

# SMALL MOLECULE AGONISTS OF EPHA RECEPTORS TO AMELIORATE DIABETES

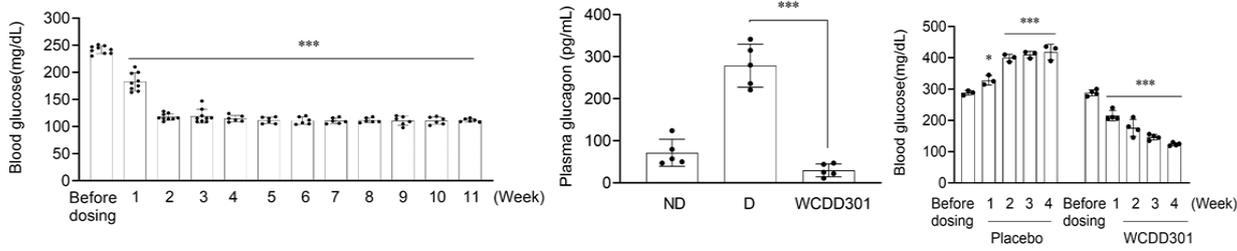
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T-020153

## T-020153 - Small Molecule Agonists of EphA Receptors to Ameliorate Diabetes

### Technology Description



*Blood glucose levels (left), post-treatment plasma glucagon (center) in WCDD301 treated NOD (non-obese diabetic) mice with moderate hyperglycemia.*

*Blood glucose levels (right) in Streptozotocin-induced mice with severe hyperglycemia.*

Researchers in David Piston's laboratory at Washington University have synthesized a series of small molecules to normalize hyperglycemia via targeting the EphA receptor.

### Stage of Research

WCDD301 is water soluble and shows strong metabolic stability in both mouse and humans with superior stability in human plasma & liver microsomes. WCDD301 outcompetes the natural EphA ligand and reduces glucagon secretion from both islets and dispersed islet cells from murine cells and human donors with long standing T1D.

*In vivo*, oral delivery of WCDD301 effectively reduces blood glucose and glucagon levels with no clinical signs of illness, hepatotoxicity, or nephrotoxicity across tested murine models without affecting the secretory functions of  $\beta$ -cells.

Prophylactic administration of WCDD301 appears to prevent the development of diabetes in NOD mice with no detrimental effects on glucose homeostatic regulators or peripheral insulin sensitivity.

Other novel compounds with similar or better affinity for EphA are currently under development and data available to share under confidential agreement.

### Publications

Asadi et al. (2024). An orally available compound suppresses glucagon hypersecretion and normalizes hyperglycemia in type 1 diabetes. JCI Insights. <https://doi.org/10.1172/jci.insight.172626>

### Applications

- Metabolic diseases, particularly hyperglucagonemia-hyperglycemia in the context of diabetes.

### Key Advantages

- **Alternative and/or complementary to insulin-only therapies.**
- **Directly targets cells with compromised signaling that leads to excess glucagon secretion.**

### Patents

- Provisional patent application filed.