RESEARCH PROJECT FOR SUMMER 2014

TITLE: Treatment effects of novel mTOR inhibitors in PTEN wild-type cancer cells

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RESEARCH PROJECT DESCRIPTION (brief overview of background, hypothesis, methods, role of medical student, funding and relevant publications)

The mammalian target of rapamycin (mTOR) pathway is significantly indicated in human cancers. Hyperactivated mTOR signaling has been associated with disease progression and poor prognosis. mTOR activity is negatively regulated by PTEN, a phosphatase that is frequently silenced in cancer. In tumor cells, mTOR controls multiple malignant phenotypes such as proliferation and survival. The pivotal role of mTOR in cancer makes it a suitable target for therapeutic interventions. There are two classes of mTOR inhibitors that are currently under clinical evaluation. These two types of drugs have different action mechanisms hence result in varied treatment consequences. Interestingly, the traditional inhibitors (such as rapamycin) have been shown to be more effective in tumors that lack PTEN. However the impact of PTEN status on the therapeutic potential of the second class ("next-generation") mTOR inhibitors has not been studied. We therefore hypothesize that the next-generation mTOR inhibitors are able to inhibit cancer cell proliferation irrespective of cellular PTEN status. Experiments will be designed to evaluate the anti-proliferative effects of novel inhibitors that are in clinical evaluation on human cancer cells with different PTEN status, using an in vitro cytotoxicity assay. In addition, mTOR associated signaling molecules will be detected after drug treatment by Western blotting. In this project, the medical student will be involved in culturing human cancer cells, performing cell-based experiments and if time allows, conducting some molecular works such as Western blotting. This project is funded in part by the UF Metastasis Program.
