

Small Molecule Inhibitors of Sortilin

Researchers at the University of South Florida have developed novel compounds capable of binding to sortilin or related analogs to treat hypercholesteremia, hepatic steatosis, and Alzheimer's disease.

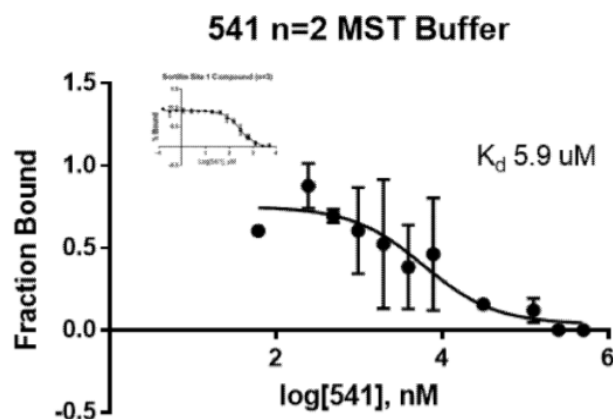
Sortilin is a protein that plays many roles in the human body. Elevated circulating sortilin levels have been associated with an increased risk of coronary artery disease and diabetes mellitus. Further, sortilin deficiency has been shown to reduce hepatic steatosis (fatty liver) in mice, and a variant of the sortilin gene has been associated with Alzheimer's disease pathogenesis. Due to the many roles that sortilin plays in cardiovascular and metabolic diseases, it is an ideal disease biomarker and potential therapeutic target.

USF researchers have developed compounds capable of binding to sortilin and disrupt its interactions with various effector proteins, such as proprotein convertase subtilisin/kexin type 9 (PCSK9). Treatment with the novel sortilin inhibitor reduced PCSK9 secretion and thereby lowered low-density lipoprotein (LDL) cholesterol. Targeting this interaction can also increase the amount of LDL receptors, subsequently minimizing the associated cardiovascular disease risks. Additionally, these compounds can affect apolipoprotein E, which has been indicated in Alzheimer's disease. The small molecule inhibitors may potentially be effective in the treatment of cardiovascular disease and hepatic steatosis.

ADVANTAGES:

- Modulates sortilin-ligand interactions
- Affects sortilin stability
- Potential treatment for hypercholesteremia, Alzheimer's disease, and hepatic steatosis

Compounds that Target the Interaction Between Sortilin and its Binding Partners



Binding of Compound 541 to Sortilin

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