Antonio Galeone, Eur J Exp Bio, 7:5
DOI: 10.21767/2248-9215-C1-002

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

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NGLY1 (N-glycanase 1) encodes an evolutionarily conserved enzyme that catalyzes the cleavage of N-glycans 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.

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 Nanobiotechnology 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.

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