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Identification of sirtuin inhibitors as promising anticancer agents: From screening to activity assays

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Sirtuins (SIRTs) are a family of enzymes able to catalyze the deacetylation of the N-acetyl lysines of both histone and non-histone substrates. Inhibition of their catalytic activity was recently reported in the literature as being beneficial in aging-related diseases such as cancer and neurodegeneration. By combining a structure-based virtual screening approach of highly diverse molecular libraries with fluorescence-based deacetylation assays, we identified new scaffolds for the inhibition of SIRT catalytic activity. For these compounds, all active in the low μM range, both mechanisms of inhibition and binding modes were elucidated. Moreover, physiochemical properties for passive adsorption and cytotoxicity data were investigated *in vitro*. We then demonstrated the capacity of these SIRT inhibitors to strongly repress angiogenesis in cells, in a FoxO-dependent fashion. Our study provided promising compounds able to target SIRTs that could be useful for both research and therapeutic purposes.

Biography

Alessandra Nurisso has completed her PhD in Structural Glycobiology from Grenoble University (France). In 2010, she joined the Pharmacochemistry Laboratory of the School of Pharmaceutical Sciences of the University of Geneva (Switzerland) as a Post-Doctoral Researcher in Computer-Aided Drug Design. She is currently Lecturer in Medicinal Chemistry at the University of Geneva, at the University of Grenoble, and, since 2013, Chair of Excellence of the University of Geneva (Switzerland). Her current research focuses on *in silico* driven strategies for the design of novel molecules targeting epigenetic enzymes.

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