Novel inhibitors of the sirtuin family of proteins

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Technology description

Summary

MARKETS ADDRESSED:
SIRT1 is a nicotinamide adenosine dinucleotide (NAD)-dependent deacetylases that removes acetyl groups from histones and non-histone proteins. SIRT1 can deacetylate a variety of substrates and is, therefore, involved in a broad range of physiological functions, including the control of gene expression, metabolism, and aging.
Sirtuins have been identified as important drug targets in neurodegeneration, obesity and fat metabolism, aging, and cancer metabolism.
Here, we report a number of compounds that inhibit the activity of SIRT1.
Cancer: It has been shown that SIRT1 is significantly elevated in human prostate cancer, AML, and primary colon cancer. Overexpression of SIRT1 was frequently observed in a variety of non-melanoma skin cancers. SIRT1 medicated deacetylation of p53 has been shown to lead to inhibited p53-mediated apoptosis induced by genotoxic stress. Treatment of cancers that overexpress SIRT1 with a SIRT1 inhibitor may reduce the acetylation of p53, making these cells susceptible to apoptosis under stress.

Advantages

Metabolic diseases: SIRT1 is an important regulator of energy homeostasis in response to nutrient availability. SIRT1 regulates lipid homeostasis by positively regulating PPARs. SIRT1 repression decreases fatty acid oxidation. It is therefore possible that inhibition of SIRT1 may be useful in the treatment of wasting diseases such as cachexia.

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