

Gene-editing: What's next after CRISPR Cas9?

Alcimed, an innovation and new business consulting firm, is committed to supporting the pharmaceutical industry in observing emerging technologies such as gene editing technologies CRISPR Cas9 and the following generations.

February, 22, 2017. Gene editing describes the process of insertion, deletion or replacing a specific gene of the genome of an organism to introduce a new function or correcting a mutation. New gene editing technologies could finally bring gene therapy to broad application and offer extremely specific modification of genes for the first time in the history of science. They may allow treating patients by directly changing their cell's genes instead of using drugs or surgery. One could even dream of delaying ageing or applying gene editing against viral infection, to make people HIV-resistant, for example.

“Gene editing has been discussed since the 90’s and is not a new approach by itself. But the new tool CRISPR Cas9 seems very promising and brings all the hopes back to actually treat patients” explains David Bariau, Alcimed Partner and Cologne Business Director. Older technologies such as Talens, Meganucleases or Zinc Fingers Proteins were not very successful due to side effects and imprecise location of the gene modification.

The CRISPR Cas9 system is by far the most famous gene-editing technology, as selected by *Science* for 2015 Breakthrough of the Year¹. It is derived from a bacterial defense system against viral DNA consisting of three stages of activity: adaption, expression and interference. Each type of CRISPR-Cas System consists of a combination crRNAs, which acts as guide RNA and Cas effector proteins. The CRISPR Cas9 can be applied to any gene location by introducing the enzyme and appropriate guide DNA to a target cell. However, a patent battle, between Feng Zhang and colleagues from the Broad Institute and UC Berkeley’s Jennifer Doudna and Emmanuelle Charpentier, limits the current use.

“I think the new gene-editing tools CRISPR Cpf1 or NgAgo could represent a game-changer since they were found to be even more efficient and versatile than CRISPR Cas9. And it gets the gene-editing field moving again”, says David Bariau enthusiastically. A Danish company has already invested in NgAgo² although reports on NgAgo were contradictory since other workgroups had difficulties to reproduce the works of a Chinese group.

Moreover, we will have to address ethical problems gene editing could cause if it can finally be applied to humans such as: Is the balance of risks and benefits given when thinking about possible off-target effects? Should we apply the CRISPR/Cas9 technique to human germlines or even embryos which would allow “designer babies”? The system was tested last year in a human-

¹ <http://www.sciencemag.org/news/2015/12/and-science-s-breakthrough-year>

² <http://www.nature.com/news/biotech-firm-backs-controversial-crispr-challenger-1.21343>

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being by Chinese scientists who injected CRISPR Cas9 modified immune cells into humans and a paper in which Chinese scientists altered DNA in human embryos was rejected by *Science* and *Nature* due to ethics concern before being published by the journal *Protein & Cell*. A public dialogue about these questions is necessary to understand if advances in gene editing should be made.

Since the field of gene-editing is very active, new tools will most probably be invented and engineered for specific applications. However, the way through clinical trials will be long and Pharmaceutical companies eagerly wait for first results of human trials and ALCIMED will support its customer along this long way.

About Alcimed

ALCIMED (www.alcimed.com) is an innovation & new business consulting firm, specialized in life sciences (healthcare, biotech, agri-food), chemicals, materials, energy; as well as aeronautics, space & defense. ALCIMED relies on a team of 200 highly-skilled individuals to help its clients with exploring and developing their uncharted territories, covering four key areas: New Technologies, Market Innovation, High-Growth Geographies, and Strategic Foresight. ALCIMED is headquartered in Paris and has offices in Lyon & Toulouse in France, in Germany, Belgium, Switzerland, the UK, the USA and in Singapore.