geometry) for binding of rotenone and three derivatives with variable conformational restrictions.

MATERIALS AND METHODS
We applied molecular dynamics simulations and the free energy methods umbrella sampling, metadynamics and linear integration energy.

DISCUSSION AND RESULTS
We find that rotenone has similar affinities to either RS and BS sites. All derivatives have low affinity, between +4 and -3 kJ/mol, to the third PS. This result indicates that the PS may be an experimental artifact due to the high rotenone concentrations used in the cryoEM preparation. Two conformationally restricted derivatives show low affinity to the RS, suggesting that the bent rotenone conformation is stabilized in the RS, favoring complex I inhibition.

CONCLUSION
Considering these, rotenone probably inhibits complex I by binding in the two sites (RS and BS) located in the Q-chamber and RS binding requires an internal flexibility to a bent geometry. We are now analysing how this internal flexibility affects rotenone transit inside the chamber.
Keywords: Molecular dynamics, Electron transport chain, Free energy methods
Supported by: FAPESP

SP-10. Biophotonics

SP-10.01 - Light-based non-thermal therapy: from basis to clinical applications

Martha Simões Ribeiro [1]
[1]Center for Lasers and Apllications, Nuclear and Energy Research Institute (São Paulo, Brazil)

Light-based non-thermal therapies are evolving as promising non-invasive and cost-effective medical technologies. These therapeutic platforms mainly encompass photobiomodulation (PBM) and photodynamic therapy (PDT), which use visible or near infrared (NIR) light to induce biological responses without any significant heating effects. For PBM, it is most commonly used red or NIR light to optimize light penetration into biological tissues. The photon absorption by natural chromophores at these spectral regions cause photophysical and photochemical reactions inside cells that trigger several biological effects such as to accelerate wound healing, reduce inflammation and relief pain, depending on light parameters and target tissue. On the other hand, PDT makes use of photoactivated drugs, also called as photosensitizers, which absorb light to induce chemical reactions that kill microbial or cancer cells by oxidative stress.

Our group have been investigating the mechanisms and several applications of PBM and antimicrobial PDT (APDT) for almost 20 years. In this lecture I will share our experience in the area to discuss how PBM and APDT could be used to revolutionize health care in the photonics era. An integrated perspective from the basic mechanisms, preclinical and clinical trials for both therapies will be presented, including PBM on cancer management and APDT against drug-resistant pathogens. The lecture will also highlight future perspectives.
Keywords: antimicrobial photodynamic therapy, photobiomodulation therapy, preclinical and clinical assays
Supported by: FAPESP, CNEN, CNPq

SP-10.02 - The water-isotopologue deuterium oxide (D2O; 'heavy' water): From biophysical properties to experimental cancer therapeutic

Jana Jandova[1], **Georg T. Wondrak[1]**
[1]Pharmacology and Toxicology, College of Pharmacy and UA Cancer Center, University of Arizona (Arizona, USA)

Since its initial discovery as a natural heavy isotope variant of dihydrogen oxide ($^{1}H_2O$), extensive research has focused on the biophysical, biochemical, and pharmacological effects of deuterated water [$^{2}H_2O$ (D_2O, also referred to as 'heavy water')]. Here, we provide a D_2O-centered perspective on biophysical properties and potential therapeutic use targeting cancer cells. Due to its unique physicochemical properties, D_2O has become a valuable biochemical probe examining various physiological parameters using MRI and isotope ratio-mass spectrometry. Biological effects of D_2O are generally attributed to altered isotopic and solvent properties, associated with an increased strength of deuterium-based hydrogen bonds. Indeed, deuteron- (versus proton-) dependent biological impact is largely attributed to alteration of biophysical properties including (i) conformational stability of proteins, (ii) fidelity of nucleic acid base pairing, and (iii) other proton-sensitive effectors including mitochondrial energy metabolism and solute channels (e.g. aquaporin and calcium). Importantly, shortly after its initial discovery by Urey in 1932, cancer-directed effects of D_2O (administered systemically) have been examined in vivo, and inhibitory effects on murine tumor growth were described as early as 1938, documenting growth inhibition of implanted carcinomas using D_2O drinking water supplementation. Cumulative evidence now confirms tumor-directed activity of D_2O supplementation in murine cancer models including pancreatic, colorectal, squamous cell carcinoma, and malignant melanoma. Using a panel of cultured melanoma and pancreatic ductal adenocarcinoma cells we have recently profiled apoptogenicity, stress response gene array expression (redox-, metabolism, and proteotoxicity-related), and