Development of Tools and Drugs Targeting Purine-Binding Membrane Proteins for Cancer Immunotherapy

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Adenosine is one of the strongest immunosuppressant agents of the innate immune system. Cancer cells and tissues can release large amounts of ATP which is immediately hydrolyzed by ectonucleotidases. These ecto-enzymes, including ectonucleotide pyrophosphatase/ phosphodiesterase 1 (NPP1, CD203a), ectonucleoside diphosphohydrolase 1 (NTPDase1, CD39), and ecto-5'-nucleotidase (CD73), are upregulated on many cancer cells leading to the production of adenosine. The cloud of adenosine formed around cancer tissues contributes to immune escape by interacting with adenosine A_{2A} and A_{2B} receptor subtypes (A_{2A}AR, A_{2B}AR) on immune cells. In addition, activation of A_{2B}ARs by adenosine enhances cancer cell proliferation, metastasis, and angiogenesis.

Our work has been focused on the identification and optimization of small molecule inhibitors of ectonucleotidases, including NPP1, CD39 and CD73 inhibitors, and adenosine receptor antagonists as novel therapeutics in immuno-oncology. Moreover, we have developed labeled tool compounds for studying these novel promising targets.