

MULTI-DOMAIN ANTIMICROBIAL PEPTIDES – PURELY ANTIMICROBIALS OR MULTI-FUNCTIONAL MOLECULES

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Antimicrobial peptides (AMPs) are short proteins which have an *in vitro* inhibitory activity against microorganisms. Whereas the majority of AMPs are short peptides, an increasing number of AMPs are longer and contain regions within the molecule having clearly different characteristics. In our lab we have isolated several multi-domain AMPs from the crustacean *Hyas araneus*. Two of these belong to the well defined crustin family within *Crustacea*, which are cysteine-rich AMPs containing a whey acidic protein domain. This domain has been shown to have a multi-faceted role. In addition, we have isolated AMPs with novel primary structures, but which consist of domains with some similarities to domains found in already known AMPs. Arasin 1 has two distinctly different regions, with an N-terminal end enriched in proline and arginine residues, and a C-terminal end containing two disulphide bridges. Hyastatin is a 115 amino acid long AMP, containing three distinctly different regions. Both arasin 1 and hyastatin show high affinity to chitin, which enable them to contribute in wound healing and the molting process. All of these AMPs have been isolated from apparently healthy animals and they are constitutively and highly expressed in both stimulated and non-stimulated experimental animals, which strengthen the hypothesis that AMPs have additional roles than purely acting as antimicrobials during microbial invasion.

THE USE OF NATURAL BIOACTIVE PEPTIDES

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Short bioactive peptides are responsible for different functions in nature and have activities and properties that might be developed and exploited for commercial purposes. Different challenges and strategies will be focused on in the presentation.

The activities of peptides in animals are very broad and varied. The potential is huge as the activity can expand from antimicrobial and antitumoral activities, immune regulating properties, enzymatic or enzyme-inhibiting activities to mention some. The peptides might be constitutively produced or produced by induction by stimuli that might be working – locally, like for instance by the invasion of microbes.

Important questions are how the different activities can be exploited commercially in drug development or for other commercial purposes? What are the limitations and how can these be dealt with to overcome unwanted effects? Limitations can be characteristics in relationship to the ability to transverse membranes to reach sites where they are intended to act, or unwanted properties like being toxic to normal cells, or proteolytic instability.

In science it is also important to study bioactive peptides and reveal their mechanism of action to discover new potential drug targets, like networks of interacting proteins, receptors and ligands. Furthermore, performing investigations to overcome or limit unwanted properties is essential. For a drug it is important to resist degradation by proteases long enough to have an effect. New methods can for instance be used to create “tailor made” or designed proteins with improved pharmacological properties. Also a range of other modification can be made to the peptides.