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Wnt Signaling Inhibitors for the Treatment of Diabetes

Summary

The Wnt/*β*-catenin signaling pathway plays a pivotal role in cell proliferation and differentiation through the regulation of the transcriptional factor *β*-catenin. The Wnt pathway has been studied extensively for cancer (colon, liver) but the role of the Wnt/*β*-catenin signaling pathway in diabetes is unknown. UMB researchers have discovered the effect of pyrvinium pamoate to inhibits the Wnt pathway in diabetic mouse models. This technology is a set of novel Wnt/β signaling inhibitors based on the pyrvinium pamoate structure and their method of use for the treatment of diabetes.

Key Investigator
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Field
Metabolic Disease
Diabetes

Technology
Small Molecules

Technology Status
Ongoing *in vivo* studies with lead compound

Status
Available for licensing

Patent Status
PCT Patent Application, filed

UMB Docket Reference
FX-2015-082

Market

The global prevalence of diabetes among adults over 18 years has risen from 4.7% in 1980 to 8.5% in 2014. In 2015, an estimated 1.6 million deaths were directly caused by diabetes and another 2.2 million deaths were attributable to high blood glucose in 2012. Due to the widespread reach of the disease, the diabetes market continues to grow. New antidiabetic drugs continue to be developed but older classes of drugs and generics are still widely being used. However, diabetes treatments often lose effectiveness after extended use and require a change in drug or a treatment must be added to the patient's regimen to manage the chronic disease. The role of the Wnt pathway has been validated for cancer (colon, liver) therapy target, but its role in diabetes is a potential novel target.

Technology

Pyrvinium pamoate, a FDA approved, anthelmintic drug for the treatment of *Enterobius vermicularis* (pinworms), was identified as a potent Wnt/*β*-catenin pathway inhibitor. Initial proof of concept studies confirmed that pyrvinium injection could significantly improve glucose tolerance and decrease body weight gain in mice fed on a high-fat diet. However, to increase the potency, metabolic stability, and bioavailability of pyrvinium pamoate, novel analogs of pyrvinium pamoate were generated and the lead candidate, YW1149, was identified. Currently, no Wnt/β–catenin pathway inhibitors are clinically available for targeted therapy.

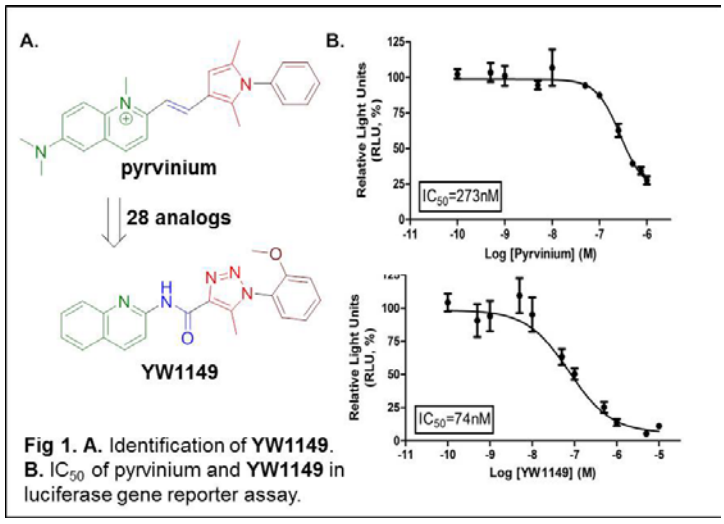

Fig 1. A. Identification of **YW1149**. **B.** IC_{50} of pyrvinium and **YW1149** in luciferase gene reporter assay.

Advantages

Novel, potent inhibitor of the Wnt/β–catenin pathway with increased bioavailability and metabolic stability.

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