SHORT COMMUNICATION

Mitochondrial dysfunction is the central node in the pathogenesis of renal injury in obstructive jaundice

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INTRODUCTION

In our latest paper, we have reviewed the underlying mechanisms, inducible agents and therapeutic strategies of kidney injury in obstructive jaundice (OJKI) [1]. Abnormal bile metabolism is the key inducement of OJKI. The kidney, as the most energy-demanding organ, requires sufficient energy to eliminate the bile and other waste in blood. About 7% of ATP energy consumption of human body is used by kidney [2]. It is closely related to the abundance of mitochondria in the renal tissue. It is doomed that mitochondria, as an important eukaryotic organelle, are of great significance to maintain the homeostasis of intracellular environment and the life activities of the organism in OJKI.

Mitochondria are organelles that hold genetic information and are primarily responsible for supplying energy and maintaining cell homeostasis [3]. It performs a wide range of tasks, including producing adenosine triphosphate, regulating calcium signaling, regulating membrane potential and controlling programmed cell death, regulating cell metabolism and proliferation, participating in cell signal transmission, and synthesizing cholesterol, which is critical for cell survival [4]. To maintain intracellular homeostasis, mitochondria must manufacture new mitochondria in a timely manner, maintain the morphology of mitochondria, and eliminate damaged mitochondria. Under pathological conditions such as stress and hypoxia, however, the disorder of mitochondrial quality control causes structural damage and dysfunction of mitochondria, such as swelling and ridge disappearance of mitochondria, decrease of membrane potential, opening of mitochondrial permeability transformation pores, ATP synthesis obstacle, excessive production of reactive oxygen free radicals, increased release of pro-apoptotic factors, and so on, which will eventually result in mitochondrial death or even cell death [5].

Mitochondria are extremely active organelles that maintain a constant balance of fusion and division. This dynamic equilibrium is referred to as mitochondrial dynamics. Mitochondrial homeostasis consists of the coordination of mitochondrial biogenesis, mitochondrial dynamics (including fission and fusion) and mitochondrial autophagy (Figure 1). The production of Reactive Oxygen Species (ROS) can be regarded as the starting factor of mitochondrial homeostasis. When ROS is produced in excess (in a state of oxidative stress), aberrant autophagy, fusion and division of mitochondria occur, resulting in mitochondrial dysfunction. Excessive ROS inhibited ATP synthesis and caused the opening of the Membrane Permeability Transition Pore (MPTP) in mitochondria, resulting in the release of cytochrome C, a shift in membrane potential, and cell death and necrosis [6].

DESCRIPTION

Studies have revealed the relationship between mitochondrial dysfunction and renal injury [7]. Showed that mitochondrial fragments in proximal tubule cells of kidney increase when kidney injury occurs [8]. In acute kidney injury, swelling and breakage of mitochondria in histopathology canbe observed [9]. Similar phenomena can also be seen in other diseases with nephropathy as a complication. In Diabetic nephropathy, which is the most common cause of End-Stage Renal Disease (ESRD) in the United States, the observed variations in mitochondrial energetics are correlated with structural changes in mitochondria [10]. As a result, persistent mitochondrial dysfunction contributes to the progression of renal disorders by undermining mitochondrial homeostasis, hence impairing normal renal function.

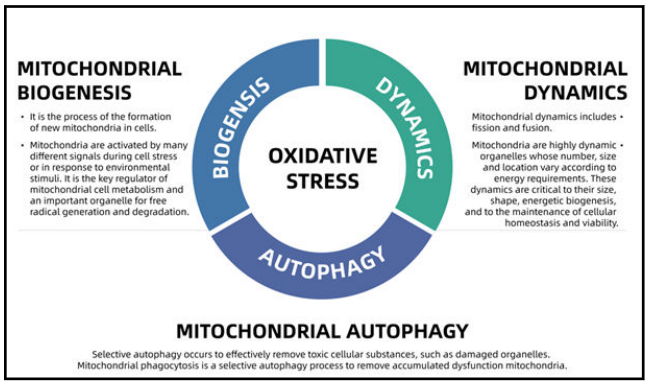

Figure 1: Diagram of steady-state relationship of mitochondria

Obviously, this is not a pathogenic phenomenon limited to a single organ or tissue. As early as studied the mitochondrial damage of kidney in rats with obstructive jaundice [11]. They found that lysosome lesion may be a possible factor of mitochondrial damage in OJKI rats. Subsequently, investigated the ultra-structural changes of isolated rat kidney induced by bilirubin and bile acid, and discovered the swelling of mitochondria and the protrusion of mitochondrial cristae [12]. In an electron microscopy study, mitochondria in kidney tissue of rats (also can be called OJKI rats) with bile duct ligation swell and rupture, even if bile returns to normal excretion, it is irreversible [13]. These studies highlight the necessity of clarifying mitochondrial dysfunction and OJKI in further research, making it a potential treatment strategy.

CONCLUSION

In conclusion, we believe that starting with mitochondria dysfunction could be a promising potential breakthrough for resolving OJKI. Because this is what our team observed in previous experiments (Although it has not been published yet). Based on this project, we also received support and funding from the National Natural Science Foundation of China. We also look forward to more researchers joining us on this clinical issue that deserves more attention. Finally, thank you to the editors for inviting us to provide a global platform to share our ideas and results with researchers from all over the world.

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