UNIVERSITÀ DEGLI STUDI DI CAGLIARI

Dipartimento di Scienze chimiche e geologiche
Dipartimento di Scienze della vita e dell'ambiente

Seminar announcement

First lecture: February 16th 2023, at 11:00 a.m.
Cittadella Universitaria di Monserrato, blocco A, room 109

Second Lecture: February 17th 2023, at 11:00 a.m.
Cittadella Universitaria di Monserrato, blocco A, room 112

Prof. Margherita Brindisi
Department of Pharmacy (DoE 2023-2027),
University of Naples Federico II, Naples, Italy

Biography

Margherita Brindisi received her PhD from the University of Siena. In 2010-2011 she worked as a post-doctoral fellow at Purdue University on the development of aspartyl protease inhibitors under the supervision of Prof. Arun K. Ghosh. From 2012 to 2015 she was appointed as a fixed-term Researcher at the University of Siena working on the development of novel agents against cancer, parasitic diseases, and brain disorders. In 2016-2017 she again moved to Purdue University as a Visiting Researcher. Margherita Brindisi is co-author of more than 100 papers in reputed journals. Starting April 2022, she is an Associate Professor of Medicinal Chemistry at the Department of Pharmacy of the University of Naples Federico II.

Date: February 16th 2023, **Time**: 11:00,
Venue: Cittadella Universitaria di Monserrato, blocco A, room 109

Structure-based drug design as an enabling tool toward novel therapeutics in cancer, neurodegenerative disorders and infectious diseases

ABSTRACT. Structure-based drug design (SBDD) represents a crucially important strategy in all the different steps of the drug discovery path, including hit identification, hit-to-lead transition, potency and selectivity modulation, reduction of off-target liability, and optimization of drug-like properties. The use of SBDD in medicinal chemistry has been increasingly growing, hand in hand with significant advances in molecular biology, the production of high-quality proteins, and X-ray crystallography techniques. SBDD has the potential of addressing the challenges of modern medicinal chemistry for traditional drug targets as well as for newly identified druggable targets. Moreover, it has the potential to strongly boost drug discovery approaches aimed at tackling the complexity of multifactorial diseases through the design of multitargeting ligands.

Different aspects of SBDD leading to biologically active compounds will be covered based on my personal experience in drug discovery. In particular, several facets and applications of SBDD will be discussed, from hit/lead generation based on the structural knowledge of the target (X-ray or homology modelling), to synthetic chemistry, and structure-activity relationships for ligand optimization. These applications of SBDD range from several drug targets relevant to cancer therapy up to neurodegenerative disorders and infectious diseases. Finally, a focus on the intertwining of enabling technologies (eg. flow chemistry and mechanochemistry) with drug discovery projects will be provided.

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Selective histone deacetylase 6 inhibition: tracking the journey from established anticancer strategy to innovative therapeutic option in rare diseases

Epigenetic regulation orchestrates many cellular processes and greatly influences key disease mechanisms. Histone deacetylase (HDAC) enzymes play a crucial role either as biomarkers or therapeutic targets owing to their involvement in specific pathophysiological pathways. Beyond their well-characterized role as histone modifiers, HDACs also interact with several nonhistone substrates and their increased expression has been highlighted in specific diseases. The HDAC6 isoform, due to its unique cytoplasmic localization, modulates the acetylation status of tubulin, HSP90, TGF-β, and peroxiredoxins. HDAC6 also exerts noncatalytic activities through its interaction with ubiquitin. Both catalytic and noncatalytic functions of HDACs are being actively studied in the field of specific rare disorders beyond the well-established role in carcinogenesis. The seminar will track the journey of HDAC6 inhibitors from established anticancer strategy to innovative therapeutic option in rare diseases, such as Rett syndrome, idiopathic pulmonary fibrosis, and cystic fibrosis, highlighting their therapeutic potential as innovative and targeted disease-modifying agents.