New Drugs for Enhancement of Memory Formation

OTT#1392

APPLICATION

Novel HDAC inhibitors (HDACis) to improve memory consolidation.

TARGET PROBLEM

Memory deficits are common to aging and neurodegenerative diseases like Alzheimer's disease. Because the U.S. population is rapidly aging, the incidence of memory dysfunction will increase exponentially.

KEY BENEFITS

- **Specific –** The lead compound increases levels of histone 3
- **Safer –** Lead compounds are less toxic than the parental natural products they were derived from
- **Cheaper –** Synthesis of the small molecules is easy and inexpensive
- **Druggable –** The lead compounds are more soluble than related FDA approved HDACis

TECHNOLOGY

Histone acetylation is a prominent epigenetic modification linked to the memory loss symptoms associated with aging and neurodegenerative disease. It has been found that HDACis enhance learning and memory in mouse models of Alzheimer's disease. Histone deacetylase enzymes are intimately involved in the organization of DNA structure and in reducing the activity of many genes. Histone acetylation promotes gene transcription, which is required for the formation of long-term memories.

The team has synthesized a small library of potent disulfide based HDACi molecules that show good solubility and low toxicity animal models. Studies show that the compounds are crossing the blood brain barrier and traveling to the hippocampus, a critical brain region for memory formation, and are improving spatial memory consolidation in a mouse model.

INTELLECTUAL PROPERTY

US Patent **11,149,062**; New analogs under investigation.

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