Recipe for making a fruitfly

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Researchers have used mass spectroscopy to determine the absolute copy numbers of nuclear proteins and histone modifications in the Drosophila embryo. The results provide new insights into the mechanisms of animal development.

Fruitflies and humans have a lot in common. Indeed, about 60% of all fruitfly genes have identifiable counterparts in humans. Research carried out in the fruitfly *Drosophila melanogaster* has yielded a wealth of

information on the basic molecular mechanisms that control animal development. However, it remains largely unclear how many copies of each of the proteins involved are produced and essential for the orderly development of a multicellular organism. In a new study, Jürg Müller at the Max Planck Institute (MPI) for Biochemistry, in collaboration with research groups led by Axel Imhof (Professor of Molecular Biology at LMU's Biomedical Center) and Michiel Vermeulen (who is based at Radboud University in Nijmegen), have quantitatively characterized the set of proteins required to regulate the development of the Drosophila embryo. More specifically, the measured the absolute copy numbers of all proteins and the chemical modifications on histone proteins in the cell nuclei of the embryo. Their findings appear in the current issue of the journal *Developmental Cell*.

The genomic DNA in the cell nucleus is tightly wrapped around particles called nucleosomes, which are made up of histone proteins. This causes each of the long DNA molecules to condense into a highly compact form, which is collectively known as chromatin. In other words, all of the genomic information that directs the orderly differentiation of the fertilized egg into a multicellular organism is packed in nucleosomes. Jürg Müller, leader of the Chromatin Biology Group explains: "The development of an embryo is a fascinating process. Unlike in humans, model systems like the fruit fly allow us to describe this process and to investigate how it is altered in genetically mutated animals. The organization of chromatin changes dramatically as embryonic cells become more and more restricted in their developmental potential. So, we wanted to understand whether and how the abundance of different chromatin proteins and chemical marks on histones change during these critical phases." Müller and his colleagues determined the copy numbers of almost 4000 proteins and chemical tags on histones at two different stages during in the development of the Drosophila embryo. This information is vital for an understanding of embryogenesis. Just as a cake recipe needs to specify not only the ingredients but also the

amounts of each one, the relative concentrations of the proteins involved in controlling development are an important factor in the outcome of the whole process.

The results of the study revealed that many regulatory proteins are present in much lower numbers than expected, whereas others are much more abundant. These observations shed light on how the genomic DNA is packed in chromatin, and how its accessibility is regulated to enable genes to be selectively expressed in differentiating cells. According to the authors, the new findings will lead to a reconsideration of current views of how chromatin works.

More information: Jacques Bonnet et al. Quantification of Proteins and Histone Marks in Drosophila Embryos Reveals Stoichiometric Relationships Impacting Chromatin Regulation, *Developmental Cell* (2019). DOI: 10.1016/j.devcel.2019.09.011

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