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Mini Review

Mitophagy and its Importance

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Abstract

Mitophagy is referred as a process in which removal of dysfunctional mitochondria takes place by autophagy. Mitochondria contains some proteins which helps in achieving this process that are PINK1, PARKIN, NIPSNAP 1, NIPSNAP 2. However, NIPSNAP 1 and NIPSNAP were discovered after initially it was assumed that only PINK1 and PARKIN proteins are only responsible for mitophagy but now it is cleared after series of experiments. Mitophagy is a crucial event in terms of health of a living cell because it ensures proper cellular functions. Here we will focus on pathway which a mitochondrion goes under to achieve mitophagy and we will also see how mitophagy is important for an organism.

Keywords: Mitophagy; Mitochondria; Organism

Introduction of Mitophagy

Mitophagy is a kind of autophagy i.e. A catabolic process which degrades the cellular proteins and damaged or excessive organelles through a formation of double membrane structure called auto phagosome which further fuses with lysosomes and forms autolysosomes. Autophagy was first discovered in yeast as a form of cellular self-digestion so that it can provide nutrients to the cells in order to avoid starvation.

There are three types of autophagyon the basis of the genes and the enzymes they are associated with macroautophagy, microautophagy and chaperone mediated autophagy. So, mitophagy is actually macroautophagy where a double membraned structure or you can say vesicles called autophagosomes envelope around the entity (which has to be degenerated) and it further fuses with the lysosomes resulting into the digestion of that entity.

Macroautophagy is divided further into two types Bulk(Non-selective) and Selective autophagy.

Non-selective autophagy comes into action only in response to starvation or nutrient deprivation to provide cells with essential amino acids and nutrients whereas selective type of autophagy comes into play during the removal of a specific worn out or dysfunctional organelle or removal of protein aggregate even under nutrient rich conditions. So, we can see that mitophagy is a selective autophagy.

In mitophagy double membraned autophagosomes enclose whole mitochondria, or selectively target the damaged areas.

Using the budding yeast saccharomyces cerevisiae as a model identified and characterized many proteins involved in this process which are termed as Atg (autophagy related) proteins. Selective mitophagy requires a specific receptor protein here Atg32 behaves as a mitophagy receptor [1].

In mammalian cells there are different pathways which induces mitophagy in them but PINK1 and Parkin pathway is most accepted pathway among them. This pathway includes two proteins PINK1 and PARKIN both proteins functions together to accomplish mitophagy.

Initially the pathway deciphers the difference between healthy and damaged mitochondria. PINK1(PTEN-induced kinase 1) protein is used in this pathway to do so basically it detects the quality of mitochondria. It is a mitochondrial serine or athreonine containing protein kinase induced by the PINK1 gene. It is present inside the cytoplasm of the mitochondria and it serves as a scout to probe for a dysfunctional mitochondrion.

It allows the parkin protein to bind with the dysfunctional mitochondria after the identification of one by PINK1 protein so that its autophagy can be done. This identification is easily carried out because the damaged mitochondria lacks a sufficient potential required for transportation of the PINK1 into the inner membrane where it is taken care by another protein PARL which cleaves PINK1 protein and stops the build-up of PINK1 protein on the outer membrane of mitochondria but due to insufficient potential the PINK1 protein accumulates on the outer membrane of mitochondria due to which then PINK1 protein recruits parkin protein for its digestion [4].

Parkin is an ubiquitin protein ligase which then initiates mitophagy by recognizing PINK 1 protein which was previously thought but now after some research scientist have found out that it also recognizes the presence of two more proteins that are NIPSNAP 1, NIPSNAP 2.

Previously it was believed that only these two proteins are responsible for degradation of mitochondria bur recent researches have shown that more two proteins are responsible for this process i.e. NIPSNAP 1 and NIPSNAP 2 they are present in healthy mitochondria. When the normal functioning of the mitochondria is hindered due to any reason so these proteins are not imported into the matrix and functioning of import system dysfunctions and they start getting accumulated on the surface of the mitochondria functioning as "eat me signals" for the digestion of dysfunction mitochondria. Researchers studied human HeLa cells where the functions of the NIPSNAP 1 and NIPSNAP 2 were discarded and it was seen that the parkin protein was unable to digest the dysfunctional mitochondria this experiment shows that both these proteins are also important for mitophagy. So at last we can see that PINK1, NIPSNAP1, NIPSNAP2, PARKIN proteins are required for autophagy of a dysfunctional mitochondria [3].

Importance of mitophagy

Mitochondria is an essential cell organelle as it serves as an energy source for an organism except bacteria because they are devoid of mitochondria.

The prime function of mitochondria is to convert the air we breathe and the food we eat into the energy. The energy which is produced is then used up by our body which helpsour cells to grow, divide and function.

They are often called as the "Powerhouse of the Cell" but rather than producing energy they are also responsible for various functions like cell signalling, regulating vital calcium levels, producing heat and killing off cells that have become unviable. Mitophagy prevents the accumulation of dysfunctional mitochondria which can lead to cellular degeneration.

Due to defective functioning of mitochondria causes a loss of efficiency in the electron transport chain and reduction in the synthesis of high energy molecules such as ATP. Due to decrease in energy levels of the bodyrate of aging increases and it also causes many chronic diseases like Alzheimer disease, Parkinson's disease, Huntington's disease, cardiovascular diseases, diabetes etc.

Due its high significance quality control of mitochondria is essential to maintain homeostasis and the regulation of mitochondria is achieved by mitophagy which shows that how important is mitophagy for an organism. This process is regulated by PINK1 and Parkin pathways which shows how really important this pathway is for our mammalian cells but its deformity can lead to a problem or we can say a disease although we are aware of a such disease called Parkinson's disease which occurs due to the loss of the function of PINK1 and Parkin in our mammalian cells. Parkinson's disease is a neurodegenerative disorder in which accumulation of damaged mitochondria and aggregation of proteins occurs due to the loss of the function in either of these genes [5].

We can see that how decisive is mitophagy in terms of our stromal(body) cells but mitophagy is also known to be crucial for cancer cells. The question which arises in our mind is that mitophagy promotes or inhibits the cancer growth is a tricky one to answer because its function highly depends upon the type of the cancer and the protein which is involved.

For example, BNIP3 (a protein involved in the pathway) suppresses the tumour cells in breast cancer however it promotes the tumour cells in melanoma.

Cancer cells need to plastically rewire their metabolism so that they can fulfil their basic needs which are ATP (to maintain energy status), metabolic precursor supply (to meet the high rate of macromolecule biosynthesis), maintenance of an appropriate cellular redox status. So, cancer cells use variety of fuel sources to cope up with metabolic and nutrient stresses. Growing evidences show that mitophagy supports the metabolic plasticity of cancerous cells by providing them the required materials by the degradation of carbohydrates, proteins, lipids, and nucleotides [2].

This concludes how important is mitophagy for our stromal cells as it maintains the homeostasis functioning on a pathway by the help of proteins and how can it affect our stability on cellular level because of its dysfunctionality and the way how it regulates cancerous cells shows the potential of further research in cancer.

Conclusion

This article covered the topic of mitophagy that how it is carried out in our body and which mechanisms are involved in it. The various proteins (PINK1, PINK2, NINSNAP1 and NINSNAP2) which

carries out the mitophagy in our body are also mentioned in the article. It also shows that how really important the process mitophagy is for our body which helps in maintaining the homeostasis and how its dysfunction can affect our body and cause many diseases.

Bibliography

1. Kanki T., *et al.* "Atg32 is a mitochondrial protein that confers selectivity during mitophagy". *Developmental Cell* 17.1 (2009): 98-109.

2. Monica Vara-Perez., *et al*. "Mitophagy in Cancer: A Tale of Adaptation". *Cell* 8.5 (2019): 493.

3. https://www.sciencedaily.com/releases/2019/04/190411145152 .htm

4. https://www.ncbi.nlm.nih.gov/ubmed/?term=Catherine%20E.%20Rodger%2C%20Thomas%20G.%20McWilliams%2C%20and%20Ian%20G.%20Ganley

5. Um JH and Yun J. "Emerging role of mitophagy in human diseases and physiology". *BMB Report* 50.6 (2017): 299-307.