**Lysine Acetylation: A switch for OPA1-mediated membrane remodeling**

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## Abstract

Mitochondrial dynamics are regulated by coordinated fission and fusion events that rely on key proteins and lipids organized spatially within the mitochondria. The dynamin-related GTPase Optic Atrophy 1 (OPA1) is essential for inner mitochondrial membrane fusion and cristae structure maintenance. While post-translational modifications, particularly lysine acetylation, are emerging as critical regulators of mitochondrial protein function, their impact on OPA1 remains poorly characterized. In this study, I explored the effects of lysine acetylation on the short form of OPA1 (s-OPA1) using acetylation and deacetylation mimetic mutations. Through a combination of in silico analyses and functional assays, I identified lysine residues in s-OPA1 that are conserved across species and significantly influence protein stability, GTPase activity, and oligomeric assembly upon acetylation or deacetylation. Using cryo-electron microscopy and helical reconstruction, I solved the structure of s-OPA1 K328Q, elucidating the conformational changes in the G-domain upon acetylation mimetic mutation. Furthermore, I performed cryo-electron tomography which provided mechanistic insights into OPA1-mediated mitochondrial membrane remodeling and fusion.