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Sugarcoating fruit fly development

Scientists discover that sugar tags on nuclear proteins have an important developmental function

Heidelberg, 28 May 2009 - Proteins are the executive agents that carry out all processes in a cell. Their activity is controlled and modified with the help of small chemical tags that can be dynamically added to and removed from the protein. 25 years after its first discovery, researchers at the European Molecular Biology Laboratory (EMBL) in Heidelberg have now gained insight into the role of one of these tags, a small sugar residue, that is found on many different proteins across species. In the current online issue of *Science* they report that the addition of this sugar tag to proteins in the nucleus of a cell is vital for normal development in fruit flies.

Over 25 years ago scientists discovered that many proteins in the nucleus and cytoplasm have a small sugar molecule, called GlcNAc, attached to them. The enzyme that adds this sugar is called Ogt but since its discovery it has remained elusive why attaching GlcNAc to proteins is important. Researchers in the group of Jürg Müller at EMBL have now discovered that flies lacking Ogt show dramatic developmental defects. In the absence of Ogt cells do not develop into the appropriate cell types and body segments do not differentiate according to plan.

“Expressing the right genes at the right time is critical for a developing organism,” says Jürg Müller. “It is the appropriate

combination of genes that tells a cell to turn into muscle, nerve or skin. This is why a tight control system regulates gene expression throughout development.”

One important component of this control system is a group of regulatory proteins, called Polycomb proteins. They switch off developmental genes when and where their activity is not needed and thereby prevent the formation of specialised tissues and organs in the wrong places.

The scientists found that in the absence of Ogt, Polycomb proteins are no longer able to inactivate developmental genes. They showed that one specific Polycomb protein, called Polyhomeotic, is modified with the sugar tag by Ogt and might be the link between Ogt and development. Further investigations are necessary to find out how the sugar tag affects the function of Polyhomeotic.

“Our findings were very surprising. GlcNAc has been found on so many different proteins in mammalian cells that we expected many processes to go wrong in a fly lacking Ogt. Instead we see a very specific effect on development in fruit flies that is likely brought about by a single nuclear protein that needs the sugar tag to function properly,” says Maria Cristina Gambetta, who carried out the research in Müller's lab. ●

Source Article

M.C. Gambetta, K. Oktaba & J. Müller, Essential Role of the Glycosyltransferase Sxc/Ogt in Polycomb Repression. *Science Express*, 28 May 2009

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About EMBL

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