Docket #: S24-233

Small molecule inhibition of the PTER/N-acetyltaurine pathway to treat obesity

Stanford scientists have discovered a series of compounds that inhibit PTER and leads to weight loss. They found that inhibition of PTER, a key enzyme that regulates N-acetyltaurine metabolism, leads to N-acetyltaurine accumulation and a reduction in food intake. Therefore, the use of PTER inhibitors may be an effective way of treating obesity and other metabolic disorders.

N-acetyltaurine is an abundant endogenous metabolite whose levels are dynamically regulated by diverse physiologic perturbations that increase taurine and/or acetate flux, including endurance exercise, alcohol consumption, and nutritional taurine supplementation. Interestingly, taurine supplementation has been reported to reduce mitochondrial redox stress, enhance exercise performance, and suppress body weight. PTER, an orphan body mass index-associated enzyme, was shown to have N-acetyltransferase/hydrolase activity and be capable of converting taurine to N-acetyltaurine. Genetic ablation of PTER and/or pharmacological administration of N-acetyltaurine in mice resulted in suppressed body weight and adiposity.

Iterative screening for and optimization of PTER inhibitors resulted in the discovery of small molecule inhibitors with a > 250-fold selectivity for PTER. Importantly, treatment with the lead compound caused an increase of N-acetyltaurine in mice and an acute decrease in food intake. Consequently, PTER inhibitors can potentially be used as a method of treatment for obesity and other cardiometabolic disorders.

Stage of Development:
Research: *in vivo*

Applications

- Treatment of obesity and other metabolic disorders
- Energy balance and body weight control
- PTER inhibitors can be administered as a therapeutic

Advantages

- Novel inhibitors of energy balance linked to taurine metabolism
- PTER activity can be inhibited as a method of increasing N-acteyltaurine levels to treat obesity

Publications

- Wei Wei, et al. (2024). A PTER-dependent pathway of taurine metabolism linked to energy balance. *bioRxiv* 2024.03.21.586194.

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