Developing a Selective SUV39H1 Inhibitor to Improve Cancer Prognosis

Kim, David (School: North Carolina School of Science and Mathematics)

Standard treatments for gliomas, such as surgery, chemotherapy, and radiotherapy, are often ineffective. Research has shown that the enzyme SUV39H1, which is involved in DNA methylation and has been linked to the aggressive behavior and poor prognosis of cancer cells, is a promising target for the development of small-molecule inhibitors for glioma and carcinoma treatment. Chaetocin, a small molecule derived from fungi, is a widely used inhibitor of SUV39H1, but it has several limitations, including low bioavailability, complex synthesis, low water solubility, high molecular weight, and toxicity to healthy cells. This study aims to develop novel, selective inhibitors of SUV39H1 that are easily synthesizable, water-soluble, and non-toxic to healthy cells. A homology model for SUV39H1 and validated models for other proteins were used to test the selectivity of these novel inhibitors using molecular docking in Maestro software. A computational analysis led to the development of a novel group of 65 compounds predicted to selectively inhibit SUV39H1 and exhibit improved drug-like properties and lower cytotoxicity compared to existing inhibitors. After evaluating the synthetic viability of these 65 compounds and identifying promising candidates, one of these compounds was chosen, and the first step of its synthesis was validated using NMR spectroscopy. This novel group of inhibitors for SUV39H1 may be effective in inducing apoptosis in tumors and reducing the migration of cancer cells, and their selectivity makes them useful for cellular assays in the broad field of methyltransferase inhibition.

Awards Won:
Fourth Award of $500