Reagents and Methods for Detecting Sirtuin Enzymatic Activity and Screening Sirtuin Modulators

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Technology description

This invention provides methods and compositions for preparing a sirtuin complex and detecting a sirtuin in a sample, as well as methods and compositions for screening and identifying compounds which inhibit or activate the enzymatic activity of a sirtuin.

Sirtuins are NAD^+ dependent acetyl-lysine deacetylases. Sirtuins are responsible for the regulation of a broad range of cellular processes, including energy metabolism, DNA-damage response and cellular stress resistance. The protective effects of these enzymes in age-related pathological processes, such as metabolic syndrome and neurodegenerative disorders, has fostered a tremendous interest in studying the enzymatic activity of the sirtuins, and in the development of specific modulators of these enzymes . Thus, the development of a tool to specifically probe sirtuin activity in biologically and pathologically relevant contexts, as well as in screening modalities is of high practical use for assessing libraries for effects on sirtuin activity, as well as understanding how cellular perturbations can alter sirtuin function. These are more precise approaches to measure sirtuin activities, rather than using downstream cellular effects as an activity readout.

Cornell researchers have developed a novel chemical approach to rapidly isolate and detect the specific sirtuin enzymatic activities. A pan-sirtuin inhibitor reacting on sirtuin active sites and a modified NAD^+ are used to form a chemically stable complex. This complex can subsequently be cross-linked to an aldehyde-substituted biotin. The biotinylated sirutin complex can be retrieved by streptavidin beads and subsequently followed by gel electrophoresis. This method enables simultaneous detection of active sirtuins, isolation and molecular weight determination. This method is sensitive to activity of sirtuins.

The approach can be used to screen compounds which inhibit or activate the enzymatic activity of a sirtuin. The compounds may be useful for the studies of sirtuins as well as for therapeutics.

Additional Information

Mechanism-based affinity capture of sirtuins. Org. Biomol. Chemistry, 2011, 9:987-93 .

Application area

Research kits for isolate and detect the sirtuin enzymatic activities
Screening for compounds inhibiting or activating the enzymatic activity of a sirtuin for research or therapeutics

Advantages

Simultaneously and rapidly isolate and detect enzymatic activities
Detect enzymatic activities in a biologically and pathologically relevant context, instead of using downstream cellular effects as an activity readout

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