The ribbon-like Golgi architecture. Its roles in development and the molecular determinants of its evolution

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Abstract

The Golgi apparatus, a universal feature of eukaryotes, is involved in several cellular processes, the most studied of which is exocytosis. Golgi's functional unit is the stack, a pile of membranous cisternae. Across species, the number of stacks per cell is variable, occurring in one to several copies. When present in multiple copies, stacks are found in two major arrangements: they remain separate or coalesce into a single structure, known as the Golgi ribbon. While it is widely believed that the ribbon-like organization of the Golgi is restricted to vertebrate cells, very recent work in our lab shows that this cellular architecture is present across several animal groups. The functions of the Golgi ribbon are currently unknown; however, its disruption is often observed in human pathologies, ranging from viral infections to neurodegenerative diseases and cancer. As we observe that during early embryogenesis the Golgi switches from separate stacks to a ribbon-like organization in sea urchins, sea squirts, lancelets, and mammals, formation of the ribbon architecture may play a developmental role. Golgins and GRASP are structural proteins that localize at the Golgi. Based on a body of evidence from mammalian systems, we identify a possible molecular mechanism driving the evolutionary emergence of the ribbon-like architecture in animals. Specifically, we hypothesize that Golgin-45 evolved the capability to bind GRASP, leading to Golgi stack tethering, which is necessary for ribbon formation. This hypothesis is backed by structure modelling of Golgin-45/GRASP complexes across the animal tree. While both echinoderms, sea urchin and starfish diverged more than 500 million years ago. Comparative studies in these two organisms are bound to be informative in terms of evolutionary conservation of biological processes and molecular mechanisms. Using sea urchin and starfish as experimental organisms, the aim of this PhD project is to deploy a combination of genetic, cell biological and pharmacological approaches to investigate the functions of the ribbon-like organization in development and test the role GRASP/Golgin-45 interaction in its evolution of this Golgi structural arrangement.