Editorial corner – a personal view

Polymers to permeate lipid bilayer membranes

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Polymers capable of entering cells across lipid bilayer membranes receive increasing attention in various different technological approaches.

Gene therapy, the insertion of genes into the cells of patients to fight diseases, holds great promise. However, safe and effective carrier structures to deliver DNA (desoxyribonucleic acid, the polymer that contains all the genetic instructions) into the cells still present a major challenge. Non-viral systems employ assemblies of DNA and cationic macromolecules. The polymers explored include degradable and non-degradable types, such as chitosan and poly(amidoamine) dendrimers, and are selected for targetability, cellular uptake and minimal toxicity. The primary purpose of introducing genes into cells is the expression of encoded proteins. In parallel to the ongoing related efforts to introduce genes, the direct delivery of proteins across the cell membranes has been investigated successfully for a variety of systems. Arginine-rich, cell-penetrating, peptide tags attached to various proteins have been shown to boost their membrane permeability. The combination of amino acids with cationic and hydrophobic side chains was reported to increase the efficacy of the peptide tags. Recently, this approach has even been applied successfully to cellular reprogramming, i.e., in the generation of human pluripotent stem cells via the delivery of a set of modified transcription factors.

Antimicrobial peptides, a range of naturally occurring and synthetically generated peptide structures, take this even further and not only disintegrate bac-

teria but also protozoa, fungi and viruses by disrupting their lipid bilayer membranes. The related peptides consist of 12 to 50 amino acids, including at least two – often more – cationic amino acids plus hydrophobic amino acids in varying amounts. Importantly, being effective against microorganisms, the peptides are compatible with tissue cells, facilitating their use in the protection of medical devices against microbial settlement and colonization without triggering microbial resistance mechanisms. These advantages motivate both the immobilization of cationic peptides onto polymeric surfaces as well as the incorporation of related antimicrobial motifs into synthetic polymer structures.

Despite all the recent progress, the targeted development of membrane-penetrating polymer structures requires a more detailed mechanistic understanding of the permeation process, and the required structural and environmental conditions. Joint theoretical and experimental efforts are emerging to resolve these issues in carefully selected model systems.

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