

Advances in segmented helical reconstruction and insights from oligomeric and polymeric autophagy receptor complexes

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Helical protein assemblies present a fundamental architecture of structures involved in diverse cellular processes such as cytoskeleton assembly, endocytosis, signalling and autophagy. I will illustrate based on previous and more recent examples of how direct electron detector technology and image processing have been essential in this method development [1], [2]. Our recent efforts in combining traditional Fourier-Bessel procedures with single-particle algorithms provide a comprehensive approach to structure determination of helical specimens [3]. In my talk, I will present a series of medium to high resolution cryo-EM structures that have advanced our understanding of the molecular mechanism of how cargo is recognized by the selective autophagy machinery. We showed that autophagy receptor p62/SQSTM-1 assembles into flexible helical filaments and provide insights into the molecular basis of polymer formation [4]. EM based structure elucidation in vitro and in situ reveals large oligomeric and polymeric cargo receptor complexes giving rise to higher-order structures that constitute the scaffold for autophagosome formation [5]. The organization of small receptor proteins into helical assemblies provides a cellular mechanism for high selectivity in cargo recognition and a fundamental architecture that enables cargo encapsulation of various sizes from molecular to cellular scale.

References

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