DESIGN, SYNTHESIS AND ANALYSIS OF SMALL MOLECULE AURORA KINASE INHIBITORS AS POSSIBLE CANCER DIAGNOSTICS AND THERAPUTICS

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BACKGROUND:

Numerous studies have shown that overexpression and gene amplification of Aurora kinases (AKs) can induce tumorigenesis. AKs have been found to be interconnected with an array of human malignancies. The AK family consists of three serine / threonine kinases, known as Auroras A, B and C. These AKs play an essential role in mitosis and meiosis of human cells. Aurora kinase inhibitors (AKIs) have been shown in-vivo to inhibit the development and activity of malignancies. Thus, AKs represent a unique approach to both diagnostics and pharmacotherapeutic treatments of human malignancies. Synthesizing and evaluating novel AKIs for their possible use as cancer diagnostics and treatments could epitomize some of the restrictions of current cancer diagnostics and treatments.

METHODS:

Molecular docking analysis was first used to evaluate potential AKIs and their probable binding affinity. Next, respective AKIs will be synthesized using standard organic synthesis techniques. Crude AKIs will be extracted and further purified using standard chromatography practices. ^{1}H-NMR spectroscopy will be used to evaluate and confirm the structure of the newly synthesised AKIs. Finally, IC_{50} testing will be used to examine the binding affinity of the newly synthesized compounds to their respective AK targets.

OBJECTIVES:

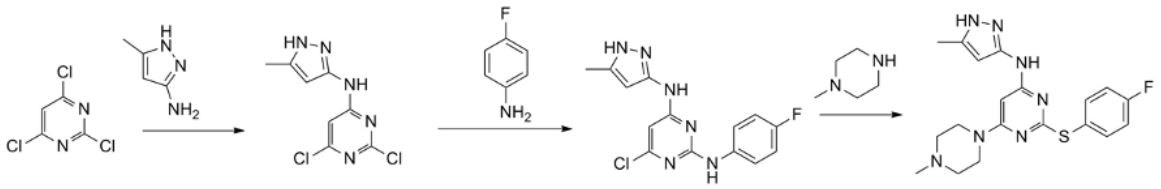

Figure 1: Proposed Synthesis of the Respective AKI

CONCLUSION:

The intent of this research is to synthesize novel AKIs that will allow for new pharmacological therapeutic agents that can be used to treat and diagnose human malignancies. Due to the overexpression of AKs in human malignancies, small molecules that selectively bind to AKs may be useful in cancer diagnostics when radiolabelled with Flourine-18 and evaluated using Position Emission Tomography. In the future, further synthesis and analysis of AKIs as well as further research regarding the molecular pathways of AKs and AKIs will allow for more possibilities regarding the anticancer and diagnostic potential of AKIs.