Modulators for Sirt2 in Cancer Therapeutics and Assays for Screening Same

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Technology description

The invention provides methods, assays and compounds associated with sirtuins, specifically Sirt2 mechanisms, for treatment and prevention of cancer.
The Lin group at Cornell has developed assays to screen for Sirt2 or Sirt5 modulators. Inhibitors that selectively target Sirt2 and Sirt5 have also been identified, and some of them have been shown to be able to control cancer cell proliferation.
Sirt2(D-5625)
The researchers have gained evidence supporting human Sirt2 protein as a new target for cancer treatment. The D-5625 invention describes a new group of small molecule inhibitors for treatment of cancer through targeting Sirt2, the only cytosolic sirtuin. SIRT2 specific knockdown can efficiently and completely inhibit breast cancer cell (MCF7) proliferation, as well as triple-negative breast cancer cells (MDA-MB-231 and MDA-MB-468), suggesting that Sirt2 is a potential target for treating breast cancer. The researchers' data show that a Thiomyristoyl lysine compound (TM) - an isolated inhibitor with high specificity for Sirt2 - inhibits many cancer cell lines in soft agar assay and effectively shrinks tumor in a mouse xenograft model. TM is then a potent Sirt2-specific inhibitor with a broad anticancer effect in various human cancer cells including brain, lung, breast cancers, and mouse models of breast cancer. Furthermore, mechanistically Sirt2 inhibition promotes c-Myc ubiquitination and degradation and it has been demonstrated that TM can effectively decrease the levels of c-Myc in many cancer cell lines by promoting the proteolytic degradation of c-Myc without affecting its transcription.

Application area

Sirt2-specific inhibitor as an anti-cancer drug candidate

Advantages

Thiomyristoyl compound (TM) presents high affinity, high selectivity, and high specificity to Sirt2
Inhibition of cancer cell proliferation with minimal effect on normal cells.

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