Q&A – CRISPR-Cas licenses free of charge

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Wageningen University and Research announces that it will provide potential partners with free licenses to use our gene-editing CRISPR-Cas technology for non-profit applications in plants. This will allow CRISPR tools to contribute to healthier, more sustainable, equitable, affordable and resilient food production for all. We hope the move will inspire a worldwide change in CRISPR-Cas IP policy and regulation.

INTELLECTUAL PROPERTY PROTECTION

- **How do patents / licenses work?**

When someone discovers a new technology or application, they will often want to protect their 'intellectual property' through patenting, so they have control over the development and application of the technique by third parties Patents may also lead to potential financial gains. The patent holder can sell licenses to allow certain parties to use the patented technology, provide the license for free, or cross license with other parties. Patents provide also important information for others working in the same field, as the applicant has to disclose information.

- **Why free licenses?**

Worldwide, there are over 3.000 CRISPR-Cas related patents and patent applications, of which WUR also holds several. For five of them (which are jointly owned with Dutch Research Council NWO), WUR decided to provide free licenses. Free licenses may benefit non-profit parties, small seed companies, farmers, and consumers, especially in low-income countries. We hope that CRISPR tools will contribute to healthier, more sustainable, equitable, affordable and resilient food production for all.

- **Why does WUR take this action (now)?**

In our view, the full potential of this technology can only be achieved through long term partnerships. That's why - when prof. Van der Oost took this initiative – he and Louise Fresco quickly realized the potential to make a concrete contribution to the Sustainable Development Goals.

That's important, because the world needs a transformation to healthier, more sustainable, equitable and resilient food systems. This will also be the focal point during the UN Food Systems Summit on September 23rd. CRISPR and other biosciences could accelerate this transformation.

It therefore fits perfectly with the WUR mission: *to explore the potential of nature to improve the quality of life*. CRISPR, a bacterial defense system to viruses is a great example. A WUR team, led by prof. Van der Oost has been studying it since 2006.

- **Are you planning to release more patent licenses? For CRISPR-Cas or other applications?**

This is a start. We will see how it develops. We hope this will encourage other institutions to do the same.

- **Who will be eligible for these free licenses?**

We will consider potential partners that will use this technique for non-profit applications in plants. Examples include scientific institutions and universities in low income countries, humanitarian organizations, NGO's and possibly private sector organizations.

CRISPR TECHNIQUE

- **What is CRISPR-Cas?**

CRISPR-Cas is a technology that enables genetic material of microorganisms, plants and (cells of) animal, including humans, to be changed relatively simply, very accurately and efficiently. This can be done by making genetic changes that result in altered properties, or by adding entirely new genetic information. The technology allows to develop crops with new traits over a shorter period of time with lower costs.

CRISPR-Cas was first discovered in the DNA of bacteria in the 1980s, and in 2005-2008 it was found that they corresponded to a microbial anti-virus system. It is present in the genomes of 40% of the bacteria and 85% of archaea. It rapidly became clear that there is a huge diversity of CRISPR-Cas systems.

CRISPR - Clustered Regularly Interspaced Short Palindromic Repeats
Cas – CRISPR-associated genes & proteins

- **How does CRISPR-Cas work?**

CRISPR-Cas is a tool for precision genome editing. Look at it as a pair of scissors. With this pair of scissors we are able to find and replace pieces of DNA to alter functionality in plants, animals or bacteria.

- **What is special about this WUR-patented ThermoCas9?**

ThermoCas9 is a Cas variant that was discovered (during a WUR / NWO-TTW project) in a thermophilic bacteria. As the word thermophilic implies, the bacteria grows optimally at temperatures of 50–60C. This means the enzyme is very stable. It also means the optimal activity is at 50-60C, but it will still work within plant cells.

- **What are applications of CRISPR-Cas?**

For instance, when you have a strain of tomato DNA and you have located the piece of genome that defines the red color of the tomato, we could change that piece of DNA and make a yellow tomato. While changing the color of tomato is not of much use to the world, editing the drought resistance of the plant, or the resistance to diseases is.

Some other examples:

- ✓ In plants, based on insights in plant physiology and genetics, the production of compounds such as fats and oils can (hopefully in the near future) be adjusted very precisely, so that the plants produce the best ingredients. And wheat gluten can be modified so that coeliac patients can safely eat wheat and wheat products.

- ✓ Animal diseases can also be prevented. For example, African swine fever, the result of a viral infection, is deadly to domesticated pigs, whereas wild boars barely display any symptoms. By making appropriate genetic adjustments, we can make domesticated pigs resistant.

- ✓ We can also turn off particular genes. Disabling the gene CD163 means pigs are no longer affected by the PRRS virus, a respiratory infection. In plants, we can turn off genes that predispose them to disease. For instance, we can develop potato varieties which are not susceptible to *Phytophthora*, the cause of potato blight, so farmers will need to apply less pesticides. Domestication of the wild tomato to the one that is even better than the one we

eat every day, has been done by disrupting 6 genes simultaneously by CRISPR editing.

- **Is CRISPR-Cas safe?**

There are no indications that there are special, additional risks compared to currently used approaches for gene editing for food applications. CRISPR speeds up processes nature is already doing by itself and enables us to do so in a more precise manner. New crops developed by CRISPR are assessed for their safety as other crops are as well.

- **What is the status of (EU) legislation?**

A 2018 ruling from the Court of Justice of the European Union decided that crops obtained from techniques that altered the genetic material (including CRISPR) should be subject to the same rules as Genetically Modified Organisms (GMO's).

CRISPR-Cas is a gene editing technique. Gene-editing technology targets specific genes within an organism to promote certain characteristics or suppress others. This can be very subtle by changing a few nucleotides (DNA building blocks), or more drastic by introducing one or more genes. In a growing number of countries (incl. USA), only the introductions of a gene from a different species (e.g. a bacterial gene in corn, Bt-Maize) is considered to result in a genetically modified organism (GMO).

Last April, the European Commission launched a review of EU rules that states that all CRISPR-edited organisms should be called genetically modified organisms (GMOs). We would welcome a change in EU legislation, to apply the best science to help solving the problems the world faces.

- **In what way is this different to earlier 'free license' initiatives like Golden Rice?**

There have been earlier initiatives to provide licenses free of charge for non-profit applications. Golden Rice is one of them. The difference with what we are doing is that our licenses will cover not just one crop and one trait, but a technology that gives access to a whole range of applications in many crops.