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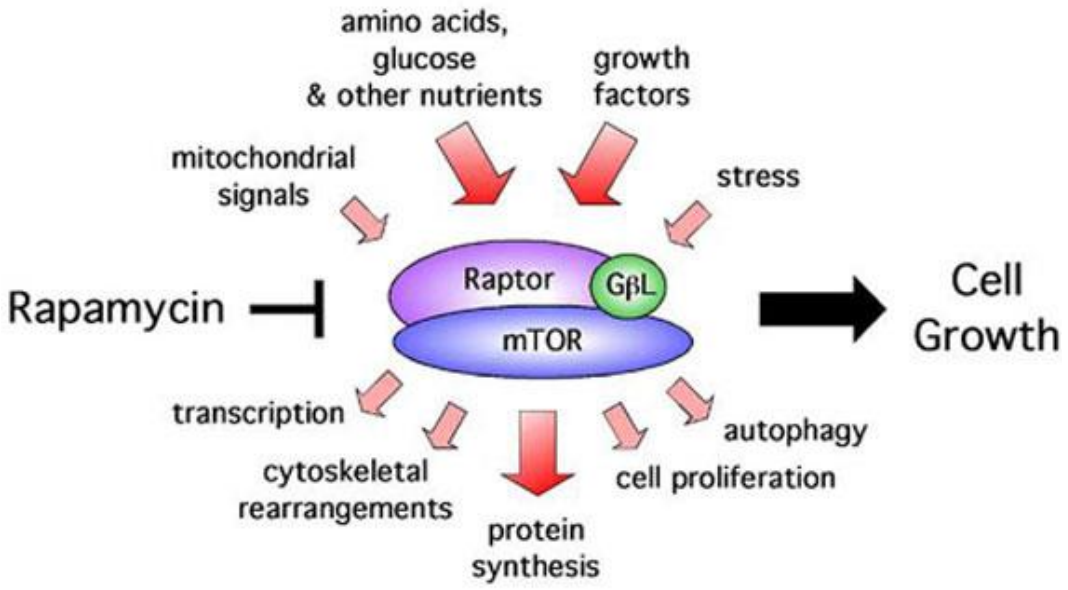
Pitt Science Blog
November 23, 2017

# There's Way More to mTOR!

Every year the University of Pittsburgh holds an event, "Pitt Science", that rivals all other scientific events in the Greater Pittsburgh Area. Generally, the organizers like to choose themes that highlight current and fundamental aspects of the science community. Previously, the themes had been focused towards differing areas of the scientific world, ranging from new and upcoming cancer treatments all the way to editing the human genome through the CRISPR/Cas system. This year the theme took on a new meaning altogether. In an era where society and the governing body of the United States does not think scientific research is important to them in any way, the organizers of "Pitt Science" simply entitled this year's conference - Science 2017. At a time when Science is under attack and the scientists who drive new discoveries and integrate what they know to help society are being oppressed, Science stands by itself. It does not require any adjectives or creative names to draw people to it because science is substantial while standing alone.

At these annual conferences, the University of Pittsburgh invites renowned scientists, whose work is impacting the scientific community and society as a whole. The scientists at the University of Pittsburgh award the Dickson Prize in Medicine to one individual, who they believed excelled in the academic area of science, but especially in Biomedical research. The 2017 awardee for the Dickson Prize in Medicine was Dr. David M. Sabatini, MD, PhD. Dr. Sabatini earned his MD/PhD degree from John Hopkins University in Baltimore, Maryland. Through his research in his graduate career, he identified an important pathway known as mTOR, or the mechanistic target for rapamycin. Identifying and ultimately characterizing this pathway has led to a hearty interest in the continuation of studying this pathway. From his studies, Sabatini and multiple other scientists have been able to tie the mTOR pathway to medical diseases and conditions and have been able to target this pathway for many treatment purposes.

To begin to understand his research presently, he mapped out his previous research and how rapamycin was linked to his studies of the mTOR pathway. Rapamycin is a common antifungal and immunosuppressive drug that has been used to arrest the cell cycle and cause various cells to shrink. Rapamycin has been examined because of its characteristics as an immunosuppressant, a cancer therapy, a preventative of restenosis of coronary vesicles, and an anti-aging formula. Rapamycin was originally identified and characterized from a soil sample that was taken from Easter Island. It was unique that Dr. Sabatini traveled to Easter Island to see the original place where they found the sample that rapamycin was created from. That shows true passion and exploration!




http://wi.mit.edu/news/archive/2003/researchers-find-new-piece-cell-growth-puzzle

As Dr. Sabatini continued to dive further into the mTOR pathway, he began to learn and see different perspectives of the pathway. Traditionally, it was believed that this specific pathway was activated by an influx of nutrients, such as amino acids or glucose, or applied stress to the cell. However, Dr. Sabatini is experimenting to see if this traditional view is truly what occurs or if there is some sort of sensor that may activate the pathway. This is vital research because mTOR is characterized as a growth pathway and there is nothing that can happen inside of a cell that this pathway does not impact.

Therefore, Dr. Sabatini developed an experiment to look at this specific pathway and he utilized mice as his model organism. He compared the liver growth in mice based solely on the activation and inhibition of mTORC1. He found through his research that the mutant mice (where mTORC1 was inhibited) had more activity when they were fed and subsequently they would exhaust their nutrients and die because they could not adapt, where mTORC1 was inhibited. He also found that the mutant offspring died once they were out of utero because they had to rely on themselves, rather than receiving their nutrients from the mother. This led to his next pathway of research to look at, which was examining the sensors that Sabatini had hypothesized were activating mTORC1.

Dr. Sabatini found that no one amino acid was sufficient enough to fully active mTORC1- rather it was a trio combination of leucine, arginine and lysine (LRK). He dove deeper into the idea that this trio of amino acids activates mTORC1 and found that there was a partial competition between leucine and arginine. He found that the C-terminal of leucine binds to the mTORC1 protein. He further found that there appears to be two gatekeeper amino acids, which allow for leucine to be the only amino acid that can bind to mTORC1. In addition to mTORC1, Dr. Sabatini's lab is examining multiple other proteins that work throughout the mTOR pathway.