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Cationic gemini and geminoid peptide amphiphiles: From transfection to Protease inhibition

Gemini surfactants are amphiphilic molecules containing two head groups and two aliphatic tails which are linked by a spacer between the head groups, or between the linker region connecting the heads and the tails. Because their critical aggregate concentration is 10^3-fold lower they are more effective surfactants than the corresponding monovalent compounds (*i.e.* classical surfactants with a single chain and a single head group), which makes them interesting for various biomedical applications.

Cationic geminis have shown to be viable agents for transfection, the introduction of nucleotides into a eukaryotic cell, thereby providing an alternative to viruses and cationic polymers. Amphiphilic peptides consisting of a peptide spacer with the N- and C-termini appended with hydrophobic groups are asymmetric geminis and are called gemini-like or geminoids. Interestingly, the SPKR geminoid with unsaturated alkyl tails can achieve transfection without the lysogenic helper lipid that is required in other cases.

The proteases involved in the maturation of the polyprotein of dengue virus to new virus particles have cationic peptide sequences as their preferred substrates. Saturated geminoids of the KG_nK and KA_nK series (n = 1 or 2) are inhibitors of dengue virus 2 protease and the host protease furin, with slight selectivity of one over the other.The inhibitors are also active against dengue virus 2 infection in a cellular context, at concentrations below which they are toxic.

Speaker Biography

Martin C Feiters graduated in biochemistry, bio-organic chemistry and food chemistry and did PhD research on structure-function relationship of the enzyme lipoxygenase, followed by postdoctoral work in X-ray absorption spectroscopy, before his appointment as Associate Professor at Radboud University (1989). He has > 150 publications and a number of patents. He has applied various kinds of radiation, viz. synchrotron X-rays and neutrons, to the elucidation of supramolecular structures such as viruses, lipid-DNA complexes, and porphyrin assemblies, as well as the coordination chemistry of metals in homogeneous catalysts, metalloproteins, and biological non-metal trace elements such as bromine and iodine. He has contributed to the development of hyperpolarization in NMR, viz. by the optimization of the catalyst and the co-substrate approach for detection and quantitative analysis by Signal Amplification by Reversible Exchange (SABRE) and high-field non-hydrogenative para-hydrogen-induced hyperpolarization (PHIP) at micromolar concentrations. He is involved in the developments of various drugs, viz. antimalarials, cyclodextrin-based steroid transporters, and amphiphilic peptides for transfection as well as, together with his spin-off company Protinhi Therapeutics, as inhibitors of viral proteases.

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