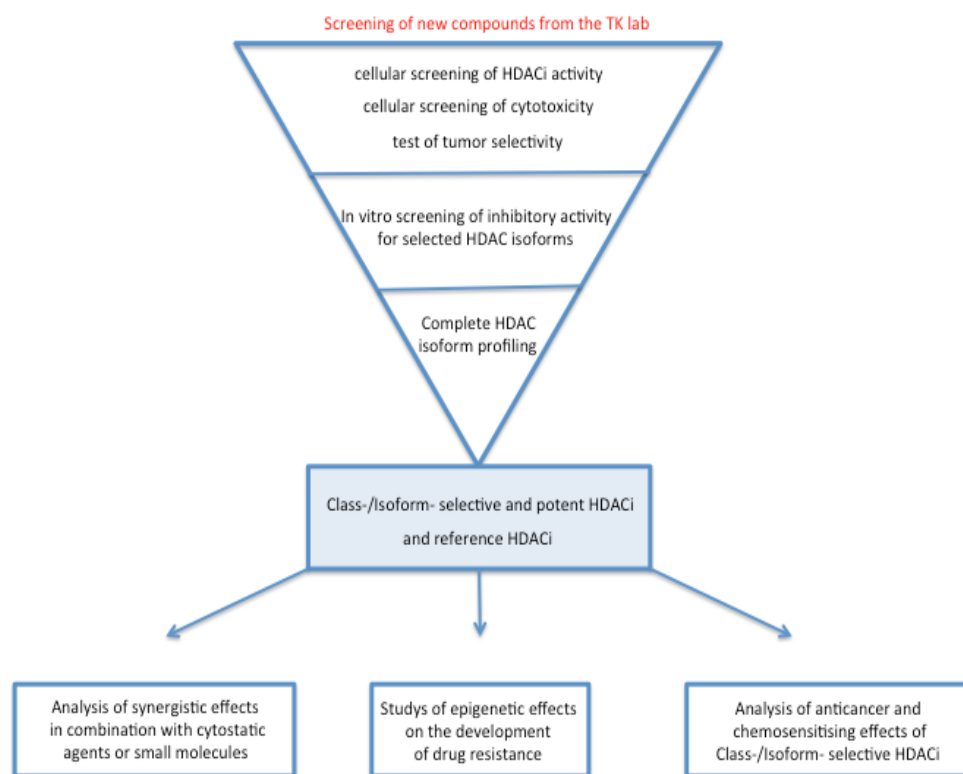


## Biological Characterization of (class IIa) HDAC-Inhibitors with chemosensitising properties as anticancer agents



Histon-deacetylases (HDACs) and histon-acetylases (HATs) belong to a family of enzymes which are crucial in the epigenetic regulation of gene expression. In tumor cells, the balance between acetylated and deacetylated histones is often impaired. Thus histon-deacetylases have been intensively studied in cancer development and progression. Based on their antitumoral characteristics, four HDAC inhibitors (HDACi) have been approved by the FDA. These inhibitors are mostly broad spectrum HDACi, which may be one reason for the observed severe side effects. Current research efforts therefore focus on the development of class- and isoform selective HDACi.

New class selective HDACi will be evaluated for HDAC inhibition, cytotoxicity, induction of apoptosis, cell cycle arrest, changes in gene and protein expression as well as acetylation status of target proteins. Reference HDACi serve as control. Cancer selectivity will be assessed with non-cancer cells. HDAC sensitivity will be tested via enzymatic HDAC assays. Also prevention and reversal of drug resistance will be tested in combination with the new compounds.