Golgi enzyme organization controls fidelity in glycan biosynthesis
Seetharaman Parashuraman

Glycans are one of the four biopolymers that cells are made of. They are built in a non-templated manner in the Golgi apparatus, on the cargoes that traverse the organelle. Despite the absence of a template, glycans produced by the Golgi are not a random collection of polymers but a set of glycans with characteristic composition and distribution pattern that is cell type and cargo specific. How this specificity is achieved by the Golgi apparatus in the absence of a template remains unclear. We used GSL biosynthesis as a model system to understand how this specificity is achieved. We observe that compartmentalized localization of GSL biosynthetic enzymes across the compartments (or cisternae) of the Golgi stack is essential to determine the specific distribution of GSLs produced by the cell. We identify that GRASP55, a Golgi matrix protein, is important for compartmentalized localization of two key GSL biosynthetic enzymes that act at branch points in GSL biosynthetic pathway. GRASP55 regulates their localization by actively preventing their entry into COPI transport carriers and retaining them in the Golgi cisterna. Impairing this “retainer” activity decompartmentalizes the enzymes, alters cargo flux across the branch points of the GSL biosynthetic pathway controlled by the enzymes and results in an altered GSL distribution at the cell surface. This altered GSL distribution then affects cell density dependent growth of cells. We propose that compartmentalized organization of enzymes in the Golgi apparatus regulates GSL metabolic bias to control fidelity in glycan biosynthesis.

References: https://www.biorxiv.org/content/10.1101/2020.05.03.074682v1
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Contacts: raman@ibbc.cnr.it
Website(s): http://www.ibbc.cnr.it/researchers/seetharaman-parashuraman/
Other: