Selective histone deacetylase (HDAC) inhibitors with therapeutic potential for cancer, neurodegenerative diseases, and autoimmune disorders

Technology #cu12080

Histone deacetylases (HDACs) are a family of proteins that remove acetyl functional groups from histones and other cellular proteins. There are eighteen known HDACs in humans, and they play a critical role in the regulation of processes from gene transcription to protein folding. As a class, HDACs have been implicated in diseases from cancer to autoimmune disorders. HDAC6 is located in the cytoplasm and has a number of different protein substrates including α-tubulin, ubiquitin, and HSP90. Its structure and function are unique among the HDACs making it an attractive drug target, however most HDAC inhibitors are not specific to a single type of HDAC protein and are therefore toxic. This technology describes two small-molecule inhibitors that are selective for HDAC6, and provides structural information for the design of other HDAC6 inhibitors.

Small molecule HDAC6 inhibitors show no HDAC1 cross-reactivity, limiting cytotoxicity and potential side effects

The HDAC6 inhibitors described in this technology do not demonstrate cross-reactivity with the closely related HDAC1. This is critical for reducing cytotoxicity because HDAC1 regulates cell proliferation. HDAC6 participates in a diverse range of important cellular processes making HDAC6 inhibitors a treatment candidate for a number of diseases. HDAC6 plays a regulatory role in mitochondrial transport, implicating it as a drug target for neurodegenerative diseases. HDAC6 inhibitors may also target T-cells, making them a potential therapy for autoimmune disorders, and they may induce DNA damage, sensitizing cancer cells to approved drug therapies.

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Applications:
• Sensitize cancer cells to approved anticancer therapies
• Therapy for neurodegenerative diseases including Alzheimer’s, Parkinson’s, Huntington’s and Niemann-Pick type C diseases
• Therapy for autoimmune disorders including AIDS
• Research tool for understanding HDAC6’s role in disease progression

Advantages:

• Fewer side effects when compared with other HDAC inhibitors
• Reduced cellular toxicity
• Specific to HDAC6

Patent Information:

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Related Publications:


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