Daniel Ungar, J Glycobiol 2018, Volume 7
DOI: 10.4172/2168-958X-C2-014

Linking golgi organization and glycan processing

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Mammalian glycans are inherently heterogeneous due to their non-templated biosynthesis. Yet this heterogeneity hides a remarkable level of control, as demonstrated by the cell-type specificity of glycan profiles. Key for this control is expression level of glycan processing enzymes, but importantly, also the non-uniform localization of these enzymes in cisternae of the Golgi apparatus. The set of proteins responsible for the vesicle-mediated targeting of glycan-processing enzymes within the Golgi were characterized. In order to understand how enzyme sorting impacts biosynthesis, we have recently developed a computational model of glycan processing to iteratively fit simulated and experimentally determined glycan profiles to each other. At a simple level, results from this model can be used to predict how the levels and localizations of enzymes change in mutants that disrupt vesicle targeting. Importantly, the model can also explain more complex phenotypes, such as the question why core-fucosylation levels dropped in a mutant although Fut8 levels or location did not change. Finally, we will show an example of using the modelling to pinpoint functionally important glycosylation changes during cellular differentiation. We envision this model to find applications in areas as diverse as cellular glycan engineering or to design treatment strategies for congenital glycosylation disorders.

Biography

Daniel Ungar has completed his PhD at the MPI of Biophysics (Frankfurt) and Post-doctorate at Princeton University. For the past 10 years, his group at York has been investigating the vesicular sorting of glycosylation enzymes within the Golgi, and how this process inflicts on glycan biosynthesis and function.

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