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PEPTIDES, PEPTIDE-POLYMER CONJUGATES AND POLYMER-BASED PEPTIDOMIMETICS OF CELL PENETRATING PEPTIDES AND/OR ANTIMICROBIAL PEPTIDES

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Peptides are an emerging class of new therapeutic candidates. The total peptide drug market was estimated at $50 billion in 2015 and, with a projected annual growth rate of approximately 10%, is expected to exceed $70 billion by 2019. They are approved and in development in a large number of therapeutic areas, including metabolic diseases, endocrinology, oncology, gastroenterology, cardiovascular, neurology. Antimicrobial Peptides (AMPs) and Cell Penetrating Peptides (CPPs) are other promising peptide candidates with therapeutic applications. Peptides, however, have a number of shortcomings impending their direct clinical application. They are essentially a lack of oral bioavailability and metabolic stability, a reduced serum half-life, an inability, generally, to reach intracellular targets, a potential toxicity and a high cost of production. The chemical and drug developments of therapeutic peptides generally require therefore a technology addressing their clinical shortcomings. Three approaches, applied to CPPs and/or AMPs, will be discussed. They include prodrugs of AMPs, activated by disease-associated enzymes. These prodrugs can be selectively activated at sites of infection, preventing the toxicity of AMPs at normal body sites (*in vitro* and *in vivo*). Polymer conjugates of these peptides can also be used to selectively deliver AMPs with anticancer properties to tumour cells. Finally, novel polymer-based peptidomimetics of CPPs and AMPs will be presented. Their activities as transfection reagents (CPP mimetics) or antimicrobial agents (AMP mimetics) surpass, or match those of the parent peptides, respectively, while being metabolically stable and, as demonstrated with the CPP mimetics, devoid of toxicity and cheaper (30 fold) to produce.

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