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Review article

Navigating cancer therapy: Harnessing the power of peptide-drug conjugates as precision delivery vehicles

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ABSTRACT

Cancer treatment is a formidable challenge due to the adverse effects associated with non-selective therapies like chemotherapy and radiotherapy. This review article primarily centers on the application of Peptide-Drug Conjugates (PDCs) for delivering cancer treatment. PDCs represent a promising class of precision medicines, harnessing the unique attributes of peptides in conjunction with non-peptide components. The covalent linking of peptides and drugs through specialized connectors characterizes PDCs. These constructs play a pivotal role in delivering drugs directly to tumor sites with high precision. PDCs encompass three pivotal components: a targeting ligand, a cytotoxic ligand, and a carefully chosen linker. The selection of these elements is crucial to maximize the efficiency of PDCs. PDCs offer a multitude of advantages over conventional drug molecules, including enhanced specificity, reduced off-target effects, and an improved therapeutic profile. The peptide component within PDCs can be customized to specifically adhere to disease-specific receptors or biomarkers, facilitating targeted drug delivery and accumulation in afflicted cells or tissues. This targeted approach enables the controlled release of therapeutic payloads at the localized site, resulting in heightened effectiveness and minimized systemic toxicity. Diverse linker strategies are employed to ensure the stable connection between the peptide and non-peptide components, ensuring controlled drug release at the desired location of action. The peptides utilized in these treatments encompass cell-penetrating peptides, peptides designed to target tumor cells, and those aimed at the nucleus of cancer cells. While certain clinical trials have been conducted, and some PDCs are currently in use for cancer treatment, it's essential to acknowledge that PDCs have their limitations, such as low stability in plasma, fast elimination and limited oral bioavailability. Ongoing research endeavors seek to surmount these challenges and further establish PDCs as potent agents for cancer treatment. This review sheds light on recent advancements in the design, delivery, and applications of PDCs, while also highlighting the prevailing challenges and charting a path for future research directions.

1. Introduction

Despite significant advancements in cancer treatment techniques, cancer remains one of the main causes of death worldwide. Among the various types of cancer studied, lung and prostate cancer have been identified as the most fatal in males, while breast cancer and colon & rectum cancer are the most fatal in females. Approximately 18 million new cancer cases and about 10 million deaths were reported in 2018 worldwide [1]. Such a huge numbers indicate that the presently used therapeutics are not adequately efficacious against the complexities of cancer and there is a pressing need for more effective and novel therapies. Available treatments namely chemotherapy, radiotherapy, immunotherapy, and hormone therapy, all are often accompanied by detrimental after-effects. Even though there is a large pool of cytotoxic agents available and are approved by the FDA (Food and Drug Administration) to treat cancer, these conventional chemotherapeutic agents, while effective in treating cancer, have several limitations that can impact their therapeutic outcomes. Some of the key limitations include non-specific targeting (Fig. 1), development of resistance that restricts the long-term effectiveness of a drug, poor pharmacokinetics (PKs) and

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