Exploring the secondary structure of Host Defense Peptides in their biological environment. A Molecular Dynamics approach.

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Host defense peptides (HDPs) are short cationic peptides that have a critical role in the innate immune response across all living organisms [1]. Their primary mode of action does not depend on protein receptors, but instead on their ability to target and disrupt the membranes of various pathogenic and pathological cells, such as those found in cancer, bacteria, or even our own senescent cells. These structures are characterized by their specific compositions, typically containing a relatively high concentration of anionic lipids. Upon encountering a pathogenic/pathological lipid membrane, the peptide's secondary structure undergoes a transformation, promoting its adsorption through electrostatic and hydrophobic interactions [2]. The membrane's functionality is compromised depending on the concentration of HDPs, which may also lead to the disruption of its structure. The general interaction mechanism between HDPs and lipid membranes is still not fully understood; however, understanding the peptide's structure in the presence of the membrane is a critical initial step towards synthesizing new artificial peptides with enhanced activity.

Predicting the secondary structure of HDPs from their sequences is particularly challenging, primarily due to the significant influence of the environment, specifically the presence of the membrane. Furthermore, there is a significant lack of structural information available for HDPs: solving the structure of a peptide in the presence of a membrane is a difficult task, resulting in sparse data compared to that for proteins. The use of Molecular Dynamics (MD) simulations may compensate the shortage of experimental results, as it is able to describe the complex interactions between the peptide and the environment and reach the typical microsecond scale of the folding processes.

References

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