In Vivo Tumor Reduction in Mice

Conor T.Ronayne
Swenson College of Science and Engineering
University of Minnesota Duluth
Ronay013@d.umn.edu

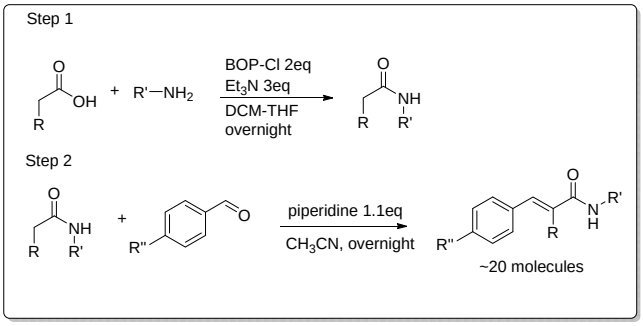
Summary

For the past year I have been doing research under the supervision of Dr. Venkatram R. Mereddy. The main focus of this research has been the synthesis and biological evaluation of anti-cancer molecules. This includes extensive organic synthesis, *In vitro* biology with numerous cancer cell lines, and finally *In vivo* biology with mice. The In vitro work includes mainly cytotoxicity assays against three main cancer cell lines; MDA-231 (triple negative breast cancer), MCF-7 (estrogen receptor positive breast cancer), and LnCAP (androgen receptor positive prostate cancer). After initial lead molecules are identified for their toxicity against each respective cell line, IC-50 values of these compounds are to be determined to get a comprehensive assessment of the toxicity of each respective series of molecules.

Respective lead molecules from each study can then qualify for *In vivo* studies. Currently, privileged molecules are being screened for general *In vivo* toxicity in mice. This initial screening is done by injecting our compounds (10% DMSO solution) into the lower abdomen. This study is done for 21 days and toxicity is noted by observing the weight of the animals every three days over the course of the study. Following toxicity evaluation, the molecules will be screened for their *In vivo* tumor reduction capabilities. Nude mice will be injected with cancer and tumors will be developed. Our molecules will then be injected *In situ*, and tumor reduction will be noted.

The mentioned studies are those currently being established. Plenty more In vivo studies are still to be done in order to result in a molecule making it to the clinic for the overall purpose of cancer patient health benefits.

Organic Synthesis



The reaction scheme above has been applied to 20+ derivatives of a molecule. Step one involves condensation of a carboxylic acid and an amine, and step two involves the coupling of and aldehyde with the newly formed amide. Purification was done largely through acidification and filtration, however, each derivative had to be treated slightly different in each case according to the functional groups present. Purity of each compound was confirmed by proton NMR spectroscopy.

Discussion

Overall, the objectives presented in this project have been achieved. The process of organic synthesis went very well in that 20+ derivatives have been prepared and purified, according to proton NMR spectroscopy. Also, in vitro biological studies of each molecule on three cancer cell lines (noted in the summary) have been completed. This gives us a good indication of which molecules can and should be tested further with animals. Also, an In vivo model has been established to test the general toxicity of the compounds in mice, which will lead to further indication of their effectiveness as a chemotherapeutic agent.