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Commentary

D-ribose-L-cysteine Activated Autophagic Related Protein Pathway: A Possible Therapeutic Mechanism for Attenuating Testicular Maladaptive Responses

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ABSTRACT

Testicular maladaptive responses caused by toxicant induced Autophagic Related Protein-7(Atg7) and Mammalian Target of Rapamycin (mTOR) pathway deactivation is becoming a common fertility emergency that requires prompt therapeutic intervention in other to avoid potentially serious sequelae including loss of germ cell, deranged acrosome biogenesis to decreased male fertility, increased embryonic loss, and higher calf mortality. We therefore hypothesized that activation of a mTOR and Atg-7 may be a potential mechanism by which DRLC protects testicular cells and tissues from oxidative stress damage.

Key words: mTOR; Atg-7; Apoptosis; Reproductive cells and Oxidative stress

ABOUT THE STUDY

A testicular maladaptive response is a common adverse deleterious effect of numerous toxicants and chemotherapeutic medications, affecting both the human endocrine and exocrine processes of the testis [1-4]. Numerous researches have revealed links between toxicant exposure and testicular maladaptive responses, including decreased fertility, increased embryonic loss, and higher calf mortality [5-6]. Most currently, the effects of toxicant exposure on male fertility have been thoroughly studied in both human and experimental animal studies [4,7-11]. Hence, It is therefore of considerable interest to recognize that, the potential of D-Ribose-L-repropharmacological cysteine's actions for the treatment of reprotoxicant-related repropathologies is gaining attention [4,12-16]. D-ribose l-cysteine is a ribose and cysteine derivative that was created as a pro-drug to increase GSH synthesis [16]. It has been patented specifically for increasing glutathione levels and as a dietary supplement to protect against diseases associated with toxicant invokes oxidative stress [17]. D-ribose l-cysteine efficiently travels through the digestive track and gives the fragile cysteine molecule to the cell, allowing glutathione to be produced efficiently and naturally. GSH is known to form oxidized glutathione (GSSG) and other disulfides, thus helping to scavenged Reactive Oxygen Species (ROS) mediated cellular oxido-inflammatory flux and apoptosis via activation of autophagic related protein [4].

Activation of autophagy is another key Atg-7 and mTORC1-regulated process that probably has a central role in promoting cell longevity. Autophagy is a major degradation pathway in eukaryotic cells that is essential for removing damaged organelles and macromolecules from the cytoplasm and recycling amino acid. Autophagic related protein like mTOR and Atg-7 act as a defense and oxido-nitrergic stress management mechanism which involves the sequestration, transport, bulk degradation and recycling of cytoplasmic components as indicated in a recent animal investigation carried out by Oyovwi et al.[4]. More so, increasing scientific based evidence indicates that Autophagic related proteins are activated in oxidative stress environment [18]. Recently, a lot of studies have been done on the relationship between Autophagic related protein, oxido-

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inflammation and apoptosis, and it is demonstrated that autophagic related protein can act as a globozoospermic related protein required for acrosome biogenesis during spermatogenesis as well as sperm cell survival mechanism to protect cells from apoptosis through modulation of p53-dependent apoptosis in germ cells [4]. Under oxido-nitrergic stress condition, autophagic related proteins can acts primarily as a pro-survival pathway to protect sperm cells and testicular tissues from oxidative damage, inflammation and apoptosis [4]. Therefore, autophagic related protein may play an important role in the repropharmacological effect of D-ribose-L cysteine against testicular maladaptive responses.

Autophagic related protein-7 (Atg-7) and mammalian target of rapamycin (mTOR) signaling pathway is a vital regulator of autophagy, apoptosis and its activation is responsible for spermatogenesis and metabolic function. It is well known that D-ribose-L cysteine activated mTOR and Atg-7 pathway alleviates reproductive disruption induced by toxicant mediated oxido-nitrergic stress, inflammation and apoptosis [4]. All these evidences indicate that it is necessary to pay attention to autophagic related protein such as mTOR and Atg-7 pathologies related infertility.

CONCLUSION

We therefore hypothesized that activation of a mTOR and Atg-7 mediated inhibition of apoptosis and inflammation may be a potential mechanism by which DRLC protects testicular cells and tissues from oxidative stress damage. Herein, by examining how DRLC activated autophagic related protein pathway in reproductive cells, and by determining the role of mTOR and Atg-7 in DRLC-mediated antioxidant responses, our previous study indicates that treatment with DRLC triggers autophagic survival response of reproductive cells and tissues against testicular maladaptive responses caused by toxicant.

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