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LS-2-P-1957 The secretory pathway in electron microscopy: Sec16 and ER exit sites

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Generating the cellular surface, and in many cases also the extracellular environment is fundamental to all cells from bacteria to eukaryotes and essential for the multicellular organization of tissues and organisms. Consequently, disruptions of the underlying process, secretion, can cause malformations and diseases. The secretory pathway starts with newly synthesized proteins and lipids leaving the ER at distinct structures termed ER exit sites (ERES), defined by the presence of Sec16. Sec16 is a large membrane-associated protein supposed to create a platform for the generation of COPII-ensheathed vesicles at ERES. The COPII vesicle coat consists of Sec23/Sec24 forming the inner shell and Sec13/Sec31 comprising the outer layer. COPII-coated vesicles transport the cargos to the Golgi where they are processed before being routed to their final destinations. To study the morphological relationship of involved organelles in the early secretory pathway we are have investigated Trypanosoma brucei, the causative agent of African sleeping sickness. T. brucei is good model since it contains only a single ERES and Golgi at a defined location in a specific state of its live cycle. Phenotypic analyses of trypanosome cells following Sec16 knockout, depletion or overexpression revealed an intriguing link between ERES and Golgi size. In particular, increased levels of Sec16 resulted in larger ERES, and concomitantly a larger Golgi whereas decreased levels had the opposite effect. We are now exploring the changes in size and shape of these organelles in 3D using electron tomography. In a second approach, and to link secretion with medically relevant conditions, we are investigating the early secretory pathway and the structure of the extracellular matrix during cartilage degeneration (osteoarthritis).