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KRAS G-quadruplex stabilisation by porphyrin based compounds: A powerful tool against pancreatic cancer

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KRAS, a frequently mutated proto-oncogene is accountable for almost every type of cancer which can form a G-quadruplex structure in the promoter region. G-quadruplex structures are one of the most important drug targets for modern targeted cancer therapy for their unique structure and specificity. Several synthetic porphyrin-based compounds have been screened as potential KRAS-promoter/G-quadruplex stabilizing ligands, using molecular modeling and docking studies. Two novel porphyrins: Porphyrin-1 (Cobalt containing) and Porphyrin-2 (Palladium containing) evidenced high affinity towards KRAS-promoter/G-quadruplex. *In silico* results were further validated *in vitro*, using techniques like fluorescence and CD spectroscopy. As KRAS mutation is prevalent in pancreatic cancer, the efficacy of these ligands against human pancreatic ductal carcinoma cell line PANC-1 and MiaPaCa-2 were examined. Both Porphyrin-1 and Porphyrin-2 exhibited significant cytotoxicity towards both cell lines, accompanied by the induction of apoptosis, inhibition to colony forming abilities and migratory properties of cancer cells. These two porphyrins block metastasis via blocking of Epithelial to mesenchymal transition. Moreover, *in vivo* studies confirmed, both porphyrin compounds to be very much effective against mice solid tumor model but with significant low toxicity against normal swiss albino mice. Interestingly the expression of KRAS protein in porphyrin-treated PANC-1 and MiaPaCa-2 cells was drastically reduced at both protein and RNA levels. Thus interaction of porphyrin-based ligands with G-quadruplex. DNA at the promoter region of KRAS might be responsible to inhibit the proliferation of pancreatic cancer cells which may have significant implication in cancer research.

Biography

Rudradip Pattanayak has completed his Master's degree from the Department of Biochemistry, University of Calcutta, India. He is the final year student of PhD under the guidance of Prof Maitree Bhattacharyya in the Department of Biochemistry, University of Calcutta in collaboration with Jagadis Bose National Science Talent Search, India. He has published 7 research papers in reputed journals. He is currently working on G-quadruplex mediated regulation of oncogenes.

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