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Design and synthesis of small hybrid molecules targeting G9a and HDAC as anticancer agents.

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Recent studies correlate many cancers to the epigenetic modifications; epigenetics refers to the heritable changes determined by how the DNA is accessed in various stages of the cell growth. Accessibility of the DNA is restricted due to the tightly bound chromatin proteins,but this can be relaxed by various post translational modifications (PTM) like methylation, acetylation etc. In this work we are focused on developing a dual inhibitor targeting two PTMs; histone H3 lysine 9 (H3K9) methylation promoted by G9a and the overall histone deacetylation promoted by HDAC. These modifications are directly correlated with many cancer including leukemia, prostate carcinoma, hepatocellular carcinoma and lung cancer.12In this work we bring forward a single molecule possesses the pharmacophore of a G9a inhibitor and HDAC inhibitor by substituting the lipophilic cap of the HDAC inhibitor with a G9a inhibitor core. Complex diseases like cancer have a multifactorial basis that involves both genetic and environmental risk factors, a balanced modulation of several therapeutic targets can provide a superior therapeutic effect and a lowered side effect profile compared with monotherapies.

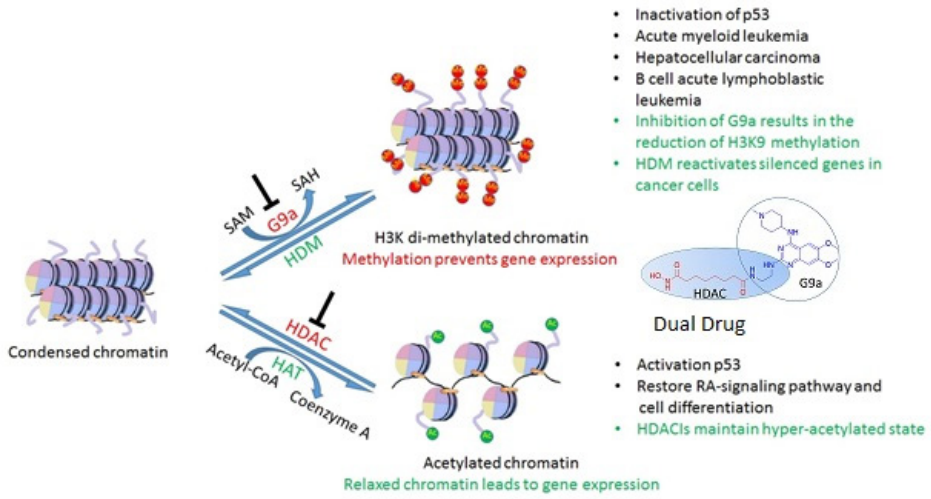

Fig1: An overview of post translational modifications on H3K9 and its significances in various cancer development.

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