St. Joan Antida High School SMART Team

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Mitochondrial Fis1's N-Terminal "Arm" Orientations

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Abstract:
Mitochondria provide over 90% of the energy needed to maintain healthy cell function. Mitochondrial fission is essential to mitochondrial health. Mutations in mitochondrial proteins are implicated in diseases such as heart disease and diabetes. Current research is exploring the role of Mitochondrial fission protein 1 (Fis1) and key interactions with Dynamin related protein 1 (Drp1), and Mitochondrial dynamics protein of 51 kDa (MiD51). Preliminary data suggests that Fis1 competitively binds MiD51, relieving MiD51 inhibition and indirectly stimulating Drp1 activity to activate mitochondrial fission. These processes assist in removal of damaged mitochondria and support apoptosis during high cellular stress levels. Potential ligands that interact with Fis1 have been found to be MiD51 and Drp1, which may be regulated by Fis1's intramolecular interactions. Using 3D printing technology, the St. Joan Antida SMART (Students Modeling a Research Topic) Team modeled cytosolic domain of Fis1 and the twice-repeated tetratricopeptide (TPR) repeat motif which is the predicted binding interface for Fis1-MiD51. TPR1 contains helices 2 & 3 and TPR2 contains helices 4 & 5. Residues 1-8 of the N-terminal arm are modelled in two orientations – "arm open" and "arm closed" – representing potential blocking of the active site within the concave pocket formed by TPR1&2 of Fis1. Current research hypothesizes sidechains of Asn6 and Arg83 to be responsible for "arm" orientation blocking the active site. Elucidating the role of Fis1-MiD51 axis in mitochondrial fission in the context of healthy and diseased models can lead to developing better therapeutics and treatments for heart disease and diabetes.