

## One, Two, Three, "mTOR"

-Will King

Annually, the University of Pittsburgh awards a leading biomedical researcher the Dickson Prize in Medicine. This year, this prestigious award was given to Dr. David M. Sabatini or, as his twitter bio (@DMSabatini) ever so affectionately refers to him, as the mTORman. His discovery of mTOR, also known as the mechanistic target for rapamycin, and further studies of the characterization of the pathway has earned him this prestigious award. This pathway has played an essential roles in understanding many molecular mechanisms in the human body, as well as found itself in the students notes who stumble into any Biochemistry class around the world.



Dr. Sabatini started his talk by taking us an adventure to the Easter Island. While at first images of Stone Heads and maybe for the less educated images of baskets, pastels, and freshly painted eggs appear he drew us to a different sight. He brought us into the dirt and the soil discussed the discovery of an essential antibiotic, rapamycin. Discovered in 1972, this antibiotic has been studied for it several properties including its immunosuppressant effects. This antibiotic was isolated from a personal favorite genus of bacteria, *Streptomyces hydroscopicus* on the island of Rapa Nui (The namesake for Rapamycin) (1). This discovery and further studies of rapamycin is what sparked Dr. Sabatini's work.

One of the main questions he addressed in his talk was identifying signaling molecules in the mTOR pathway, and what they responded to. The mTOR pathway responds to several different signals, but all the players in the pathway have yet to be identified. He established the importance of this pathway by previous studies in which he established the role of the pathway in terms of nutrition recognition. He now began to examine what signaling molecules were present, and what they were activated by.

He began to identify two signals that are associated with the lysosome, one of the signals from inside of the cytosol, while the other is from inside the lysosome. He then began to examine what specific amino acids affect signaling. He discovered that there is not a single amino acid that activates signaling of the mTOR pathway, but rather three. A combination of Leucine(L), Arginine(R), and Lysine (K) are needed to activate the pathway. He then he began to examine how these amino acids actually effected the pathway. He first identified how these amino acids and their effects play into the mTor pathway. He found two arginine receptors that help regulate the mTor pathway. One of these receptors in the presence of arginine inhibits a protein known as CASTOR, an inhibitor of GATOR1, which allows the pathway to be activated. Previously, which amino acids activated this pathway was slightly unclear

Overall, Dr. Sabatani gave a highly engaging talk and truly showed the beauty of science. While it seems like many pathways are fully characterized and just common knowledge, he showed us the complexity it takes to identify the players in pathways and the role that they play in the story. He also showed us that there are always more questions to be asked, interesting things to learn, and new things to be discovered. He was an excellent speaker who was equally informative and entertaining, so shout out to Dr. Sabatani for all his work and progress Also, feel free to check him out on twitter for some quality mTOR humor.



#### References:

Seto, B. (2012). Rapamycin and mTOR: a serendipitous discovery and implications for breast cancer. *Clinical and Translational Medicine*, 1, 29. <http://doi.org/10.1186/2001-1326-1-29>