ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

DIPARTIMENTO
DI FARMACIA
E BIOTECNOLOGIE

AVVISO DI SEMINARIO

Il giorno **14 Marzo 2024**
alle ore 14:30

Prof. Michele Mazzanti

Università degli Studi di Milano
(ospite di Prof. Stefano Ferroni)

terrà un seminario dal titolo:

Chloride Intracellular Channel 1 as a privilege receptor mediating metformin antiproliferative action on glioblastoma cells

Area tematica:
Neuroscience, Cancer Biology

in presenza:
Aula A Farmacologia, via Irnerio 48, Bologna BO

e/o in streaming:
https://teams.microsoft.com/l/meetup-join/19%3aN09c0NIyEssBnF7ObCyDOQwkgDWm1qdd9f7F2nJV9fw1%40thread.tacv2/1631519544944?context=%7b%22Tid%22%3a%22e99647dc-1b08-454a-bf8c-699181b389ab%22%2c%22Oid%22%3a%225a941351-ef41-4aa4-8771-fa50a6d62ca1%22%7d

Colleghi e studenti sono cordialmente invitati

ABSTRACT

Metformin is the first-line drug for type-2 diabetes. Retrospective analyses, based on diabetic patients' clinical data, demonstrate that daily assumption of metformin reduces the incidence of several kinds of solid tumors. Even though it is widely agreed that metformin must be internalized to accomplish its pharmacological activity, direct evidence about metformin membrane permeability and/or the presence of a specific membrane receptor in cancer cells is still missing. Here, we show that the transmembrane form of Chloride Intracellular Channel 1 (tmCLIC1) works as a privileged metformin receptor in glioblastoma stem-like cells. We found that metformin impairs tmCLIC1 activity by a specific binding coordinated by arginine 29. Its mutation, preventing metformin to bind and block tmCLIC1, abolishes the biguanide inhibition of glioblastoma cell proliferation in 2D and 3D models and metformin dependent effect on mitochondrial respiration. In addition, we demonstrate the direct binding between the drug and its target, and by in vivo experiments on zebrafish embryos and mice orthotopically engrafted with glioblastoma cells and treated with metformin, we prove that metformin binding to tmCLIC1 is crucial for metformin antineoplastic effect. Considering tmCLIC1's contribution to glioblastoma progression, the present work provides the fundaments for future development of strategies aimed at improving metformin-tmCLIC1 interaction to further increase metformin therapeutic potential.

BIOGRAPHICAL SKETCHES

Michele Mazzanti graduated with a thesis in muscular biomechanics from the Institute of Human Physiology at the University of Milan. He then obtained his Ph.D. in Biophysics through a joint project between the laboratory of General Physiology at the University of Milan and the laboratory of Membrane Biophysics at Emory University, in Atlanta. During his staying at Emory University, he spent 3 years as a post-doc and 3 years as an Associate Professor. After returning to Milan, he worked as a researcher at the University of Wurzburg in Germany, the New South Wales University in Australia, and the University College London (UCL). Meanwhile, he became an Associate Professor at the University of Rome La Sapienza and subsequently a Full Professor of Physiology. For several years, he has been associated with the University of Milan (Department of Biosciences), where he leads the laboratory of Cellular and Molecular Physiology. Since completing his Ph.D., Prof. Mazzanti's work has focused on investigating the electrical properties of cellular membranes. Initially, he studied cardiac and neuronal cells, and later, he delved into intracellular membranes. In recent years, his research has centred on the physiology of brain tumours.