

Architecture of the yeast Elongator complex

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The highly conserved eukaryotic Elongator complex performs specific chemical modifications on wobble base uridines of tRNAs, which are essential for proteome stability and homeostasis. The complex is formed by six individual subunits (Elp1-6) that are all equally important for its tRNA modification activity. However, its overall architecture and the detailed reaction mechanism remain elusive. Here we show the structures of the yeast Elp123 sub-complex and fully assembled Elongator solved by negative stain electron microscopy, showing that two copies of the Elp1, Elp2 and Elp3 subunits form a symmetric two-lobed scaffold, which binds Elp456 asymmetrically. Furthermore, we use crosslinking mass spectrometry to identify the global interaction network of Elongator and employ an integrative modeling approach to localize all individual subunits and generate a topological model of the full complex. We validate our model, which is consistent with previous studies on the individual subunits, by complementary biochemical analyses. Our study provides a structural framework on how the tRNA modification activity is carried out by Elongator.