Contribution ID : **226** Type : **Poster Presentation**

On the allostery of european ALDH2 enzyme: an in-depth computational investigation

Allostery is a biological phenomenon that plays a pivotal role in regulating the metabolic pathways, such as feedback inhibition and feedforward activation, in which the three-dimensional structure of proteins could create surface pockets recognized by modulators. The binding of modulators elegantly affects the orthosteric pocket via a dense connection of amino acids between the allosteric and active sites. Thus, the knowledge of such allosteric pathways is fundamental to enhance the design of promising pharmaceutical molecules for personalized medicine. Mitochondrial Aldehyde Dehydrogenase 2 (ALDH2) is a key enzyme in the cellular detoxification of aldehydes after alcohol assumption, and its malfunctioning is associated to mitochondrial anomalies, alteration of the energy production metabolism and cardiomyopathies. The focus on the allosteric inhibition is driven by the well-substantiated advantages of the allosteric modulators with respect to the competitive ones, such as the high specificity and minor adverse effects, vital for the design of a drug [1]. In this study, European ALDH2 modulation is deeply investigated, starting from experimental evidence of two inhibitors of its enzymatic activity, quercetin and one of its metabolites [2]. Molecular dynamics simulations and molecular docking provide the means to deepen highlight the structural effects after the inhibitor binding and to propose a novel allosteric pocket, thorough the application of MD analysis tools. Furthermore, it was applied a Python package, MDiGest, which is a potent object-oriented toolkit to target protein hubs, amino acid communities and allosteric networks of biological systems through pairwise correlations extrapolated from the MD simulations [3].

Primary author(s) : Ms. DODARO, Alessia

Co-author(s) : PREJANÒ, Mario; RIVALTA, Ivan; CIARDULLO, Giada; MARINO, Tiziana

Presenter(s) : Ms. DODARO, Alessia