

Parenti MD, Bruzzone S, Nencioni A, Del Rio A (2015). Selectivity hot spots of sirtuin catalytic cores. *Mol. Biosyst.* 11:2263-72.

Sirtuins are NAD(+)-dependent deacetylases with several biological roles in DNA regulation, genomic stability, metabolism, longevity and immune cell functions. Numerous disease conditions are linked to sirtuins including metabolic disorders, inflammatory and autoimmune processes and cancer. Although few specific small molecule modulators have been reported to date, the need to identify selective ligands would be crucial not only for the development of active pharmaceutical ingredients for new targeted therapies but also as a tool for dissecting the biological roles of sirtuin family members. Herein, we report a comprehensive study aimed to classify and identify the selectivity hot-spots for targeting the catalytic cores of human sirtuins using small molecule modulators. Our selectivity analysis suggests that catalytic cores can be divided into different clusters that can constitute the basis for the development of selective ligands. The ensemble of hot-spot information is expected to be helpful to devise new selective chemicals targeting sirtuin family members.