

Project Title: Discovery of Novel Heterocyclic Compounds with Anticancer and Antiparasitic Properties

Project Mentors: *Dr. Moses Lee, Dr. Dereje Desta, Dr. Sameer Chavda, and Dr. Balaji Babu*

Project Description:

Chalcones are simple organic compounds related to combretastin A4, a compound known to be active as an anticancer agent that is presently undergoing phase II clinical trials. Chalcones are known to inhibit the polymerization of tubulin in cells thereby causing significant toxicity against rapidly dividing cells, such as cancer cells and human pathogenic parasites, such as *Plasmodium*, *Trypanosoma*, and *Leishmania*. Even though both combretastatin A4 and chalcones are biologically active, their usefulness as potential medicines is hampered by their lack of solubility in biological aqueous media. The use of chalcones is further hindered by their susceptibility to detoxification by glutathione. Consequently, there is an international effort to develop novel analogs of combretastatin A4 and chalcones that (1) retain their potent anticancer and antiparasitic properties, (2) exhibit enhanced solubility in aqueous media, and (3) can be synthesized readily and efficiently. Accordingly, the goals of this project are as follows: (1) we will design and synthesize heterocyclic analogs of combretastatin A4 that should have improved water solubility, and (2), we will evaluate the anticancer and antiparasitic activity of the compounds.

This summer, we plan to recruit two high school students to work on this project. These students will work alongside two Hope College students, three PhD level scientists, and myself. Specifically, the students will execute multiple two-to-three step syntheses to produce a mini-library of a new class of diarylheterocyclic compounds. Upon determining the ability of these compounds to kill cancer and parasitic cells grown in culture, a structure-activity relationship on a series of diarylheterocyclic compounds will be constructed. The most active compound(s) will be further tested for their ability to inhibit tubulin polymerization in cells. With the excellent chemistry and biology facilities at Hope College, and in-house expertise, we will be able to achieve the goals as indicated above during the six-week summer research program.