Antimicrobial Peptides (AMPs)

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Abstract: Antimicrobial peptides are short peptides recently discovered that belong to the first line of **defense against invading pathogens**. They have been described from bacteria, insects, plants and vertebrates, and are classified in several groups depending on their structure. Several mechanism of action have been proposed to explain the interaction with bacterial membranes, but in general, they cause lytic pores. In most of the cases, these peptides are ribosomally sintethized, some of them as pre-proteins. Several applications have been proposed to control bacterial infections, especially skin infections or in the mucosal areas.

Distribution:

AMPs can be found in many different species, most of them came from **vertebrate animals** but there are a lot of AMP produced by plants, microorganisms, insects, marine invertebrates and others.
Nowadays Scientifics are studying AMPs from different species to use them as therapy against a wide spectrum of diseases.

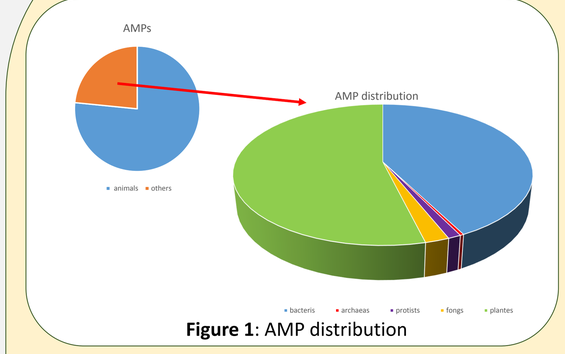


Figure 1: AMP distribution

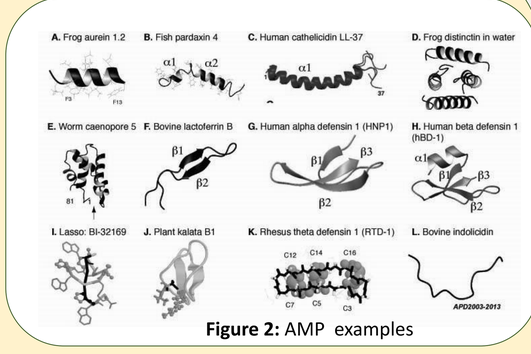


Figure 2: AMP examples

Classification:

AMPs can be classified in **four grups**: alfa-helix, cisteine rich peptides, betta sheet, high aminoacid content. Some peptides can have modified aminoacids in their structure, like D-aminoacids.

Mechanism of action

AMPs show different ways to interfere in cell viability.

1) Interfering in metabolic pathways or dna synthesis.
2) Producing pores that kill cells by lisis.

Once the critical peptide concentration is reached in membrane the peptides interact to create a pore .

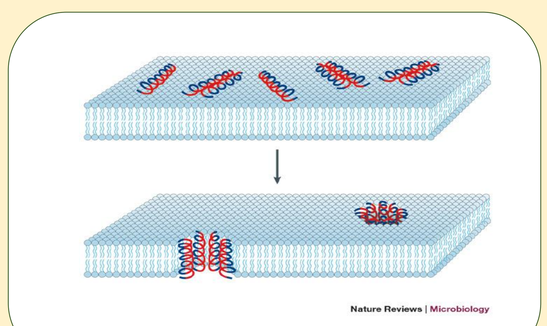


Figure 3: pore formation via AMP

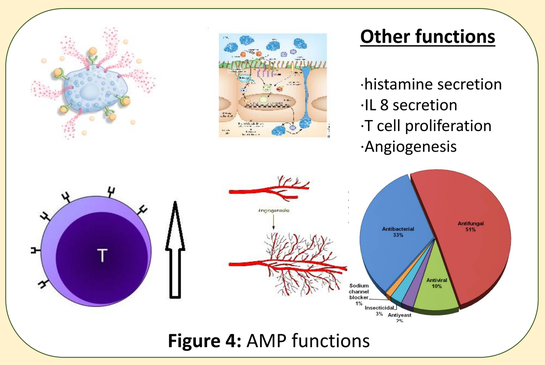


Figure 4: AMP functions

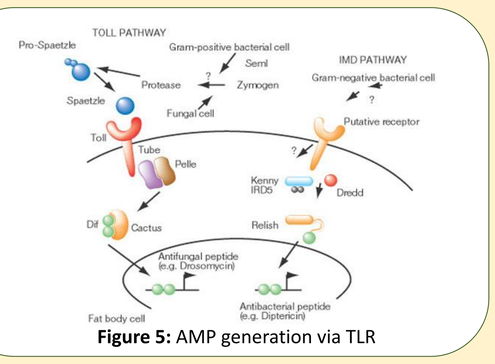


Figure 5: AMP generation via TLR

- Surface charges alteration
- Alterations in lipid A,
- Membrane protein changes
- Proteolithyc enzimes
- Membrane fluency reduction
- PAM neutralitzation
- Membrane transporters

Figure 6: resistance mechanisms

Functions:

- Antibacterial Peptides
- Antiviral Peptides (Anti-HIV Peptides)
- Antifungal Peptides
- Antiparasitic Peptides (Antimalarial)
- Anticancer Peptides
- Anti-protist Peptides
- Insecticidal Peptides
- Spermicidal Peptides
- Chemotactic peptides
- Antioxidant peptides
- Protease inhibitors

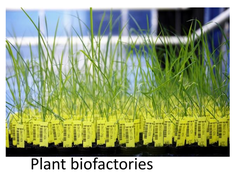
Genes expression:

PAMs are synthesized as large precursors that contain **one or more copies** of the active segment cleaved via proteolythic processing. The release of the N-terminal signal peptide leaves free the active part, but generally one or more anionic segments are removed during the process. There are two expression patterns: 1) Constitutive
2) Induced expression by TLRs

synthesis

Optimized chemical or enzymatic

Microbial fermentation



Plant biofactories

Limitations

- Short peptides
- No postraductional modifications
- Low yields
- High costs

how can we solve this?

alternative

Heterologus expression via stable transfected *sf9cells*

Resistances:

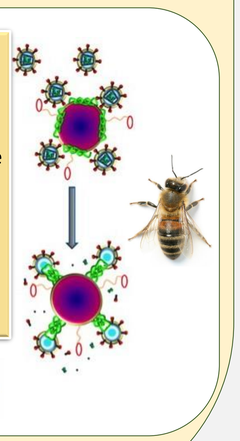
Two types of resistance are described: **intrinsic** resistance or **constitutive**, and **adaptive** resistance or **inducible.** In the first the factors involved are always present, in contrast to the inducible activation occurs microbial factors needed to survive in sub-lethal levels of AMPs.

Production

Nowadays AMPs are mainly produced via chemical synthesis, or microbial fermentation. These two methods present some **limitations** like: peptides without post-translational modifications, length limitations, toxicity, low yields and expensive costs.

- Activity comparable to conventional antibiotics
- Biocompatibility
- Biodegradability
- Mecanisms of action with low risk of development of resistance on target
- Possibility of reducing production costs and environmental impact using biotechnology procedures

Melittin is a toxic peptide that is present in the venom of bees. Scientists have already used it to attack cancer cells, taking advantage of their potential to create holes in cell membranes. In Washington university, nanoparticles loaded with melittin were used to attack the viral envelope VIH.[1]



Applications

AMPs can be applied to many different types of industries as: **pharma, veterinary, plants, food, biomaterials, biocides, cosmetics, or antimicrobial materials**. The peptides used in each industry are going to be different, so it might be a good idea to find a standard system to produce them for future applications.

References:

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