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The goal of this project is to find out how our immune system responds to endolysins and further how to modify molecular elements of endolysins that determine this response.
Importance of this problem refers directly to the problem of drug-resistant infections. In the EU alone, more than 25 000 patients die from infections by multidrug-resistant bacteria every year. This problem has even been called the threat of a return to the pre-antibiotic era. Endolysins are antibacterial enzymes derived from bacteriophages. Antibiotic-resistant bacteria can be sensitive to endolysins since cross-resistance is not observed. Endolysins are proposed as an alternative to the insufficient antibacterial drugs arsenal.
Any drug proposed for human treatment must be well characterized in terms of safety and efficacy. These are strongly dependent on pharmacokinetics and interactions with immune system. Endolysins, though well characterized in the field of structures, biochemistry and microbiology, have not been described in terms of immunogenicity (or other interactions with the immune system). Data on endolysin interactions with the immune system are very limited. This fact limits the perspective of their effective use in vivo, since mammalian immunology is a key factor determining pharmacokinetics and effectiveness of drugs. This project proposal underlines the first attempt to identify and to design immune-reactivity of endolysins, for optimization of their activity, stability and safety in vivo. First, immunogenic elements of endolysins will be identified by laboratory testing followed by bioinformatics analyses. Next, new enzymes with low-immunogenicity will be designed in silico and then produced and tested in laboratory. As a result, new low-immunogenic endolysins will be proposed.
Cooperation will also enable scientific exchange of younger scientists/researchers (PhD students and/or postdoctoral fellows), thus educational aspects which will be the added value of the project.