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Repositioning of heterocyclic derivatives as sirtuin 5 activators

Abstract:

Sirtuin 5 (SIRT5) is a nicotinamide adenine dinucleotide (NAD⁺)-dependent enzyme belonging to HDACs family, primarily present in mitochondria. Besides to the deacetylase activity, SIRT5 catalyses the desuccinylation, demalonylation and deglutarylation in particular of negatively charged acyl lysine residues. SIRT5 modulates the activity of various enzymes involved in the metabolism of ammonia and glucose, the amino acid degradation, the electron transport chain and apoptosis, contributing to maintain cellular redox homeostasis and to control ROS levels. Furthermore SIRT5 dysregulation has been related to different pathologies as metabolic disorders, cardiovascular and neurodegenerative diseases, infections, cancer and to the modulation of the inflammatory response. Since drug repositioning is considered among the effective tools in developing potentially active molecules, with the aim to discover novel SIRT5 activators, we applied this approach to our in-house library compounds. Their biological evaluation led to the identification of some heterocyclic derivatives endowed with SIRT5 activation but not exhibiting antiproliferative activity. The most significant data will be proposed.

Biography

Arianna Gelain is Assistant Professor at University of Milan, Faculty of Pharmacy. She graduated in Pharmaceutical Chemistry and Technology and obtained the Ph.D. in Medicinal Chemistry at University of Milan. Her scientific activity concerns the design, synthesis and the related structure-activity relationships studies of novel small molecules as signaling pathway modulators (in particular STAT3 inhibitors) and potential antimicrobial (antitubercular, anti-biofilm and antimalarial) agents. She is author and co-author of 60 scientific publications in peer reviewed and SCOPUS indexed international journals, one chapter book and over 60 contributions (oral and poster communications) presented at national and international congresses.