

Tissue-specific regulation of BMP signaling by *Drosophila* N-glycanase 1

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Abstract

NGLY1 (N-glycanase 1) encodes an evolutionarily conserved enzyme that catalyzes the cleavage of N-glycan's from glycoproteins. Mutations in human NGLY1 cause a rare congenital disorder with severe developmental delay, delayed bone age and osteopenia, gastrointestinal dysfunction, small hands/feet and absent tears. However, the mechanism by which NGLY1 deficiency causes the above-mentioned clinical phenotypes is not known, and neither has NGLY1 been linked to any major developmental signaling pathway. Here we show that *Drosophila* Pngl encodes an N-glycanase and exhibits a high degree of functional conservation with human NGLY1. Loss of Pngl results in developmental midgut defects reminiscent of midgut-specific loss of BMP signaling. Tissue-specific knock-down and rescue experiments indicate that Pngl is primarily required in the mesoderm during *Drosophila* development. The enzymatic activity of Pngl is essential for BMP autoregulation in the visceral mesoderm mediated by Dpp as ligand and Tkv as receptor. Genetic and phenotypic analyses indicate that loss of BMP signaling in Pngl mutant midguts results from a requirement for Dpp homodimers in this tissue, suggesting that the heterodimer form of Dpp with Gbb, the other fly BMP ligand, is not affected. Indeed, biochemical data show that loss of Pngl results in a severe decrease in the level of Dpp homodimers, suggesting a role of Pngl for Dpp homodimer formation and/or stability. summarized.

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Biography

Antonio Galeone is a Post-Doc Associate in the Department of Molecular and Human Genetics at Baylor College of Medicine (BCM). He has received BS and MS in Molecular Biology from University of Salento-Italy in 2008. He has completed his Graduate work in Pompa and Cingolani's Lab at Italian Institute of Technology (IIT), where he focused on the understanding of the interaction between nanomaterials

and living systems using *Drosophila melanogaster* as model. He has graduated in Nano biotechnology in 2012 and has completed a short-term Postdoctoral training at IIT funded by the European Commission. He has joined the Jafar-Nejad's lab in September 2013 at BCM. Currently, he is involved in the NGLY1 project and aims to study the pathophysiology of NGLY1 deficiency using a fly model.