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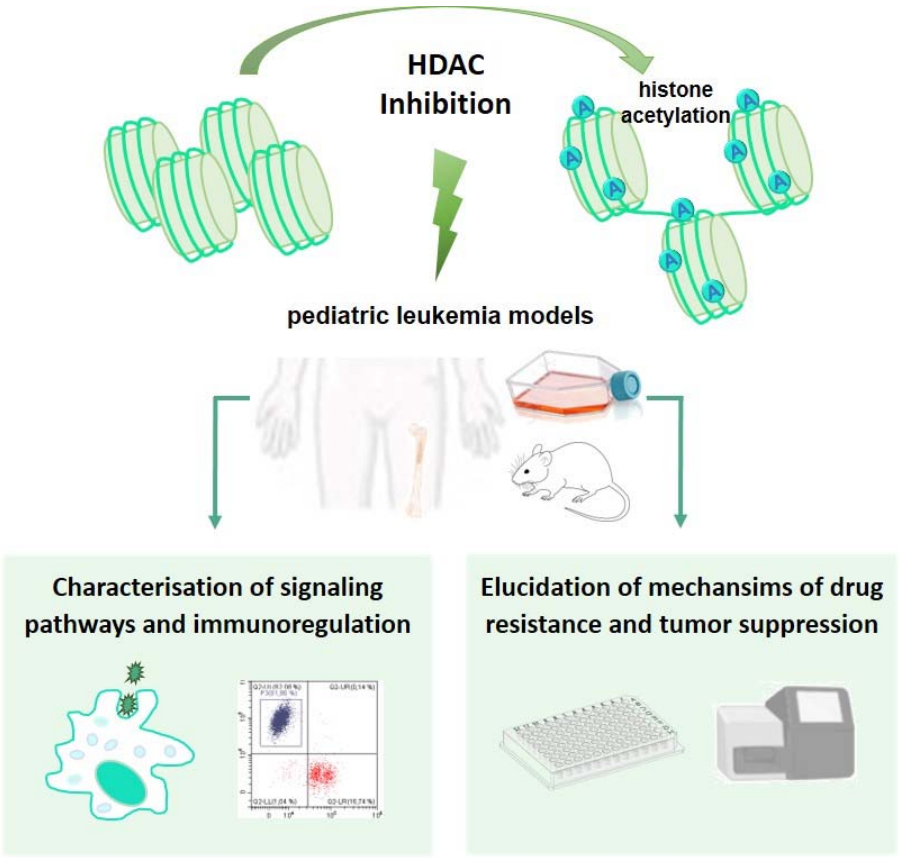
Preclinical development of natural product-based HDAC inhibitors to overcome therapy-resistant acute childhood leukemia



Histone deacetylase (HDAC) enzymes act as an epigenetic regulator of the genes that have been widely studied with their crucial roles in post-translational protein modification. There is evidence suggesting that aberrant chromatin remodeling due to dysregulated histone (de)acetylation prominently contributes to tumorigenesis. While a variety of pan-HDAC inhibitors have shown therapeutic efficacy in childhood leukemia treatments, the indication of refractory issues in patients still frequently occurs. Thus, in this project, we attempt to further study the signaling pathways, immunoregulation and drug sensitivity in order to understand the underlying mechanisms of HDAC inhibition-mediated tumor suppression and induction of drug resistance in cell- and animal-based models. Furthermore, we also aim to test and characterize the natural products-derived inhibitors as chemotherapy agents with less toxicity and robust treatment potential in collaboration with GRK working groups.

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