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The Role of BAG5 In Post-Fertilization Sperm Mitophagy

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Mitochondria and mitochondrial genes are exclusively inherited from mother in mammals. It is not fully understood why this occurs, or what happens to the father's mitochondria during fertilization. It is known that the mitochondria from spermatozoa are degraded after oocyte fertilization, but many of the contributors to that degradation process remain unclear. BAG5 is a pro-autophagic protein which regulates the PINK1-Parkin mitophagy pathway. This pathway is known to control mitophagy in many cell types; however, it has yet to be implicated in mitochondrial inheritance. In order to assess this protein's role in post-fertilization sperm mitophagy, we used our established porcine mitophagy model from which spermatozoa and oocytes are easily obtained. To analyze the BAG5 protein, we used immunocytochemistry, quantitative proteomics, SDS-PAGE Western blotting, and a mammalian cell-free system (primed boar spermatozoa coincubated with sow oocyte extracts) which our laboratory has established. In ejaculated spermatozoa, BAG5 localizes on the acrosome of the sperm head. Sperm priming for cell-free system coincubation, which mimics sperm demembranation during early stages of fertilization, appears to unmask the BAG5 protein, now also found throughout the sperm tail, including the mitochondrial sheath. However, after exposure to the cell-free system BAG5 is no longer detected in spermatozoa. This is interpreted as oocyte-extract mitophagy elements degrading BAG5 in the sperm mitochondria and other tail accessory structures. We hypothesize that this disappearance of BAG5 allows the PINK1-Parkin mitophagic pathway to degrade the sperm mitochondria shortly after fertilization. This study can be used as a starting point for future studies on post-fertilization sperm mitophagy. Through studying BAG5, we begin to better understand the proteomic changes that happen during post-fertilization sperm mitophagy. Understanding post-fertilization sperm mitophagy and mitochondrial inheritance can shape the way reproduction is approached in animal agriculture and human assisted reproductive therapy.