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The machinery and mechanisms of membrane protein biogenesis

Max-Planck-Institut für Multidisziplinäre Naturwissenschaften (MPI-NAT, Faßberg-Campus)

The human genome encodes ~5000 integral membrane proteins. These proteins are needed to transfer essentially all information and molecules into and out of the cell, and are the targets of most drugs used to treat human disease. Our research group has been investigating how cells embed these proteins into the membrane and fold them into functional products. For decades, it was thought that membrane proteins are inserted by the same machinery used for protein secretion: the Sec61 protein translocation channel. We have discovered that this textbook model of membrane protein biogenesis is incomplete. Instead, cells contain specialised machinery for membrane insertion that cooperates with Sec61. We and others have identified the key components of this membrane insertion machinery, determined their structures in different states, identified their substrates, and shown how these factors dynamically assemble at a membrane-associated translating ribosome. These findings have led us to a new paradigm for membrane protein biogenesis that rationalizes a wide range of observations over the past few decades and provides a new unifying framework for future studies.

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