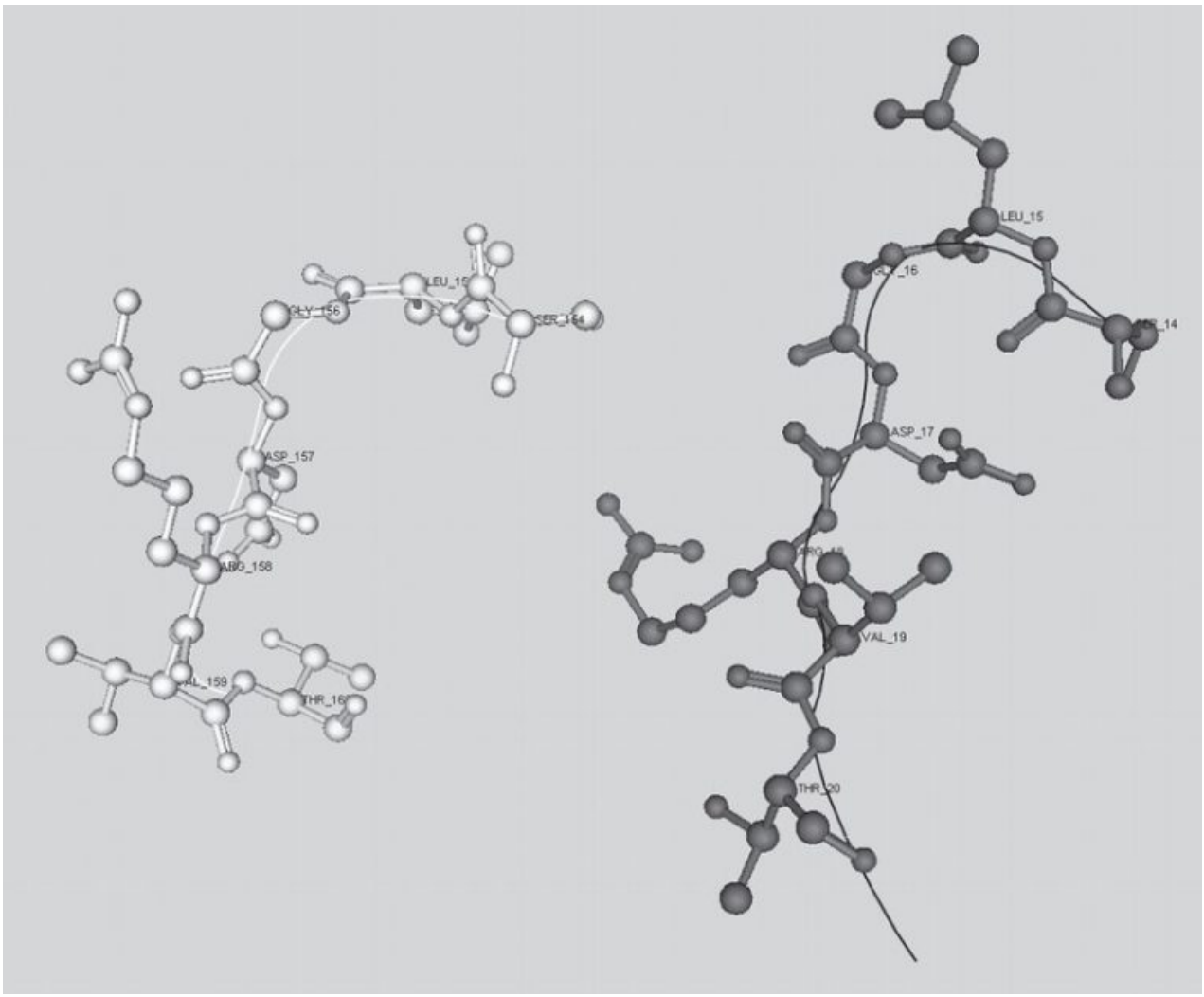
Veille citoyenne d'information sur les OGM et les semences

# Fungicide and herbicide micropeptides on Europe’s doorstep?

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Toulouse-based Micropep Technologies has just had one of its *fungicidal* micropeptides approved in the United States. The technology, developed and patented by this CNRS *spin-off, is* aiming for European approval by 2030. However, these micropeptides are raising questions about their potential impact on ecosystems.



*"We are on a mission to build a more sustainable agriculture for future generations*". This is the vision of Micropep Technologies, a Toulouse-based company spun out of CNRS, which has raised around €23 million since 2016 to develop micro-proteins called micropetides (miPEPs). On the strength of its first approval in the United States for what it calls a "*biofungicide*", it is aiming to enter the European market within 5 to 6 years. However, this technology raises major environmental issues and will have to comply with current European regulations.

## *The "miPEPs"* technology

Micropep Technologies published its original research results in the journal *Nature* in 2015[1]. Technically, these miPEPs are micro-proteins, small chains made up of 10 to 30 amino acids. They are distinct from proteins, which are also made up of amino acids, but are longer. Micropep is mainly interested in the fungicidal and herbicidal properties of these molecules, but is also developing miPEPs to selectively inhibit the growth and overcome the resistance of weeds to conventional treatments. In particular, the Toulouse-based biotech company is testing molecules against Palmer amaranth in North America, a weed that has become resistant to glyphosate (due to the excessive use of Roundup on GMOs), and field vulpine in Europe[2].

The miPEPs are involved in a range of biological processes, including the regulation of gene expression, the control of enzyme activity and cell signalling. Laurent Thomas, CEO and co-founder of the company, explains: "*The miPEPs control the microRNAs that play an essential role in plant development. Some control microRNAs involved in fixing atmospheric nitrogen, while others are involved in the immune response. We can apply miPEPs directly to a plant and stimulate the expression of the corresponding microRNAs to help or protect the plants*"[3]. According to the company, miPEPs, sprayed directly onto fields, would improve plant resilience to environmental stresses, enhance growth and development, and increase crop productivity.

The miPEPs are developed using a *patented platform* based on IT tools. This system identifies potential miPEP sequences, and algorithms are used to select and rank candidate molecules according to a set of criteria predefined by the company. A few hundred candidates are then tested in internal efficacy trials. The selected miPEPs are then manufactured by chemical synthesis and studied to test their cell penetration properties to reach their target when sprayed on leaves or deposited in the soil.

## Micropeptides to "*save the planet*"

Micropep Technologies' communication combines technological promise with environmental promise. Its miPEPs are said to be a less toxic and more targeted alternative for combating crop diseases, such as fungi and bacteria that thrive in field crops. The Toulouse-based company claims that its miPEPs are "*safe, effective and sustainable natural solutions to help adapt our farming systems to the impact of climate change and save our planet... the next generation of sustainable crop protection and crop stimulation tools that farmers are looking for*". A communication full of promise, on behalf of all farmers. Yet many farmers are questioning or even refusing to use patented products in their fields.

Micropep entered the commercial phase in 2022, targeting the US market. With success, since its fungicide targeting, among other things, soybean rust and mildew, was classified as a "*biochemical active ingredient*" (MPD-01) by the EPA (Environmental Protection Agency) in February 2024. This approval gives it access to a simplified US regulatory route to registration by 2026, after further crop trials. The Toulouse-based company is also targeting the European market, where it will also

have to follow a regulatory authorisation procedure.

## The European market: between regulations and environmental risks

Products must be marketed or even introduced into the European Union (EU) in compliance with the law. Among other things, this involves guaranteeing that they are harmless to the environment and to consumers, as well as being effective. There are a number of legal instruments that could affect miPEPs, such as the Regulation on plant protection products (no. 1107/2009), the Reach Regulation on the protection of human health and the environment against the risks related to chemical substances (no. 1007/2006) or the Directive on biocidal substances (no. 528/2012).

Above all, according to MicroPep, these micropeptides are produced by bacteria. Therefore, while these micropeptides are not GMOs as such (they are not organisms), they are products of GMOs, genetically modified micro-organisms (GMMs) to be precise. They will therefore necessarily be subject to the requirements of European legislation on GMO micro-organisms.

Although Micropep promotes its miPEPs as a '*safer and more sustainable*' solution, their potential long-term impact on ecosystems is open to question. Because it is recent, this technology may lack data on the evolution of miPEPs, including their environmental degradation, their potential bioaccumulation, their effects on biodiversity, particularly on non-target organisms, etc.

Asked to comment on these issues, the director of Micropep said: "*It is necessary to obtain marketing authorisations in order to market products. That's where the problem lies: European regulations take twice as long as American regulations*". Thomas Laurent goes on to praise the "*pragmatic"* spirit of the United States: "*As long as they are new technologies,... that have environmental benefits compared to conventional chemistry,... as long as they are of natural origin, they are exempt from additional studies to demonstrate the environmental benefits. This is not always the case in Europe. Nevertheless, there has been some positive progress in Europe, where a project to redefine the term biocontrol is under way, and good progress has been made"* 4.

With regard to the redefinition of "*biocontrol*", the European Commission says it wants to better integrate sustainable practices and respond to environmental issues, in particular by funding research projects on "*nature-based"* solutions, such as macro- or micro-organisms, biopesticides, etc.5

## Patented "*natural*" micropeptides

For some years now, the biotechnology sector has been trying to force through the idea that some of the molecules it develops are "*close to nature*", "*conventional*", or even "*natural*" or "*biological*". Examples include interfering RNA (iRNA)6 or GMOs/NTGs. Micropep adopts the same language, while emphasising, through the voice of its Managing Director, the potential profusion of miPEPs: "This is a *new Eldorado of innovative active substances of natural origin, which have the property of degrading in the soil"*.

However, the miPEPs technology is covered by patent rights in the United States and Europe. These cover the use of micropeptides to "*promote plant growth*" or "*modulate gene expression*". Some patents have been granted since *Inf'OGM* reported on these rights in 20187. The claims define, in particular, methods for detecting micropeptides, their use in a composition comprising a plant protection agent and, in the case of a US patent, compositions comprising micropeptides at specific concentrations. Although these patents do not explicitly cover natural micropeptides as such, the claims nevertheless cover the use of potentially natural micropeptides in particular applications.

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