology  
Intellectual property & economic issues

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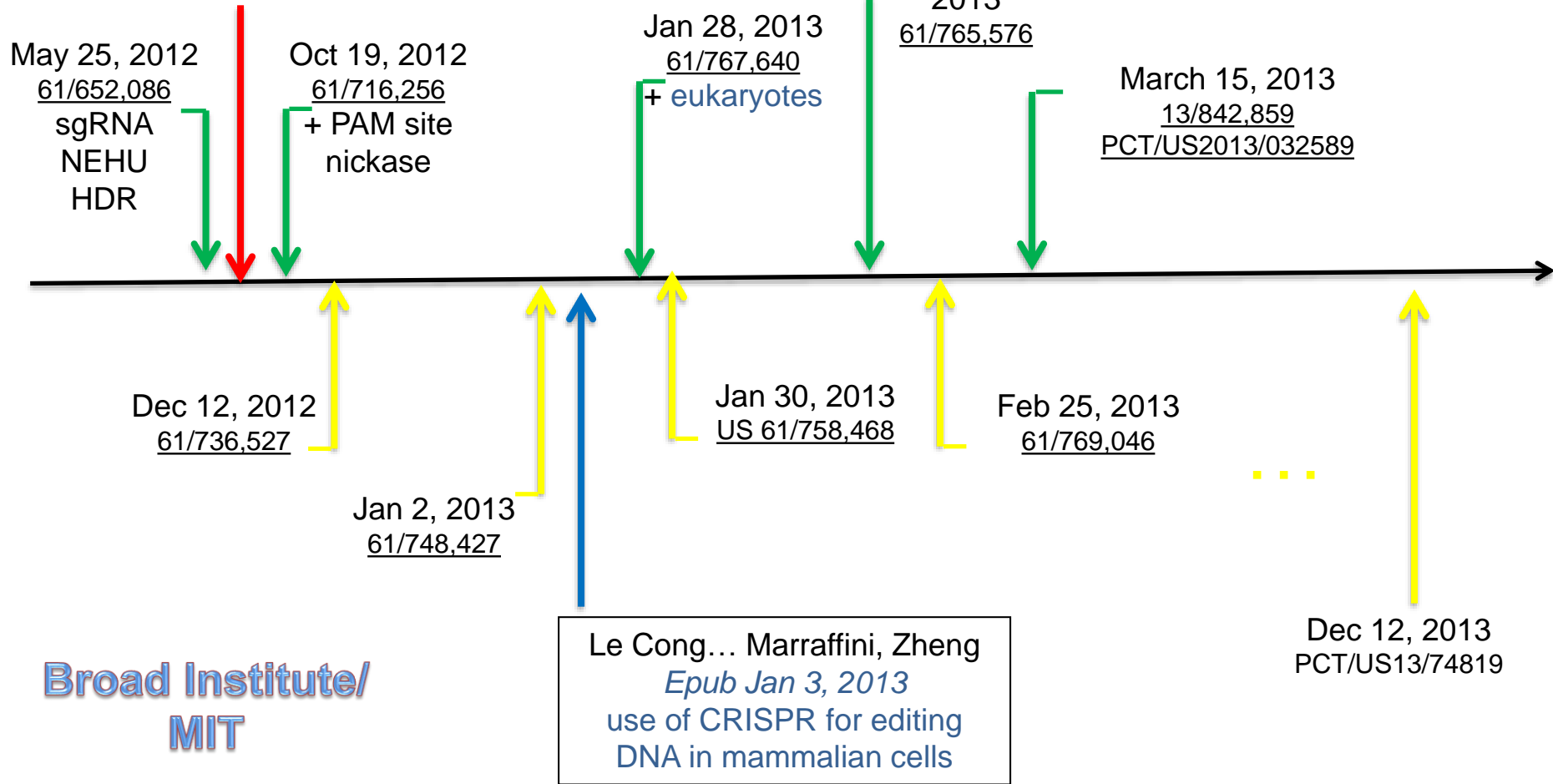
*ARRIGE kick-off meeting*

# CRISPR/Cas9 foundational patents



Jinek... Doudna, Charpentier  
*Epub June 28, 2012*  
 use of CRISPR to cut DNA

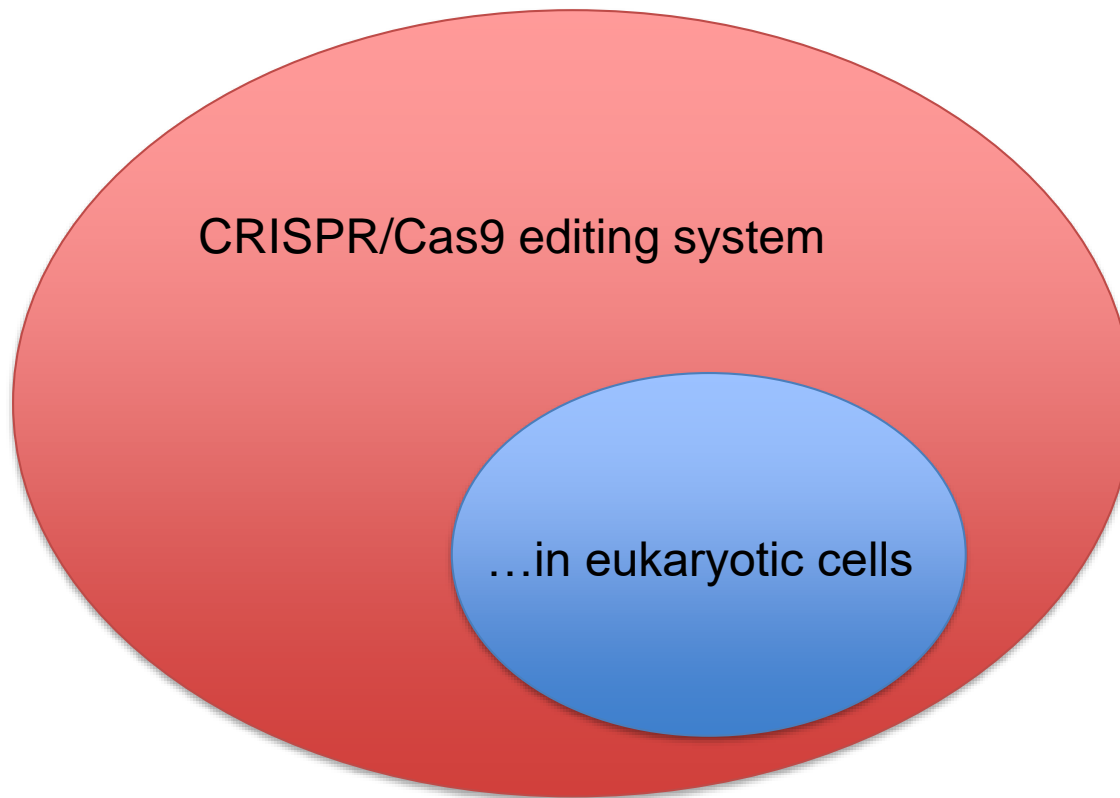
**UC Berkeley/  
 U. Vienna / E.C.**



# CRISPR/Cas9 foundational patents



**UC Berkeley/  
U. Vienna/E.C.**



*“the Broad Institute's patent is for green tennis balls but the patent we will have is for all tennis balls” (Doudna)*

**Broad  
Institute/ MIT**

# Patent law : right to patent protection



*Prior to 15 March 2013:*

A person shall be entitled to a patent unless —

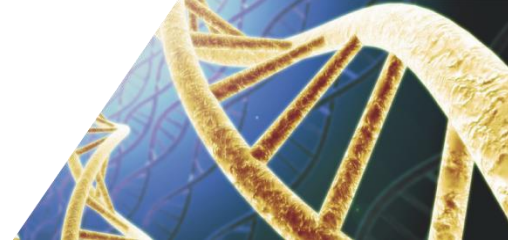
(a) the invention was known or used by others [...], or patented or described in a printed publication [...], **before the invention** thereof by the applicant for patent

=> First to invent

The right to a EP patent belongs to the person whose EP patent application has the **earliest date of filing**...

=> First (inventor) to file

# CRISPR/Cas9 : the patent dispute



**APPLICANTS** University of Vienna; the Regents of the University of California; Emmanuelle Charpentier

The Broad Institute; MIT

International patent applications	WO2013176772	WO2014204729, WO2014204728, WO2014204727, WO2014204726, WO2014204725, WO2014204724, WO2014204723, WO2014093718, WO2014093712, WO2014093709, WO2014093701, WO2014093694, WO2014093655, WO2014093635, WO2014093622, WO2014093595, WO2014093661
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Patent interference

USA Applications  
**13/842,859**; 14/685,502; 14/685,504;  
 14/685,513; 14/942,782; 15/138,604;  
 15/435,233; 14/685,513; 14/685,514;  
 14/685,516;

Patents  
**8,697,359; 8,771,945; 8,795,965; 8,865,406;**  
**8,871,445; 8,889,356;** 8,889,418; **8,895,308;** 8,906,616;  
**8,932,814; 8,945,839; 8,993,233; 8,999,641;**  
 9,790,490; 9,822,372; 9,840,713

Applications 14/105,035, 14/704,551....

EP Patents  
 EP2800811 (9 oppositions),  
 EP3241902 (opposition filed)

Application  
 EP18152360.6

Patents  
 EP2771468 (9 oppositions); EP2784162 (8 oppositions)  
 EP2896697 (8 oppositions); EP2764103 (7 oppositions)  
 EP2898075 (6 oppositions); EP2921557 (7 oppositions)  
 EP2931898 (6 oppositions)

Applications  
 EP2940140, EP2998400, EP3045537, EP3064585,  
 EP3144390

Oppositions

# CRISPR/Cas9: the patent dispute



## USPTO : Patent Interference No. 106,048

- An interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party
  
- USPTO Patent Trial and Appeal Board to determine the first to invent:
  - A method, in a eukaryotic cell, of cleaving or editing a target DNA molecule or modulating transcription of at least one gene encoded thereon...
  
- PTAB Conclusion (15 Feb. 2017):
  - Broad/MIT's claims are non-obvious over UC's claims
  - no interference-in-fact
  - no need to make a decision as to who invented first
  
- Appeal filed on 13 April 2017 by UC/U. Vienna/E.C.

# CRISPR/Cas9: the patent dispute



➤ In parallel, at the European Patent office (1/2):

❑ EP 2 800 811 B1 granted on 10 May 2017 to **UC/U. Vienna/E.C** with claims reciting:

“1. A method of modifying a target DNA , the method comprising contacting the target DNA with a complex comprising:

(a) a Cas9 polypeptide and

(b) a single-molecule DNA-targeting RNA [...]

wherein said contacting is in vitro or in a cell ex vivo[...].

4. [...] wherein the target DNA is present in ...a single-cell eukaryotic organism...a cell from a vertebrate animal”

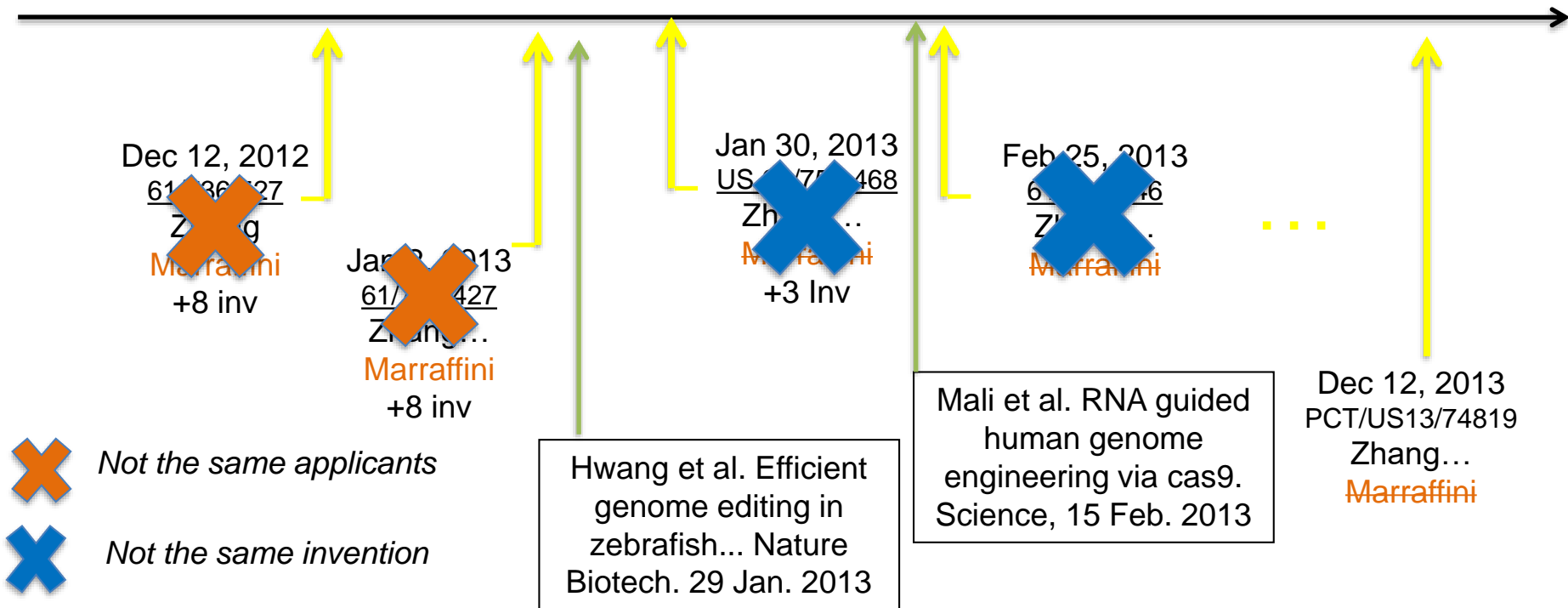
# CRISPR/Cas9: the patent dispute



▀ In parallel, at the European Patent office (2/2):

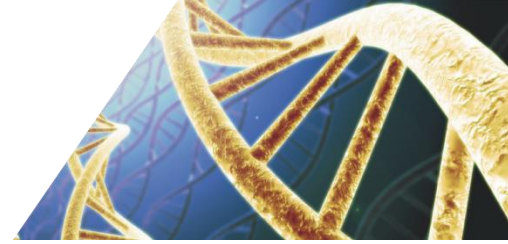
□ EP 2 771 468 B1 granted to **Broad Institute/MIT** :

Opposition division revoked the patent due to invalid priority claims, and anticipation by Mali and Hwang (17 Jan. 2018)





# CRISPR/Cas9 IP rights



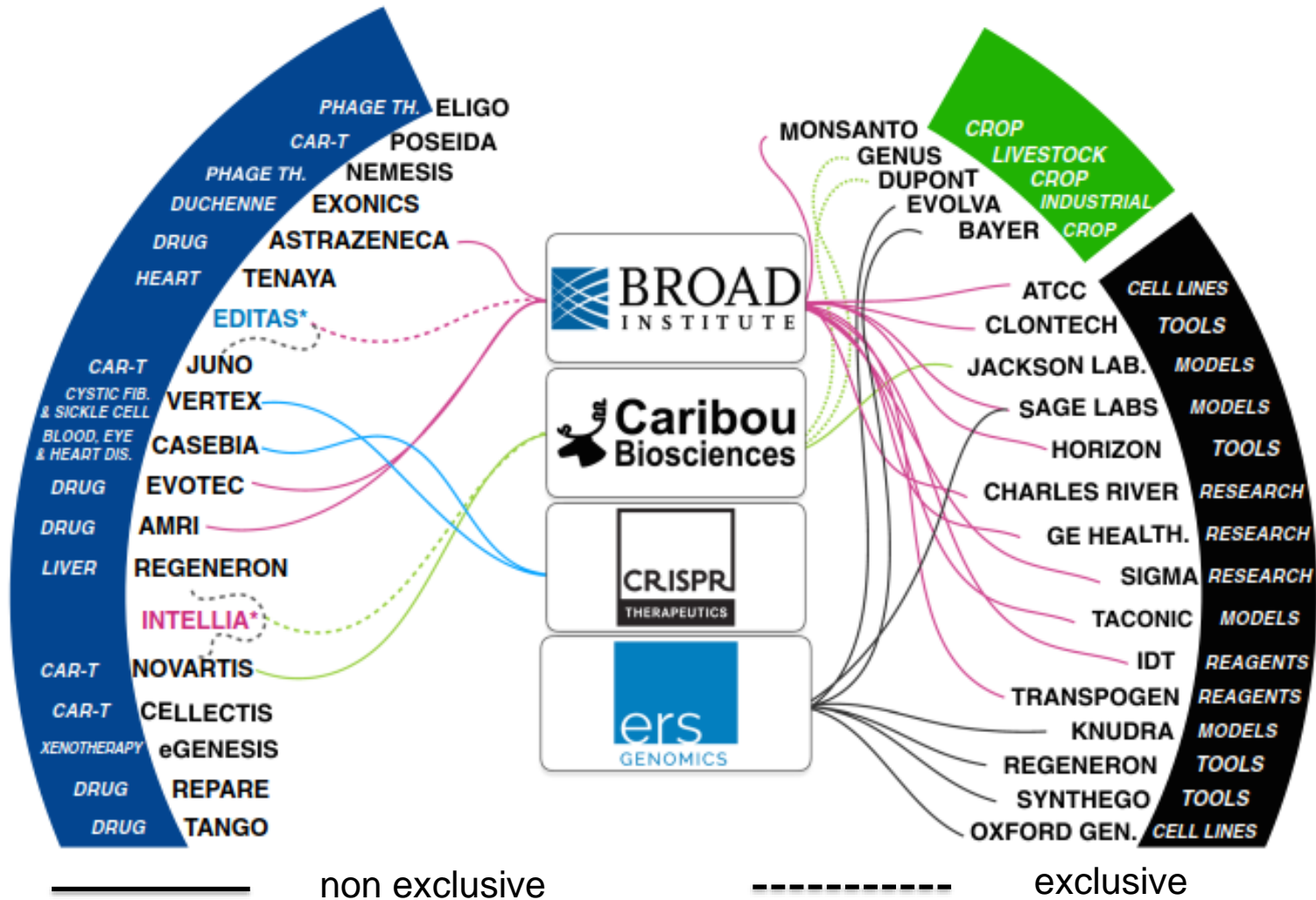
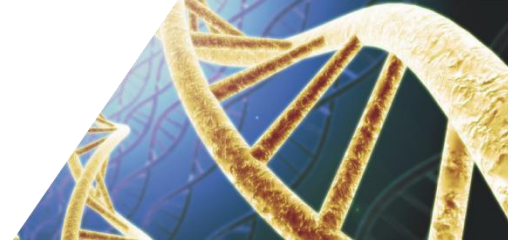
Dispute between Broad/MIT – UC Berkeley will be ongoing for a while

Other players have IP rights :

- University of Vilnius, Toolgen, Sigma Aldrich, Rockefeller University...
- Over 2200 patent families relating to CRISPR, ranging from components to delivery systems and uses thereof

⇒ the licensing situation may remain opaque

# CRISPR/Cas9 licensing



Source: Ferreira, R., David, F. & Nielsen, J. *J Ind Microbiol Biotechnol* (2018): 1-14.

# CRISPR/Cas9 licensing



## Broad Institute, MIT and Harvard

- ❑ We make CRISPR tools, knowledge, methods and other IP for genome-editing freely available to the academic and non-profit community:
  - ⇒ **No license is necessary for academic and non-profit use**
- ❑ We license CRISPR IP non-exclusively to companies to use in their own commercial research.
- ❑ We also license CRISPR IP non-exclusively to companies wishing to sell tools and reagents for genome editing.
- ❑ For **human therapeutics**, “inclusive innovation” model:
  - ❑ primary licensee, Editas Medicine, Inc. (Editas)
  - ❑ right to exclusively use the technology on targets of its choosing
  - ❑ after an initial period, other companies may apply to license certain CRISPR IP for use against genes of interest not being pursued by Editas.

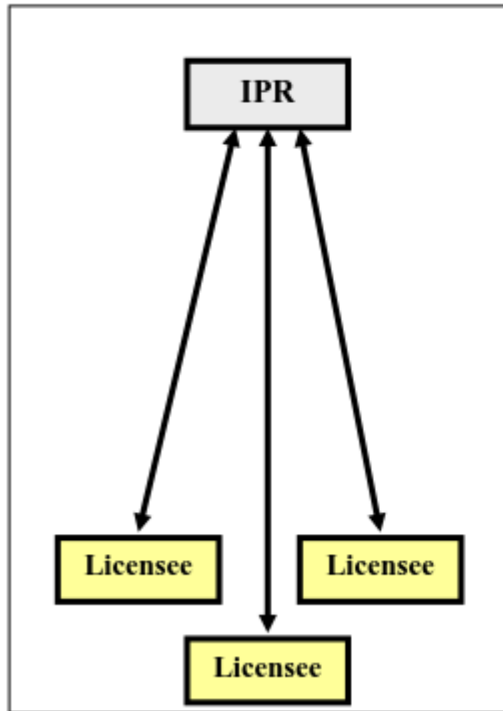
## License restrictions for ethical motifs:

- ❑ no transformation of germinal cells or embryos (Editas),
- ❑ no gene drive/sterile terminator seeds/tobacco (Monsanto)

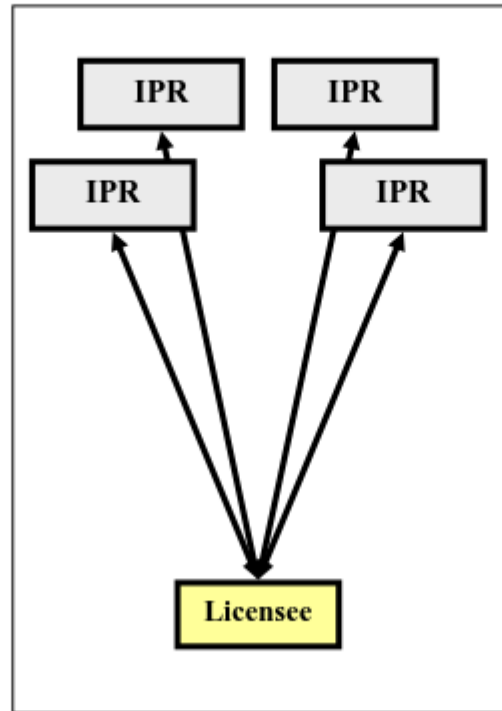
# Patent pooling



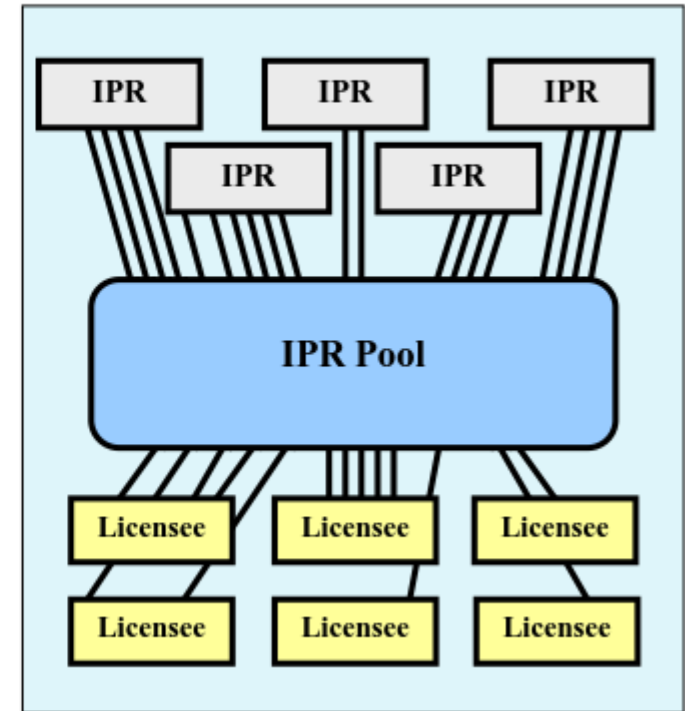
“One-to-Many”



“Many-to-One”



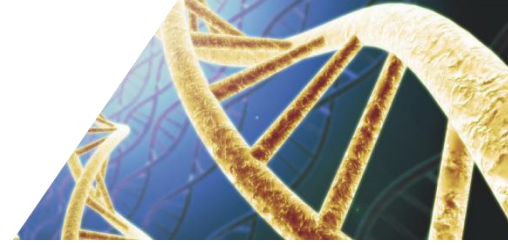
MPEG LA®  
“Many-to-Many”



Source: ["Keynote Presentation by Kristin Neuman at the LES France General Assembly"](#) (5 December 2017)

MPEG LA®: making multiple technology pieces, each of them dependent on others, easily accessible to a multi-user market

# Conclusions



- /// The patent situation of CRISPR Cas, and therefore licensing situation, is complicated
- /// Patent pooling could represent an effective solution, subject to participation of foundational patent owners
- /// For the therapeutic field where investments and risk to fail are very high: exclusive license for gene/disease specific application
- /// Priority could be given by actors in the field to follow-on gene editing tools, e.g. Cpf1 as an alternative to Cas9 (Zheng et al.)
- /// Attention is paid to broad access to the technology for academic and non-profit community, and ethical issues

# Bibliography



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- /// Ferreira, Raphael, Florian David, and Jens Nielsen. "Advancing biotechnology with CRISPR/Cas9: recent applications and patent landscape." *Journal of industrial microbiology & biotechnology* (2018): 1-14.
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- /// <https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-ed>
- /// <http://www.mpegla.com/main/pid/CRISPR/default.aspx>

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