

Proinsulin-transferrin fusion protein: An insulin analog to achieve both liver-targeting and overcoming insulin resistance

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We have recently prepared a recombinant proinsulin-transferrin fusion protein (ProINS-Tf). ProINS-Tf is an inactive form of insulin analog, but can be selectively absorbed, activated, and retained in the liver. We have demonstrated in type 1 diabetes mouse models that ProINS-Tf is a highly liver-targeted and long-lasting insulin prodrug. Due to the binding to both insulin and transferrin receptor, the liver-activated ProINS-Tf exhibited a significantly higher affinity to insulin receptor when compared with the native insulin. The bivalent binding of activated ProINS-Tf induces a longer and stronger activation of insulin receptor as demonstrated in the enhanced and prolonged Akt phosphorylation with hepatoma cells. Furthermore, ProINS-Tf can overcome insulin resistance in palmitate-treated HepG2 cells, as well as in severe hyperglycemic NOD mice. Therefore, ProINS-Tf can potentially be developed into a safe and effective insulin prodrug for the control of basal glycemia in diabetes and for the treatment/prevention of insulin resistance-associated diseases.

Biography

Dr. Wei-Chiang Shen is Professor in Pharmaceutical Sciences at the University of Southern California School of Pharmacy. His research interests focus on the development of novel systems for improving peptide and protein drug delivery. He has published more than 150 papers in different areas of biomedical sciences. He is a co-author of the textbook Immunology for Pharmacy Students, and a co-editor of the book Antibody-Drug Conjugates – the 21st Century Magic Bullets for Cancer. He was elected to Fellow of the American Association of Pharmaceutical Scientists in 1992 and Fellow of the American Association for the Advancement of Sciences in 2000.

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