EuroSciCon

DAY 1

Scientific Tracks & Abstracts

European Congress on

Advanced Chemistry

July 12-13, 2018 Paris, France

EuroSciCon

European Congress on

Advanced Chemistry

July 12-13, 2018
Paris, France

Katarina Nikolic et al., J Org Inorg Chem 2018, Volume: 4
DOI: 10.21767/2472-1123-C2-005

COMPUTER-AIDED DRUG DESIGN OF SELECTIVE HISTONE DEACETYLASE INHIBITORS

Katarina Nikolic[1], Dusan Ruzic[1], Nemanja Djokovic[1], Milos Petkovic[1], Danica Agbaba[1], Maija Lahtela-Kakkonen[2] and A Ganesan[3]

[1]University of Belgrade, Serbia
[2]University of Eastern Finland, Finland
[3]University of East Anglia, Norwich, United Kingdom

The concept of gene expression is continuously explained with epigenetic modification. Post-translational histone acetylation and DNA methylation are dominant epigenetic alterations of the genome. Histone deacetylases (HDAC) play essential role in this process and therefore are very intensively investigated drug targets. The alteration in the structure and function of HDAC isoforms are identified in the pathogenesis of inflammation, cancer, and neurodegeneration. Eleven human HDAC isoforms are sharing a highly conserved catalytic domain. Among them, HDAC6 and SIRT2 are important for a wide range of diseases, due to their unique physiological functions. In our research, we have applied pharmacophore modelling, virtual screening, molecular docking and molecular dynamic methodologies for design and identification of selective HDAC6 and SIRT2 inhibitors. Recently resolved the crystal structure of catalytic domain II of human HDAC6 discovered a wide binding site essential for the substrate recognition. We have successfully used these structural features of human HDAC6 catalytic domain II to rationally design selective HDAC6 inhibitors. Newly published X-ray structures of selective ligand-SIRT2 complexes have revealed high conformational flexibility of this enzyme, and gave us more details about mechanism of action of sirtuin 2 inhibitors. Based on these findings we have performed molecular dynamic study of SIRT2 and tried to explain the conformational changes during enzyme catalysis. Since small number of selective HDAC modulators have been reported so far, rational design of HDAC6 and SIRT2 inhibitors are essential for further progress in discovery of epigenetic drugs.

Biography

Katarina Nikolic has completed her PhD from Faculty of Pharmacy, University of Belgrade. She is an Associate Professor at Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Belgrade, Serbia. The main areas of her research involve: Molecular Modeling, Pharmacophore Modeling, Virtual Screening, Molecular Docking and Molecular Dynamic, Computer-aided Drug Design, Lead Optimisation, Synthesis, and Chemometry. Her research is currently focused on Discovery of Novel CNS Drugs and Antineoplastic Agents. Her team has long-lasting research collaboration with several leading European Universities via few Horison2020/COST projects which are focused on rational drug design and discovery. She has published more than 75 papers in reputed journals.

knikolic@pharmacy.bg.ac.rs