DESIGN AND SYNTHESIS OF AURORA KINASE INHIBITORS

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BACKGROUND/OBJECTIVES: The Aurora Kinase (AK) family is made up of three serine/threonine kinases, Aurora A, B and C, all of which are implicated in diverse cell cycle events, including mitosis and meiosis. Previous studies have shown that Aurora A and B play a major role in tumorigenesis and that both are significantly overexpressed in multiple cancers. Therefore, the targeted inhibition of AKs represents a promising approach for the development of novel anticancer agents. The aim of this research project is to design and synthesize a small organic molecule that selectively binds to AKs with high affinity and specificity. In subsequent research projects, this molecule would be radiolabelled with Fluorine-18 and its efficacy and specificity in detecting AK expression in murine malignant tumours would be detected using PET imaging.

METHOD: Small molecules with potential high binding affinity were first identified via molecular docking analyses. The molecule of interest will then be synthesized by standard organic synthetic procedures and purified using chromatographic techniques. ^{1}H-NMR and TLC data will be used to confirm the identity of the products. In subsequent investigations, IC_{50} assays will be used to evaluate the efficacy of the synthesized compounds in terms of its inhibitory effect on the target kinases.

RESULTS:

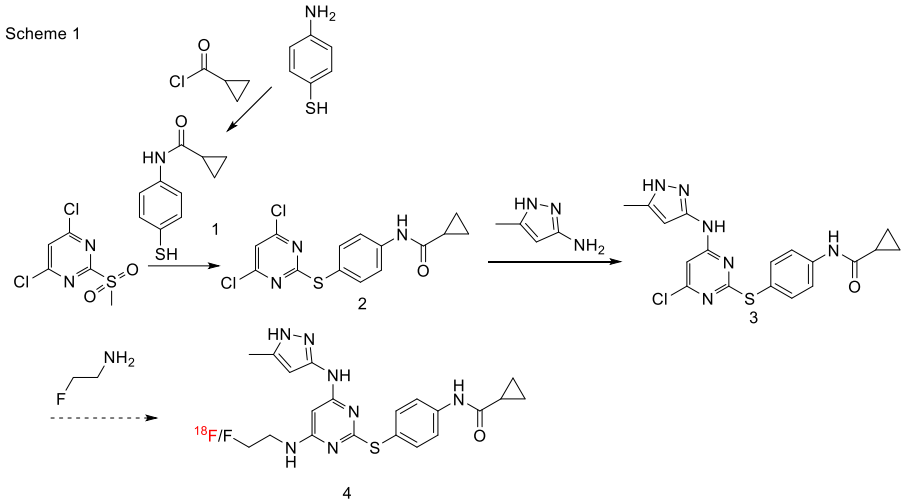

Figure 1. Synthetic Scheme for the Proposed Small Molecule Radiotracer

The above figure represents the proposed synthetic route for the synthesis of the small molecule with potential high binding affinity based on molecular docking analyses. The first three step reactions have been performed successfully.

CONCLUSION/IMPLICATION: The development of novel radiolabeled compounds that bind with high affinity and high specificity to AKs has many ramifications in the field of cancer research and in the early detection of cancer as well as in anticancer therapy monitoring in vivo.