

14th World Cancer & Anti-Cancer Therapy Convention

November 21-23, 2016 Dubai, UAE

Combinative drug therapy for cancer treatment: Exploring synergistic mode of action of amino and carboxy terminal domain inhibitors of Heat Shock Protein 90 (HSP90)

Bhaskar Kr Chatterjee

Indian Institute of Technology, Delhi, India

This work entails the characterization of how inhibitors work against the various properties of Hsp90, a eukaryotic chaperone. For decades, drugs have been designed against this molecule, as it has over 200 client proteins that include kinases and steroid-hormone receptors. Many of them have been implicated in several types of cancer, in their mutated versions. Proper folding enables mutant proteins to become functional and develop cancer in tissues. Inhibiting one or more chaperone functions will reduce amount of functional mutants. This work studies in detail how commercially used (geldanamycin and novobiocin) as well as novel inhibitors (KU compounds) affect the chaperone properties of Hsp90 viz., ATPase activity and prevention of aggregation of denatured substrates. It also investigates the effect of these inhibitors in the refolding of luciferase (model substrate) inside HeLa cells, which are given heat shock to denature luciferase. It also tries to correlate the *in vitro* data by using *in silico* models of Hsp90 bound to these inhibitors, and exploring the global and local changes that occur in MD simulations. Most importantly, it explores if two different classes of inhibitors (for example, geldanamycin & novobiocin) can act synergistically, to enhance inhibition, as compared to the inhibition of an individual drug. This can be thought of as a lab scale project to aim for a novel drug therapy for cancer treatment, as results are indicating synergistic mode of action in some of the *in vitro* assays.

Biography

Bhaskar Kr Chatterjee is currently pursuing PhD from IIT-Delhi. He is a fifth year student, working on mechanistic action of Hsp90 inhibitors both *in vitro* and in cancer cell lines. He is also involved in *in silico* studies to correlate his *in vitro* work, in collaboration with Super-Computing Facility, IIT-D. He aims to carry out animal model studies to actually understand whether synergistic mode of action is helpful in partially/fully abrogating cancerous lesions, with minimal side-effects.

bhaskarkumarchatterjee1989@gmail.com

Notes: