

## Technology Offer

### A novel system for mass production of YenTc toxin

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Sprays containing insecticidal toxins have been used for protection of crops since the 1920s, when French farmers started using the entomopathogen *Bacillus thuringiensis* (Bt) with its active Cry toxin ingredient to control flour moths. However, the intense global use of Bt has caused resistant pest populations to emerge, with a large assessment of recent studies identifying 5 of 13 major pest species as having resistant populations. One of the best strategies for mitigating this would be to deploy novel insecticidal toxins unrelated to the Bt Cry toxin. Unfortunately, very few can compete with its production levels, potency and specificity.

#### Technology

Our scientists from the Max Planck Institute of Molecular Physiology have developed a novel system for mass production of insecticidal toxins including the Tc toxin YenTc from the bacterial species *Yersinia entomophaga* (a risk group 1 organism harmless to humans but extremely lethal to insects), which can be applied to crops in the form of either intact bacteria, the entire toxin mix, or specific toxins purified from this mix.

They have discovered

- the central switch (YenR/RoeA) controlling the conversion of non-toxin producing cells to their toxin producing counterparts, which can turn the entire *Yersinia entomophaga* population of bacteria into toxin-producers/releasers when placed under control of an arabinose-inducible promotor (Ara-YenR/Ara-RoeA)
- a pH-controlled release mechanism which allows to grow the bacteria to high densities and subsequently release the toxin mix directly into protein purification buffer, with no laborious cell lysis steps required
- a genomic editing strategy for fusing in-frame affinity tags to the toxins for high-throughput purification

Using these strategies, a total amount of 270 mg pure YenTc was obtained from 1 liter of Ara-YenR/Ara-RoeA cells (compared to 21 mg using a strain with unmodified YenR/RoeA) as proof of concept. Homogeneous and well-folded YenTc complex formation was confirmed by size exclusion chromatography and negative stain electron microscopy.

**We are now looking for a licensing partner to further develop this project.**

#### Patent Information

An international PCT application was filed on Sep 8th, 2023: WO2024052546.

#### Publications

Sitsel et al., Nature Microbiology 2024, DOI: 10.1038/s41564-023-01571-z

#### Contact **Dr. Ingrid Kapser-Fischer**

Senior Patent- & License Manager

Nutritionist, M.Sc.

Phone: +49 89 / 29 09 19-19

Email: kapser-fischer@max-planck-innovation.de