A life-changing partnership: New regulatory complex turning on genes

24 June 2010

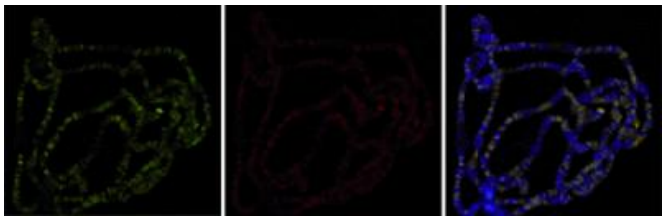

Fig. 1: These microscopy images show that a protein from the NSL complex (red) and MOF (green) both bind to all chromosomes in female fruit flies - overlap is shown in purple. Image: Asifa Akhta

(PhysOrg.com) -- Researchers from the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, and the Max-Planck Institute of Immunobiology Freiburg have identified a novel protein complex that regulates around 4000 genes in the fruit fly Drosophila and likely plays an important role in mammals, too. Published today in Molecular Cell, their findings explain how a regulatory protein can lead a double life. (*Molecular Cell*, 24 June 2010)

"This new complex seems to be one of the major regulatory complexes both in Drosophila and in mammals", says Asifa Akhtar, former EMBL group leader and now at the Max-Planck Institute of Immunobiology in Freiburg, Germany, who led the study: "Without it, flies die early in embryonic development."

The absence of the newly found complex causes early embryonic death of both males and females, so Akhtar and colleagues named it Non-Specific Lethal (NSL), in contrast to a previously known complex called Male-Specific Lethal (MSL). The MSL complex enables males to double the production of mRNAs encoded in their single X chromosome - a process called dosage compensation - by binding to the body of those genes together with a protein called MOF. Thus, male flies are able to compensate for the fact that they have only one X chromosome, while females have two. But MOF leads a double life: it also binds to the promoter regions of genes on all chromosomes, in both sexes.

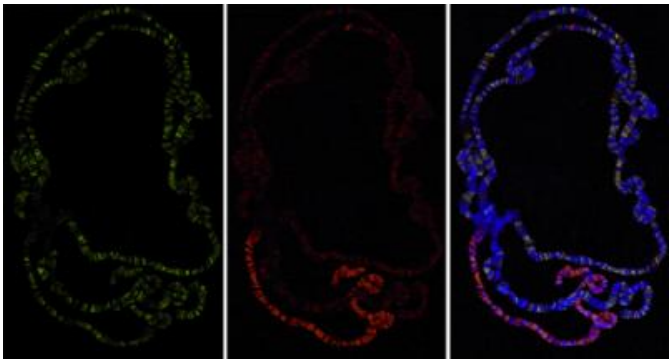

Fig. 2: The protein from the NSL complex (red) and MOF (green) both bind to all chromosomes in male fruit flies - overlap is shown in purple. On the male X chromosome, MOF binds not only to promoter regions but also to the body of the genes, generating a brighter signal (pink). Image: Asifa Akhtar

Akhtar and colleagues discovered that the NSL complex decorates all chromosomes in both sexes. They also observed that the NSL complex helps MOF to bind to promoters and thereby plays an important role in determining the life MOF will lead. If it partners up with NSL, MOF turns on genes in all chromosomes. If it interacts with MSL instead, it binds to genes on the males' X chromosome, playing its role in dosage compensation. Interestingly, NSL indirectly drives this aspect of MOF function too, by acting together with MOF to turn on the genes whose output will then be increased by dosage compensation.

"These proteins have been conserved throughout

evolution - they exist not only in fruit flies but in mammals too, meaning that everything we have discovered in flies has implications for humans and other mammals, which we'd like to investigate next", Akhtar concludes. Since MOF is frequently down-regulated in cancers, comparing how the NSL complex behaves in healthy tissues and in tumours is especially relevant.

More information: Raja, S.J., Charapitsa, I., Conrad, T., Vaquerizas, J.M., Gebhardt, P., Holz, H., Kadlec, J., Fraterman, S., Luscombe, N., & Akhtar, A.
The Nonspecific Lethal Complex Is a Transcriptional Regulator in Drosophila, Molecular Cell, June 24th, 2010

Provided by Max-Planck-Gesellschaft