ItPS Seminars

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MARC DEVOCELLE
Professor
Royal College of Surgeons Dublin

Conjugates, mimetics, prodrugs and hybrids thereof of membranotropic peptides

In less than 25 years, Cell Penetrating Peptides (CPPs) have progressed from challenging a paradigm to entering clinical trials. Counterintuitively, though charged and hydrophilic biopolymers are inherently prevented from crossing phospholipid bilayers, CPPs, peptide sequences 5- to 30-amino acid long generally displaying high net (positive) charges, possess the ability to efficiently translocate cell membranes and deliver a broad range of cargoes intracellularly. Antimicrobial Peptides (AMPs) are another group of membranotropic peptides, adding a broad spectrum of antimicrobial activities to their membrane translocation properties. They have microbicidal activities associated with high fitness cost of resistance and are currently developed in multiple antimicrobial products ranging from human medicine to biomaterials. Notwithstanding these unique features, CPPs and AMPs have a number of shortcomings, which limit in particular their clinical applications. They include notably a high cost of production and a proteolytic liability. Techniques of pharmacokinetic improvement developed for therapeutic peptides, such as conjugation, peptidomimetic conversion and prodrug modification can be applied to membranotropic peptides. Examples of candidates obtained through these approaches, developed individually or concurrently, will be presented. They are mainly aimed at therapeutic applications, but could also be extended to other products such as antimicrobial coatings.

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