

**New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT**

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Estela Jacinto**

Project Title: **Target of Rapamycin Complexes in Growth Regulation**

Description: **We will elucidate how deregulation of nutrient signals mediated by a protein (TOR), that is the target of the potential anti-cancer drug rapamycin, can lead to cancer.**

Cell growth is defined as the increase in cell size or cell mass. A proliferating cell usually has to undergo growth before dividing to maintain an appropriate cell size and conform to a normal organ/organism size. The process of growth is controlled by highly coordinated signaling events. The presence of extracellular stimuli such as nutrients and hormones initiates a cascade of signaling events culminating in the production of proteins and other building blocks that are required by a growing cell. A signaling molecule that has been shown to be important for growth signals in several organisms, including yeast and mammals is TOR (target of rapamycin). TOR is the target of rapamycin, an antibiotic that binds TOR and blocks its functions involving protein production. First discovered as an immunosuppressant by a New Jersey drug company and currently produced and marketed by a number of New Jersey pharmaceutical companies, its potential to treat various growth-related diseases has received considerable attention only recently however. Rapamycin and its chemical analogs are currently in clinical trials to treat a broad range of human malignancies such as renal cell, breast, lung carcinomas and lymphoma. Our long-term goal is to understand the mechanisms of how TOR can sense the presence of nutrients and thereby signal to the cell to undergo growth and how these signals can be deregulated leading to diseases such as cancer. Our proposed research will examine the role of phosphatases, which are proteins that can potentially inhibit TOR and are believed to be tumor suppressors. The model organism yeast is very suitable to conduct these studies due to high similarity of yeast TOR signaling with that of mammals. Yeast cells can also be experimentally manipulated easily. We will use a series of biochemical and genetic assays to address how phosphatases can block TOR activity. Eventually, we would like to address in the future how phosphatases or other signaling molecules involved in the mammalian TOR signaling pathway can be targeted for therapy against a variety of human cancers.