Dual agonist proteins for the treatment of type 2 diabetes

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Biomedical Engineering (BME)

Publication(s)

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External Link(s)

• From the lab of Dr. Ashutosh Chilkoti

Unmet Need

Over 37 million people in the United States have diabetes, and approximately 90-95% of them have type 2 diabetes (T2D). Diabetes and its related complications not only cause premature mortality and lower quality of life, but also impose a significant economic burden for countries, healthcare systems, diabetes patients and their families. However, most of the current medicines primarily address the symptoms rather than the physiology, resulting in 40% of T2D patients still failing to reach glycemic control. Furthermore, a single drug is generally insufficient for successful management of T2D, while multi-medicine coordination likely reduces patient compliance. There is a need for aggressive treatment regimens that combine two medicines into one delivery package to maximize sustainable glycemic control.

Technology

Duke inventors have developed a drug that contains dual agonist proteins to achieve synergistic therapeutic effects. This is intended to be used for the treatment of metabolic disease, especially type 2 diabetes. Specifically, fusion proteins comprising an elastin-like polypeptide (ELP) domain as a linker, with a glucagon-like peptide-1 (GLP-1) receptor agonist domain and a fibroblast growth factor 21 (FGF21) receptor agonist domain attached to the two ends of the ELP domain, can achieve robust glycemic control without a significant elevation in insulin. This has been demonstrated through *in vivo*mice studies, which showed that the dual agonist drug had potent and sustained effects on body weights and ambient blood glucose levels, outperforming the single agonist monotherapies (GLP1-ELP and ELP-FGF21). By linking two agonists into one molecule, ELP also helps increase the circulating half-life and enables sustained release of the drugs. A single injection was shown to sufficiently maintain therapeutic drug levels and protect mice from hyperglycemia and weight gain for >7 days, reducing the frequency of required administration to once weekly.

Other Applications

This technology could also be adapted to include other multiagonist drugs that allow for a broader range of metabolic applications, such as obesity, metabolic syndrome, and gestational diabetes.

Advantages

- Significantly reduces the required drug administration frequency to once weekly
- Novel method of combining two drugs with an ELP linker to increase their circulation half-lives, achieve a sustained release module, and provide a more readily injectable therapeutic with superior stability
- Demonstrated to be more effective in controlling both glycemic levels and body weights compared to single agonist monotherapies