AN INNOVATIVE THERAPEUTIC STRATEGY TO FIGHT ANTIMICROBIAL RESISTANCE

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AN INNOVATIVE THERAPEUTIC STRATEGY

The MaxImmun project aims at developing an innovative therapeutic strategy to fight bacterial antimicrobial resistance by stimulating the immune response and boosting the expression of natural human antimicrobial peptides thanks to marine bioinspired molecules. MaxImmun is a Horizon Europe project supported by the European Union, through the European Innovation Council.

WHAT IS ANTIMICROBIAL RESISTANCE?

Antimicrobial resistance is a worldwide health threat and considered by the World Health Organization to be one of the top global health priorities. In 2019, it was attributed 1.27 million deaths around the world, with 35.000 deaths per year in the US and 33.000 in the EU. Since the clinical pipeline of new antimicrobials is largely dry, the development of new and innovative therapeutic strategies to fight infections and reduce spread of antimicrobial resistance is urgently needed.

WHAT IS THE MAXIMMUN PROJECT?

MaxImmun aims at selectively boosting expression of the body own antimicrobial defense peptides naturally produced at mucosal surfaces. The novelty of our approach is based on new immuno-modulatory molecules inducing a therapeutic expression of host antimicrobial peptides, without triggering inflammation. Rather than directly targeting a pathogen with exogeneous antibiotics and the risk of resistance development, our innovative therapeutic strategy fosters a natural endogenous response of the human body through its own antimicrobial defenses. Our approach provides a sustainable solution against antimicrobial resistance development that also protects from resistance spread in the environment and among animals.

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WHAT ARE ANTIMICROBIAL PEPTIDES?

Antimicrobial peptides (AMPs) are defense proteins secreted by the human cells in response to bacterial infections. These host natural antibiotic peptides are efficient against a broad-spectrum of pathogens. Antimicrobial peptides have several advantages over current antibiotics:

- AMPs have a different mode of action and pharmacodynamics than antibiotics, lowering the risk of resistance development.
- AMPs are able to target specific bacteria, reducing the likelihood of harming beneficial body microbiota.
- AMPs are effective against antimicrobial resistant bacteria, providing an alternative or complementary approach to antibiotics.

WHAT ARE OUR OBJECTIVES?

- To evaluate the potential for resistance development to human antimicrobial peptides in antibiotic resistant bacteria.
- To identify new molecules from the marine microbiome boosting antimicrobial peptide expression without triggering inflammation.
- To characterize AMP-inducer molecules in a pipeline for enabling expedient validation of the molecules in human intestinal cells and organoids.
- To determine mechanisms of action for AMP-inducer molecules on the antimicrobial peptide regulatory circuits disconnected from inflammation.
- To chemically optimize AMP-inducer molecules in terms of activity and drug-likeness by medicinal chemistry.
- To assess AMP-inducer molecules efficacy in pre-clinical models of validation.

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WHAT IS OUR METHODOLOGY?

In MaxImmun, we are searching for AMP-inducer molecules in the underexplored marine ecosystem. Marine organisms, like sponges, with their symbiotic microorganisms such as bacteria and microalgae, are sources of a wide variety of valuable molecules. These microorganisms are not only sources of highly active natural compounds, but also of metabolites involved in communication during interspecies interactions, whose unique chemical structures are not found in terrestrial organisms. Chemical biology of the marine ecosystem constitutes a valuable source of molecules with high-potential for discovery of AMP-inducers.

WHO ARE THE CONSORTIUM PARTNERS?

With strong complementarity and minimal size, the MaxImmun consortium has the agility and breadth of expertise to tackle the transdisciplinary scope of the project:

- **Brice Sperandio**: immunologist at INSERM, group leader, and the coordinator of the MaxImmun project (Ecole Normale Supérieure, France).
- **Mark Brönstrup**: chemist, director of the Chemical Biology department, and a professor at the Leibniz University of Hannover and at the German Center for Infection Research (Helmholtz Center for Infection Research, Germany).
- **Dan Andersson**: microbiologist, and the director of the Antibiotic Center (Uppsala University, Sweden).
- **Nathalie Vergnolle**: pharmacologist, physiologist, and the director of the Digestive Health Research Institute (Institut National de la Santé et de la Recherche Médicale, France).
- **Ali Al-Mourabit**: chemist, and the former director of the Natural Products and Medicinal Chemistry department of the Institute for Natural Product Chemistry (Centre National de la Recherche Scientifique, France).
- **ImmunRise Technologies**: a biotech company with a strong experience in the screening and exploitation of the marine microbiome as a new source of molecules for the development of innovative solutions to boost the host-defense mechanisms, in plants and humans (France).

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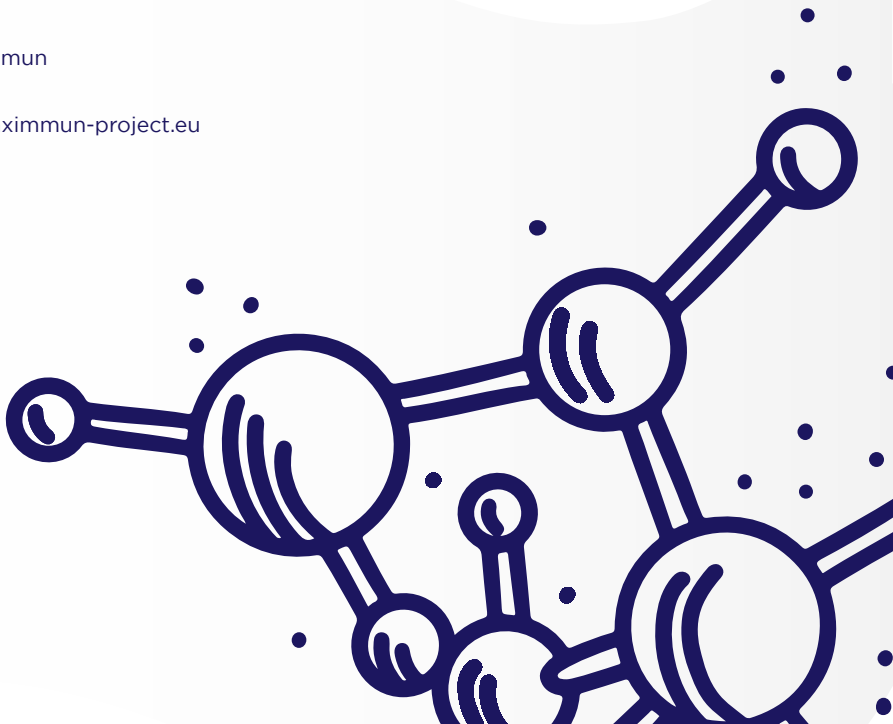

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