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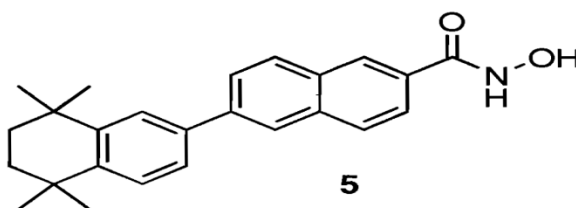


TECHNOLOGY OPPORTUNITY

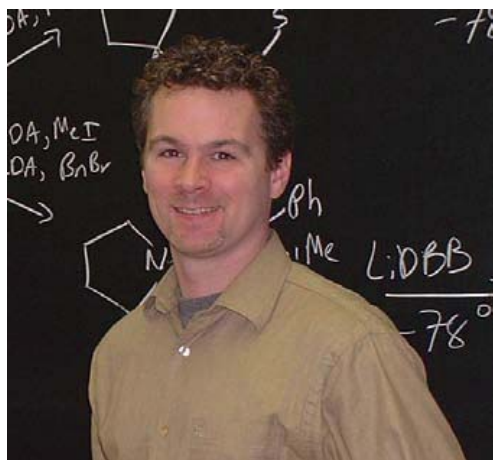
Hybrid Compounds with Retinoid Agonism and HDAC Inhibition for Cancer Therapy

Applications: Treatment of Breast Cancer, Leukemia and other neoplasms

Technology: Histone deacetylase inhibitors (HDACis) such as trichostatin A and suberoylanilide hydroxamic acid (SAHA, Zolinza) show synergistic behaviour with retinoic acid and retinoids in leukemia cancer cell lines. We have designed hybrid bifunctional molecules which possess both HDACi and retinoic acid receptor agonist properties. The lead compound, (Compound 5, below) blocks replication completely at 0.5 – 1.0 μM in the MDA-MB-231 breast cancer cell line, known for being extremely aggressive and drug resistant. A mixture consisting of of a retinoic acid receptor agonist and HDAC inhibitor was much less effective. Thus the potency of the compound resides in a high degree of synergism.



The Lead Inventor, Dr. James Gleason:



Dr Gleason's research focuses on diverse areas of organic synthesis, including the development of new synthetic methodologies, including cycloaddition strategies and methods for stereoselective quaternary carbon synthesis, the application of these novel methods in the total synthesis of bioactive natural products, the development of dynamic combinatorial libraries as a tool for medicinal chemistry and the design and development of hybrid molecules combining affinity for multiple biological targets. The latter research area involves the design and synthesis of "tricerols", hybrid molecules which combine structural features of vitamin D receptor agonists and histone deacetylase inhibitor hybrids.

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