Docket #: S22-388

Insulin receptor antagonist

Researchers at Stanford have developed a potent, insulin-based, insulin receptor antagonist that could be used as a hyperinsulinism therapeutic. Congenital hyperinsulinism (HI) is a genetic disorder of pancreas and beta-cell function characterized by the failure to suppress insulin secretion in the setting of hypoglycemia, resulting in severe hypoglycemia that can cause brain damage or death if inadequately treated. Roughly 50% of HI patients can manage their condition with the existing drugs diazoxide or octreotide, but the other 50% must undergo a pancreatectomy, leading to long-term surgical complications. Thus, there is a large unmet need for patients with congenital HI that are not candidates for current drug therapies. This newly developed insulin receptor antagonist may provide a solution, providing better efficacy and fewer complications than the standard of care for HI. The antagonist has been shown to successfully reduce the activation of the insulin receptor and downstream signaling in vitro in the low nanomolar range. In addition, mice exhibit insulin resistance following treatment with the antagonist in vivo. This invention could be used as a scaffold for a new and improved HI therapeutic.

Stage of Development
Research - in vivo

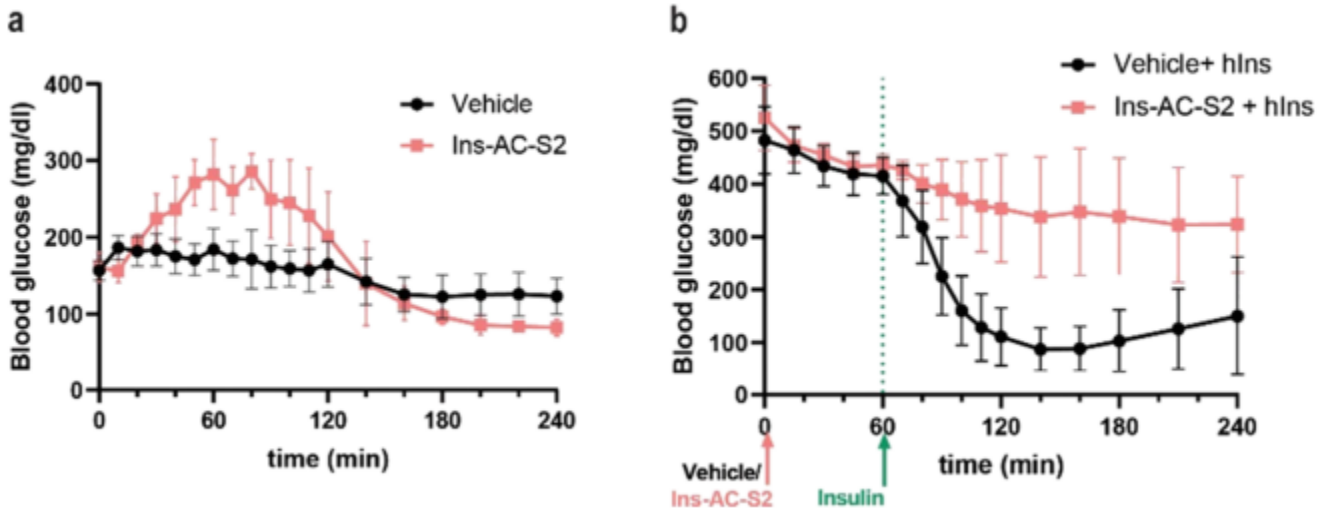

Figure description:
(a) Ins-AC-S2 alone disrupts blood glucose regulation by suppressing insulin receptor activation. (b) In mice, Ins-AC-S2 treatment leads to insulin resistance, as shown by a suppressed glucose-lowering effect of insulin compared to a vehicle control.
Image credit: Park et al., Journal of Medicinal Chemistry (2023)

Applications

- Insulin receptor antagonist for:
  - Congenital hyperinsulinism therapy
  - Diabetes research and therapeutic evaluation
  - Other uses related to the insulin receptor and downstream signaling pathways

Advantages

- Effective insulin receptor antagonist in the low nanomolar range
- Reduced complications compared to the current standard of care for HI
- Greater efficacy than current and pending HI therapies
- Distinct from a competing allosteric antagonist antibody

Publications

- Antagonistic Insulin Derivative Suppresses Insulin-Induced Hypoglycemia

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