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Solid Supported Membranes based on Amphiphilic Gramicidin Derivatives

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INTRODUCTION: Gramicidin A (gA) is a 15mer peptide antibiotic, originally derived from the soil living bacterial species *Bacillus brevis*. It consists exclusively of hydrophobic amino acids, alternating in D- and L-conformation, which leads to a rolled-up β-sheet, the so-called β-helix (1). Quaternary structure is manifested in the helical dimer or the double helical form; latter is dominant in lipid bilayers (Figure 1).

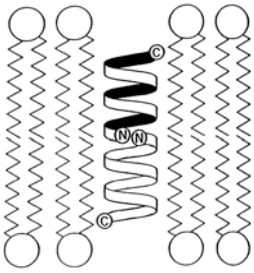

Figure 1: helical dimer in lipid membrane (1)

We attached hydrophilic sequences of oligo-lysine to the N-terminus of Gramicidin and yielded amphiphilic peptides with the ability to self-organize to membranes and vesicular structures in aqueous solution.

METHODS: All peptides were synthesized on solid phase using Fmoc chemistry. Purification was performed by preparative RP-HPLC.

Superstructural analysis was carried out using TEM, SEM, AFM, LS and CD techniques.

RESULTS: In this project, we end-functionalize Trunk-peptides with lipoic acid (2) to immobilize them on gold surfaces (Figure 2).

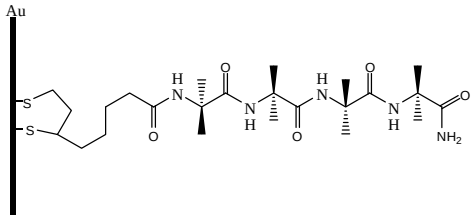

Figure 2: scheme of the chemical adsorption of a thiopeptide

We expect to observe the dimerization kinetics of our peptides by QCM experiments and its response to a variation of solvent and temperature.

Additionally, we anticipate to detect (AFM, ellipsometry and film balance) a regular molecular alignment governed by the interactions responsible for membrane formation in aqueous bulk solution (3).

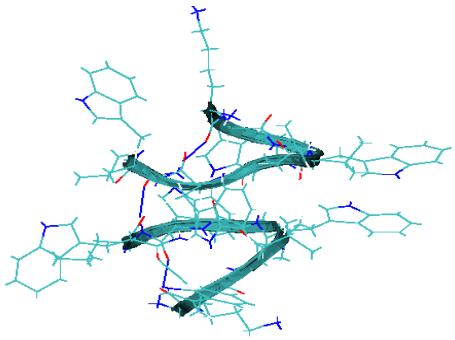

Figure 3: dimer structure of $K(WL)_3W$

MD calculations of $K(WL)_3W$ were setup with CHARMM (Figure 3) and complemented with NMR measurements to approve the hypothesized membrane structure as well as the role of the tryptophanes within.

DISCUSSION & CONCLUSIONS: The gA sequence is a suitable hydrophobic block to form purely peptidic membranes. Furthermore, we reduced the functional structure to a repetitive sequence of L-tryptophane and D-leucine amino acids. In conclusion, we propose aromatic interactions in addition to the hydrophobic effect to be held responsible for the structural characteristics of our membranes. Surface measurements on gold as well as the computational approach will give important complementary information about the membrane structure.

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