

James Rusche and Vincent Jacques
“HDAC Inhibitors for CNS Diseases: Challenges in Selectivity and Pharmacology”

Abstract: Epigenetic modification of gene expression impacts fundamental neurological processes such as cell survival from injury and consolidation of memory. Preclinical studies in behavioral and neurodegenerative disease models suggest that small molecule inhibitors of histone deacetylase enzymes (HDACi) may provide therapeutic benefit. Single gene neurodegenerative diseases represent a well defined setting for testing HDAC inhibition as a treatment target. A significant challenge is to find a pharmaceutically acceptable composition for chronic CNS treatment as all previously developed HDACi were chosen for peripheral activity as anti-tumor agents. Some aspects of the HDACi chemical structure will be discussed that impact compound selectivity and tissue distribution; two important features to achieve a safe and effective treatment for CNS diseases.

Dr. James Rusche has been at RepliGen since 1996 when the company began small molecule programs. He has directed the preclinical and early clinical development of proteins, peptides, natural products, and small molecule drug candidates for CNS, inflammation, and oncology programs.

Dr. Vincent Jacques is currently Senior Director of Preclinical Development at RepliGen Corp and has 9 years experience in R&D in the biotech industry working on magnetic imaging contrast agents and therapeutic small molecules. His responsibilities at RepliGen include medicinal chemistry, biochemical assays, in vitro ADME, and bioanalytical.