Contribution ID: **49** Type: **Poster**

Intracellular Water –an Overlooked Target of Drug Activity? Cisplatin´s Impact in Breast Cancer Cells Probed by Neutron Techniques

Friday, 2 September 2016 17:50 (1h 25m)

The first neutron scattering study of intact human cells is reported, addressing the subject of solvent-slaving to a drug by directly probing intracellular water to ascertain structural and dynamical variations upon drug exposure. This study is based on the assumption that the behaviour of cytoplasmic water determines both the conformation and function of biomolecules. Inelastic and quasi-elastic neutron scattering spectroscopy experiments with isotope labelling were performed, for monitoring interfacial water response to the widely used anticancer drug cisplatin in human metastatic breast cancer cells. This is an innovative way of tackling a drug´s pharmacodynamics, searching for alternative targets in order to improve chemotherapeutic efficiency. Intracellular water was found to behave differently in drug-free and cisplatin-exposed cells: concentration-dependent structural changes coupled to a progressive mobility reduction were unveiled, concurrent with variations in the native organisation of water molecules within the intracellular medium as a consequence of drug action. These results constitute the first reported experimental proof of a drug´s impact on the cytomatrix by neutron techniques, and lead to a better understanding of the in vivo mode of action of antitumour agents, at a molecular level, allowing a rational design of improved drugs.

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Session Classification: Poster Session