

## **The role of LONP1 in mammalian mitochondrial physiology**

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Lon is a serine protease located in metazoan mitochondrial matrix. It is nuclearly encoded and highly conserved from eubacteria, archaea, fungi to mitochondria. Lon is a member of the AAA+ protein family (ATPases associated with diverse cellular activities) These enzymes are able to degrade proteins upon cyclic ATP hydrolysis. Previous research on Lon has primarily been carried out in yeasts and bacteria. In mitochondrial matrix, Lon is essential for degrading unfolded or damaged proteins. In addition, Lon is also involved in several mitochondrial processes via degrading folded proteins. An important Lon target is the mitochondrial transcription factor A (TFAM), which is a major mtDNA binding protein. Loss of mammalian LONP1 resulted in embryonic lethality around E7.5 indicating the importance of LONP1 in early mammalian development. The aim of the project is to further understand the possible functions of LONP1. Since it is essential for development, we will establish conditional tissue-specific models in C57BL/6N mice for describing the role of LONP1 in mitochondrial physiology and its association with mtDNA maintenance via its regulation of TFAM. In mammalian cell models, we will search for new LONP1 targets by trapping catalytically inactive protein. We will investigate how LONP1 influences the cellular and tissue homeostasis during stress on mitochondrial and cytosolic levels.