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Design and discovery of novel ectonucleotidases inhibitors

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Ectonucleotidases are ectoenzymes that hydrolyze extracellular nucleotides to their respective nucleosides. They are potentially involved in decreasing extracellular concentrations of nucleotides and in generation of nucleosides. Extracellular nucleotides modulate a multiplicity of tissue functions including development, blood flow, secretion, inflammation and immune reactions. Indeed, signaling via extracellular nucleotides has been recognized for over a decade as one of the most ubiquitous intercellular signaling mechanisms. Their high expression is associated with various types of cancers, gastrointestinal disorders, neurodegenerative diseases, chondrocalcinosis and many other physiological disorders. Unfortunately, a very limited work is reported in context of selective inhibition of these enzymes. The presented study aims at identification of novel and potent inhibitors of two major families of ectonucleotidases namely ecto-5'-NT (ecto-5'-nucleotidases) and ALPs (alkaline phosphatases). We have identified new small molecules based inhibitors of ecto-5'-nucleotidases which are potent and highly efficient with K_i values in micro molar ranges. Moreover we have also discovered some new classes of inorganic and organic compounds which show high potency and selectivity in inhibiting alkaline phosphatases up to nano molar ranges of K_i values. Their comparative studies on different isozymes obtained from human and animal sources revealed their selectivity potential. Discovery of these inhibitors may lead to establishment of therapeutically important tools for treatment of cancer, neurodegenerative disorders and many other associated problems.

Biography

Rabia Raza is a Ph.D. Scholar at Bahauddin Zakariya University Multan, Pakistan. She is working on inhibitors based discovery of drugs. During her Ph.D. studies, she has published four research papers in international high impact journals. In 2011 she was awarded with research productivity award. She also won first prize on presenting her work in an International Chemistry conference in Karachi Pakistan.

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