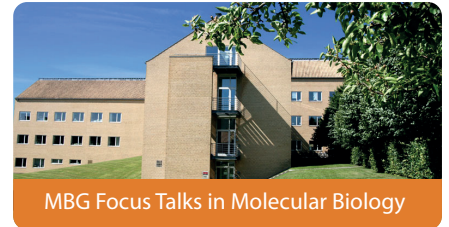


# MBG FOCUS TALK

hosted by Ditlev Brodersen and Esben Lorentzen



**Monday August 9, 2021 at 10:15 am**

Science park, conference room (3130-303)

**Ahmad Jomaa, PhD**

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## **Mechanism of co-translational nascent chain recognition and handover to the endoplasmic reticulum by the mammalian signal recognition particle**

The cell proteome consists of many membrane and secretory proteins that in eukaryotes are mostly co-translationally delivered to the endoplasmic reticulum (ER) for secretion or insertion into the membrane. This is a multi-step targeting process that involves the function of the universally conserved signal recognition particle (SRP) and its receptor (SR). The process commences by SRP binding ribosomes translating nascent proteins that need to be targeted; and this complex is then delivered to the membrane via interactions with SR, followed by the departure of SRP and the formation of a complex between the translating ribosome and the Sec translocon on the ER membrane. SRP is a ribonucleoprotein complex that binds and recognizes an N-terminal hydrophobic ER signal sequence on the nascent polypeptide chain as it emerges from the ribosome exit tunnel, while SR is a protein complex that is anchored to the ER membrane and interacts with SRP. Both SRP and SR contain homologous GTPases that form a heterodimer and mediates ribosome recruitment to the membrane during the protein targeting pathway. Since ribosomes that are translating proteins that need to be targeted are much more abundant than SRP, cargo recognition and handover has to take place efficiently to prevent the hydrophobic cargo from aggregation in the cytosol. However, due to its complexity in comparison to bacteria, mammalian SRP is mechanistically not well understood. In particular, it is not clear how eukaryotic-specific elements contribute to cargo recognition and cargo handover. Here, I will present electron cryo-microscopy structures of SRP and SRP·SR in complex with the translating ribosome. The structures reveal the specific molecular interactions between SRP and the emerging signal sequence and the elements that regulate GTPase activity of SRP·SR. Our results suggest the molecular mechanism of how eukaryote-specific elements regulate the early and late stages of SRP-dependent protein targeting.