ItPS Seminars

18th Sep 2023 2pm CEST

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Identification, production and characterization of Cryptic Antimicrobial Peptides enabled by a computational-experimental platform

Cryptides are bioactive peptides released by the proteolytic processing of protein precursors. They can show several biological activities often different from those of the respective host proteins. In particular, cryptic cationic antimicrobial peptides (CAMPs) are a still unexploited source of natural antimicrobial agents with anti-inflammatory, anti-biofilm and immunomodulating properties. We have developed a computational-experimental platform for the discovery and the production in recombinant form of novel CAMPs. The in silico tool is based on the demonstration that it is possible to assign to each peptide an "antimicrobe score" (based on the peptide amino acid composition and two bacterial strain dependent variables) which is linearly correlated to the antimicrobial potency expressed as Log (1000/MIC) where MIC is the minimal inhibitory concentration. Analyzing a library of thousands secreted human proteins, we have identified several novel human cryptic CAMPS including peptides from Apolipoproteins E and B, Pepsinogen A, Fibrinogens α, β, and γ. More recently the method has been used to develop an algorithm for the mining the whole human proteome. This analysis led to the identification of several hundreds of potential bioactive cryptides. Almost one hundred of these cryptides have been characterized and have proved to be wide-spectrum antimicrobial agents with antibiofilm and endotoxin scavenging activity. Several of the novel cryptids showed in vivo anti-infective activity in mouse models. The platform also includes methods for the production of recombinant peptides in Escherichia coli very well suited for the production of toxic molecules like antimicrobial peptides and the labelling with environment-sensitive fluorophores allowing to study the interaction of peptides with membranes, endotoxins (LPS, and LTA) and whole cells.

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