Induction of Autophagy upon Starvation

Janine Pelzer, Hui Shi, Tamerra Jones, and Amber Akbar

Abstract

When faced with starvation, autophagy is a powerful mechanism which enables an organism to live longer by degrading proteins or damaged organelles so that essential components can be reused. There are many signals by which autophagy can be induced. One of the prevalent signaling pathways is the mTOR pathway. mTor is a serine/threonine kinase that has a central role in cell growth. By inhibiting the role of mTOR, autophagy can be induced through forming phagophore.

Introduction

What is the signaling pathway that induces autophagy when the body is faced with starvation?

Autophagy is a bulk degradation process for clearance of proteins and organelles and has profound clinical implications to combat diseases. For example, autophagy is used in treating neurodegenerative diseases because it can destroy the misfolded and aberrant proteins that disrupt neuronal functions. (citation) Excessively triggering autophagy can increase the progression of metastasis of cancer while impairing autophagy causes lysosomal storage disorder and muscle disease. (citation)

A signaling pathway is a series of messages transported in the cell from the extracellular domain to the nucleus of the cell to change the gene expression. One specific receptor protein is known as RTK, which is a kinase protein that adds a phosphate to itself. The addition of a phosphate causes a conformational change to the receptor. After binding the signaling molecule, RTK dimerizes and autophosphorylates, causing a signaling cascade that transfers the signal from the cytosol to the nucleus, triggering the gene expression.

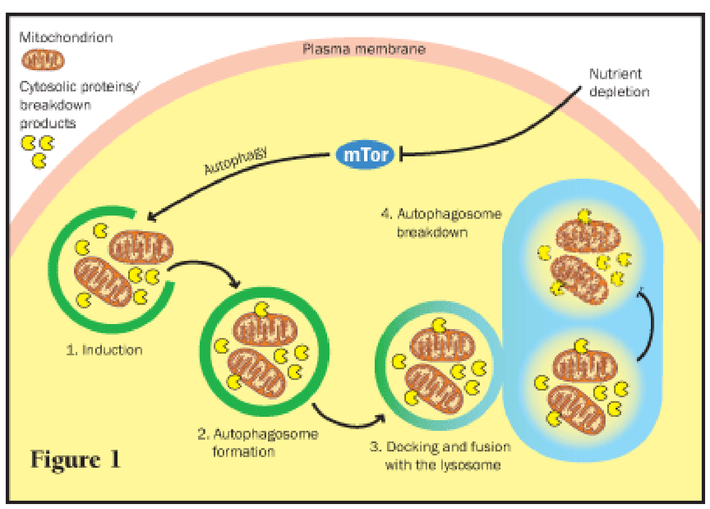
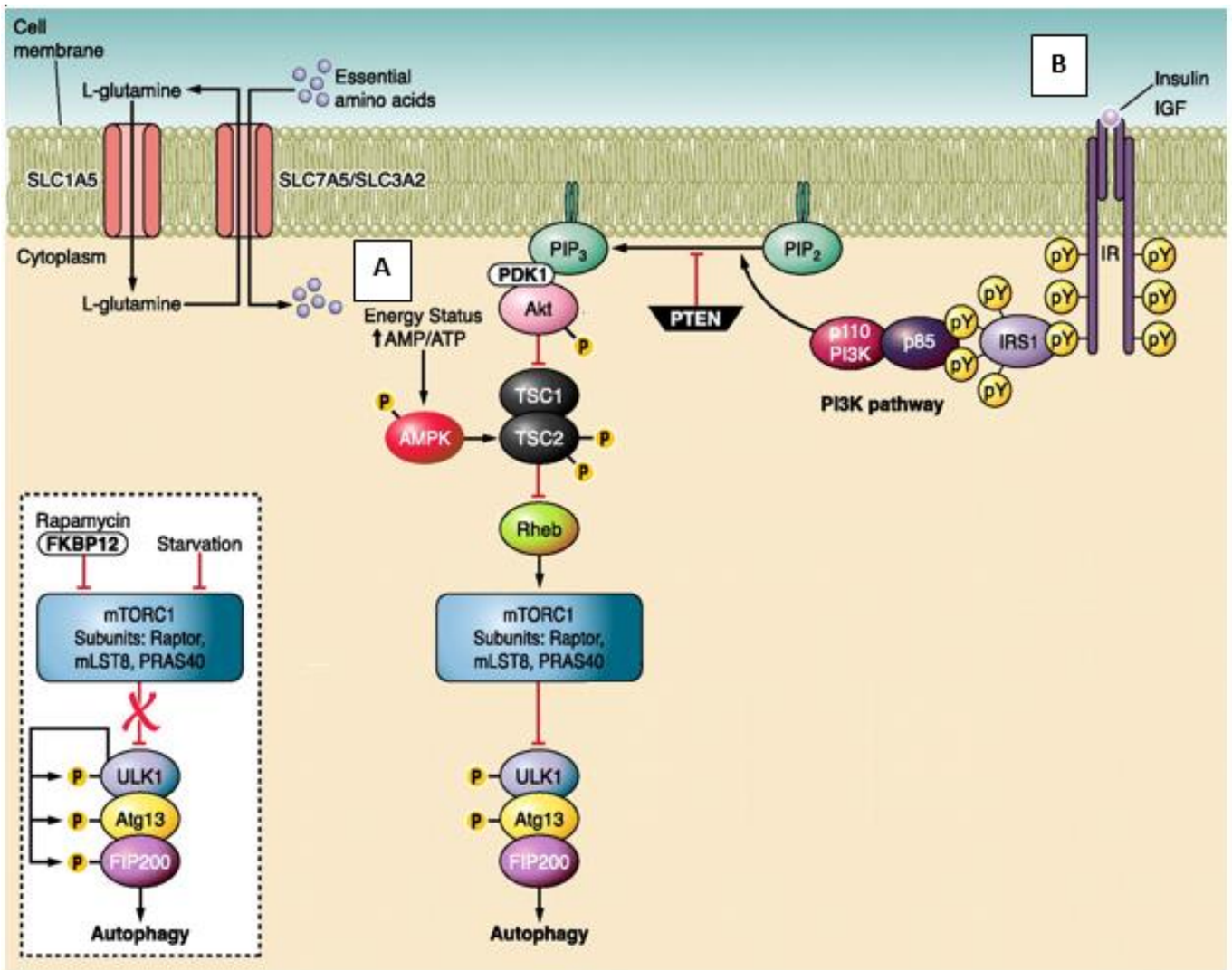


Figure 1. Overview of autophagy

References

[1]
[2]
[3] …

Approach



A During starvation, organisms face nutrient deprivation which leads to low levels of energy resulting in a high AMP to ATP ratio. This ratio initiates a phosphorylation cascade starting with AMPK, a cellular energy sensor, This leads to initiation of the formation of a phagophore.

B Another pathway is PI3K-Akt-mTORC1. Under normal conditions, growth factors stimulate RTK which leads to autophosphorylation thus activating class I PI3K-PKB kinase. This in turn leads to phosphorylation of Akt thus activating the enzyme. When starvation occurs, PTEN, a phosphatase is activated and disrupts class I PI3K from activating Akt. Upon inactivation of Akt, mTORC1 is inhibited; therefore, gene expression of autophagy genes increase which leads to the formation of a phagophore.

Future Outlook

A. Has answering this question led you to ask another question or questions?

B. Has the answer to this question explained a similar phenomena seen in another biological system?