

Job Description:

A project initially funded by ICMR Govt. of India to develop isoform selective HDAC3 inhibitor in the queue of our ongoing effort in developing different series of HDAC3-selective inhibitors aimed at enhancing therapeutic precision while minimizing adverse effects for last 15 years. Recently one promising compound (AH22) demonstrated very high potency and huge isoform selectivity, with an IC_{50} of 4 nM for HDAC3 and approximately 1100-fold selectivity over any other HDAC isoforms. These compounds were screened for cytotoxic activity across a panel of 15 cancer cell lines and 4 normal cell lines, exhibiting strong selectivity toward cancerous cells over normal human cells-underscoring their potential as safer, targeted epigenetic therapeutics that need a few translational validation experiments.

Proposal involves translational validation of AH22: assessing cell permeability (Caco-2 assay), cancer cell death mechanisms, and its ability to sensitize chemo-resistant cells. Pharmacokinetics, biodistribution, in vivo efficacy (mouse models), cardiotoxicity, and biomarker studies (western blotting) will be conducted to support its clinical readiness.

It is expected that the fellow should take the molecule towards translation and the work should be such an extensive that it will lead to get the PhD of the fellow.