

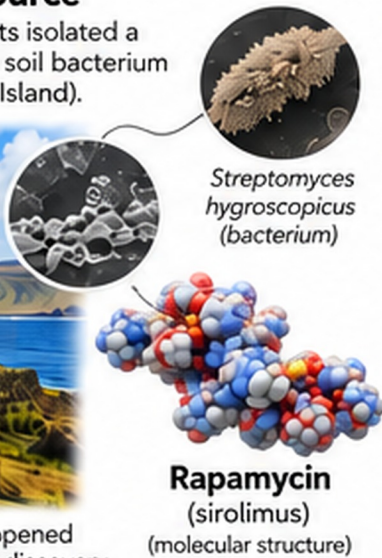
# 1 CHAPTER 1 THE DISCOVERY How a molecule from the soil revealed a hidden cellular system

## 1 A surprising source

In the 1970s, scientists isolated a new molecule from a soil bacterium on Rapa Nui (Easter Island).

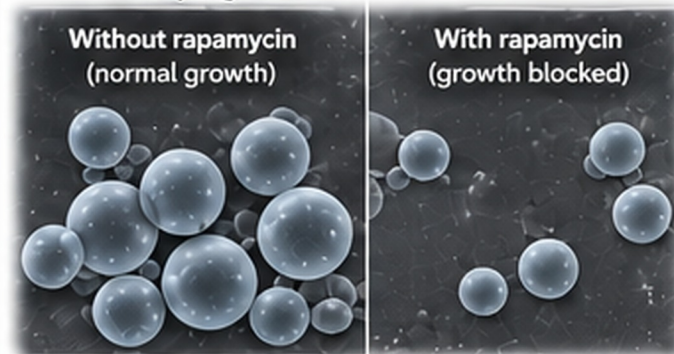


A natural product from soil opened the door to a major scientific discovery.



## 2 A powerful biological effect

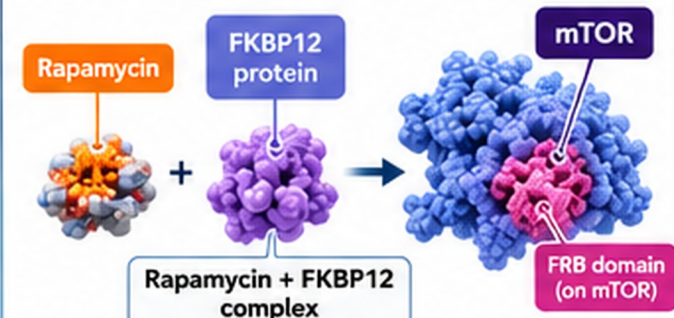
Rapamycin was first studied for its anti-fungal properties. Later, scientists noticed it could also stop cell growth in many organisms.



Rapamycin worked by targeting a key cellular system, but at that time no one knew what it was.

## 3 Finding the target

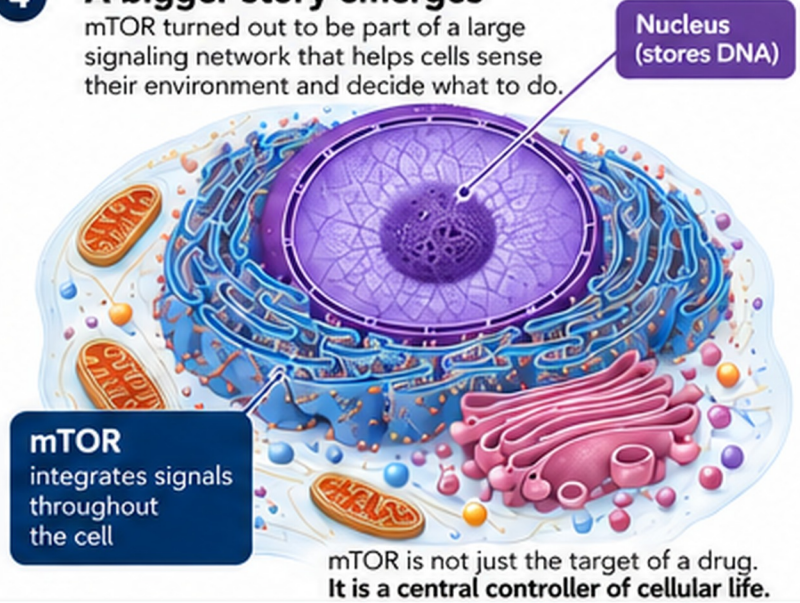
In the 1990s, genetic studies in yeast helped identify the genes TOR1 and TOR2 (target of rapamycin). Soon after, scientists found the mammalian version: **mTOR** (mechanistic target of rapamycin).



Rapamycin first binds to FKBP12, and this complex then binds to the **FRB domain** on mTOR, inhibiting its activity.

## 4 A bigger story emerges

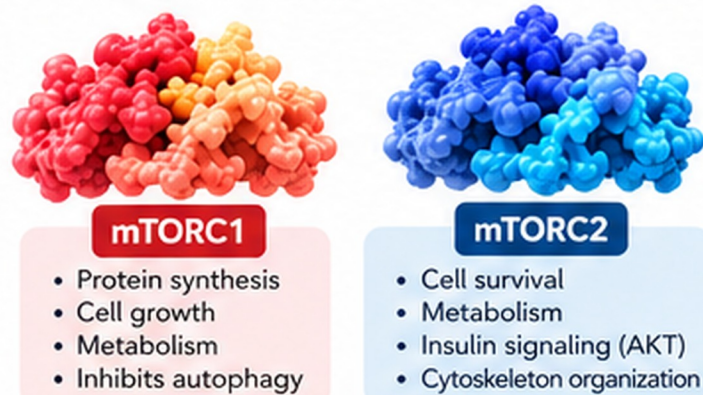
mTOR turned out to be part of a large signaling network that helps cells sense their environment and decide what to do.



# 2 CHAPTER 2 THE MECHANISM How cells decide whether to grow, conserve resources, or recycle

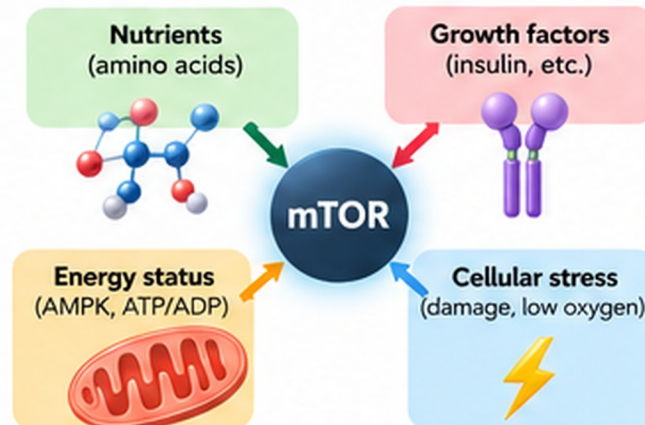
## 5 Two complexes, different functions

mTOR works in two main protein complexes with different partners and functions: **mTORC1** and **mTORC2**.



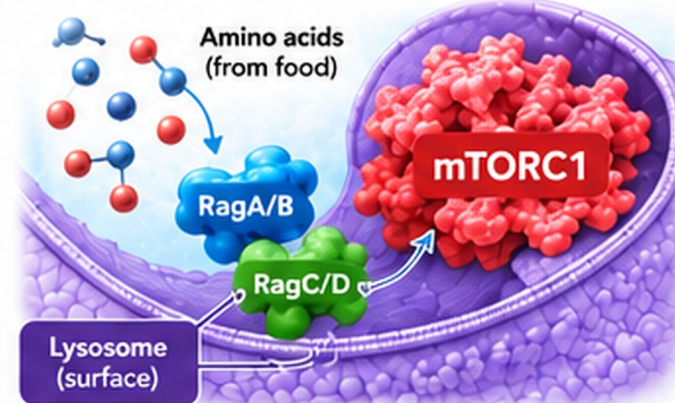
## 6 Multiple signals, one decision

mTOR integrates information about nutrients, energy, growth factors and stress.



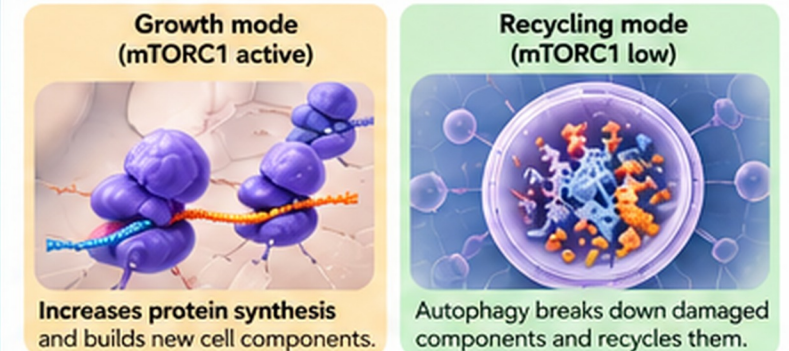
## 7 How amino acids activate mTORC1

Amino acids are sensed inside the cell, often at the lysosome, and signal through Rag GTPases to activate mTORC1.



## 8 Growth or recycling?

When conditions are good, mTORC1 increases protein synthesis and cell growth. When nutrients are scarce or there is stress, mTORC1 activity decreases and autophagy is turned on.



# 3 CHAPTER 3 THE FUTURE Why mTOR matters for health, disease and a longer, healthier life

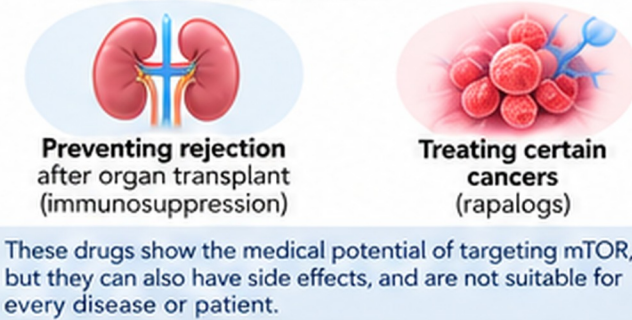
## 9 When things go wrong

Altered mTOR signaling can contribute to diseases such as cancer, metabolic disorders, neurological diseases and immune dysfunction.



## 10 From discovery to medicine

Rapamycin and related drugs (rapalogs) are already used in medicine, for example:



## 11 mTOR and aging

In many model organisms, changes in mTOR signaling can extend lifespan and improve health indicators. In humans, the picture is more complex.



## 12 An exciting future

mTOR is a key piece of the puzzle, but many important questions remain.

