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Abstract

Pioneering organelle structural biology: Golgi apparatus dysfunction and cascades of fatal pathways in cancer †

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Abstract: The Golgi apparatus (GA) dysfunctions in Parkinson's Disease (PD), neurodevelopmental disorders (NDDs), cancer, and organelle structural biology (OSB) can provide insights into therpeutic targets, gene therapy, and drug design. Primary defects and fragmentation within the GA are implicated in a wide range of neurodegenerative diseases. GA defects typically result in mislocation of proteins, accumulation of undegraded proteins, and impaired glycosylation of proteins. Inhibition of vesicular trafficking by α-synuclein (aSyn) may affect the dopamine-producing neu- rons and neuromodulators. GA regulates apoptosis during pathological mechanisms of neurological diseases and could provide new avenues in treatments through translation research. PD patients bearing the hereditary E46K disease mutation manifest the clinical picture of parkinsonism. How do we provide high resolution nanoimages of the GA during disease to capture dysfunction? Could we visualize the aSyn traffic jam between vesicles in the organelles ER and GA? OSB is emerging as a field as more technology advances and is more accessible. Structural studies of the GA will advance the field of neurological disease forward with an in depth understanding of dysfunction, fragmentation, and defects. Discoveries of the GA in PD, NDDs, and cancer would break new ground and provide translational medicine data of these diseases. Future research could be visualizing high angle annular dark field-STEM (HAADF-STEM) tomograms, cryogenic electron tomography (cryo-ET), multiplex correlative light and electron microscopy (cryo-CLEM), nanobody-assisted tissue immunostaining for volumetric EM (NATIVE) and using soft X-ray tomography (SXT) and computational reconstruction of the GA.

Keywords: structural biology; organelles; Golgi apparatus (GA); Parkinson's disease (PD); cryo-ET; alpha-synuclein; neurodegenerative diseases; soft X-ray tomography (SXT); cancer; NDDs