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Strategic PEGylation: Half-life extension of biologic drugs

The tremendous potential of biologic drugs is hampered by short half-lives *in-vivo*, resulting in significantly lower potency than activity seen *in-vitro*. These short-acting therapeutic agents require frequent dosing profiles that can reduce applicability to the clinic, particularly for chronic conditions. Therefore, half-life extension technologies are entering the clinic to enable improved or new biologic therapies. PEGylation is a commonly utilized technique to improve drug solubility and stability, prolong blood circulation time, reduce immunogenicity, and decrease dosing frequency. As with any form of molecular modification, the active site is affected and can drastically decrease the bioactivity of the therapeutic agent, especially when the modification is performed on a small molecular weight molecule like peptides and small proteins. Steric hindrance from high molecular weight PEG can lead to a dramatic loss in the biological and pharmacological activity of the molecules. The higher the molecular weight, the lower is the bioactivity. Therefore, it is generally accepted that a balance must be struck between the molecular weight of the PEG and the activity of the therapeutic molecule to reach sufficient drug efficacy. The strategic PEGylation technique introduced here offers many benefits over the conventional PEGylated forms of peptides and proteins. Strategic PEGylation signifies that a tradeoff of PEGylation for bioactivity is not necessary. Specifically, this abstract focuses on the strategic PEGylation of potent therapeutic peptides for GLP-1 analogues as a model peptide. Strategic PEGylation can be a platform technology to extend the half-life while preserving the biological activity of peptide and small protein drugs.

Biography

Kang Choon Lee is Haengdan Distinguished Professor at College of Pharmacy, Sungkyunkwan University, Korea. For over 35 years, his Drug Targeting Laboratory has been focused on immuno-targeting and bioconjugation of peptide and protein drugs. He is internationally recognized as one of the leading experts in site-specific peptide/protein PEGylation and demonstrated the therapeutic potential of novel site-specific PEGylated drugs such as GLP-1 and TRAIL for the first time. He has published over 150 papers in peer-reviewed journals and served as an invited speaker at many international conferences. He is an inventor on more than 20 patents related to specific bioconjugation and PEGylation of peptide/protein drugs. He is honored as a Fellow of the American Association of Pharmaceutical Scientists (AAPS) in 2003. He currently serves on the editorial advisory board of many international scientific journals. For the clinically translating and commercializing site-specific engineered peptide/protein drugs developed by his laboratory, he founded D&D PharmaTech, Korea and also co-founded and serves as a Board Member of Theraly Pharmaceuticals, USA.

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