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Compensasome in *Drosophila*

Ribonucleoprotein (RNP) complexes such as ribosomes, spliceosomes, primosomes and telomerases play important roles in different cellular regulatory activities. Recently, a novel RNP complex has been reported in *Drosophila*. The complex concerns dosage compensation, wherein it promotes the enhancement of transcription of single male X chromosome, so that the quantum of products produced by the single X chromosome in a male is equal to that of the two X chromosomes of females. Aptly, this ribonucleoprotein complex has been named the "compensasome" (Franke and Baker 1999).

The known protein components of the compensasome include the products of five male specific lethal genes (*msls*). They are *msl1*, *msl2*, *msl3*, maleless *mle* and males absent on the first – *mof*. MSL1 is a novel acidic protein, MSL2 a putative zinc binding RING protein, MSL3 a chromo domain protein, MLE a DNA/RNA helicase of the DEAH subfamily and MOF is a protein with an acetyltransferase domain (reviewed by Lucchesi 1998). The non-coding RNA component of the compensasome is coded by two genes, *rox1* and *rox2* (Amrein and Axel 1997).

Two successive steps have been visualized for the recognition of the X chromosome by these components of the machinery. The MSL1 and MSL2 interactions initiate the formation of the complex. They are found to associate with 30–40 sites present all along the X chromosome; subsequently, they recruit other MSL proteins to these sites. Of these sites on the X chromosome, two encode *rox* RNAs, and the *rox* RNAs are incorporated into the growing MSL complex. In the next step, the MSL–RNA complex associates with chromatin entry sites specifically on the X chromosome and spreads to other sections of the X chromosome (Kelley *et al* 1999). Elegant immunoflurescent studies involving *rox* antisense RNA and MSL antibodies have shown colocalization of these on the single X chromosome of males and their absence on the double X chromosomes of females (Franke and Baker 1999).

The MSLs appear to function through chromatin remodelling of the X chromosome. Under the influence of the MOF protein, histone H4-Lys 16 acetylation occurs. Histone acetylation and gene transcription are related. Many proteins designated as transcriptional cofactors possess histone acetyl transferase activity (Brownell *et al* 1996). With regard to role of *rox* RNAs, the following possibilities are being tested. They may act as contact point between MSLs and the X chromosome, or its interaction with RNA polymerase or other components of the chromatin remodelling machinery to enhance transcription within a stipulated time.

In contrast to the coordinate upregulation of the single male X chromosome in *Drosophila*, the equalization of X-linked products between the sexes (dosage compensation) takes place by two other (and different) mechanisms in humans and nematodes (*Caenorhabditis elegans*). In humans, it is through inactivation of one of the two X chromosomes in females while in the nematode it is achieved through hypoactivation of both the X chromosomes in females (reviewed by Lucchesi 1998; Lyon 1999). With the conceptualization of compensasome in *Drosophila*, attempts have been made to analyse the nature of compensasomes in an inactivated (humans) and hypoactivated (nematode) dosage compensation system. Preliminary reports show parallels between *rox* RNAs of *Drosophila* and *xist* RNAs of man.

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Size control in development: lessons from *Drosophila*

As long back as in 1927 J B S Haldane pointed out that "The most obvious differences between different animals are differences in size, but for some reason the zoologists have paid singularly little attention to them" (Haldane 1927). Almost three quarters of a century later, one of the most important and fundamental aspects of development – how the size of a multicellular organism is determined – remains as mysterious as ever. The final size reached by an adult organism is a consequence of changes in the size and number of cells during its development. The critical factors thus are how many cells there are, how big a cell is on average and the amount of extracellular matrix and fluid present.

Early studies on the yeasts *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* provided indications that growth could continue in the absence of cell division. Therefore growth was not simply a matter of increasing cell numbers; control of cell size was important too. Unfortunately, while much attention has directed to the analysis of mechanisms which regulate cell numbers, cell size regulation seems to have received a less than fair treatment by researchers. However, recent studies on the fruitfly *Drosophila melanogaster* have shown that mutations that block cell cycle progression tend not to arrest cell growth (Conlon and Raff 1999). Therefore the mechanisms that regulate the sizes of the imaginal discs (sacks of epithelial cells which reorganize during metamorphosis into external body parts such as the antennae, wings and legs) during larval development must be acting primarily by regulating cell size and not by regulating cell numbers. How then is size regulated? We know that growth depends on intrinsic cues as well as extrinsic factors which can stimulate intracellular pathways and induce biosynthetic processes. In vertebrates the insulin-like growth factor IGF-1 is one such extrinsic factor that regulates cell growth and proliferation. Molecules involved in the insulin signalling pathway in vertebrates – for example, insulin receptor, insulin receptor substrate and phosphatidylinositol 3-kinase – also regulate cellular growth rate and/or cell size in *Drosophila* (Leevers 1999).

In a recent report Montagne *et al* (1999) identify *Drososphila* S6 kinase (*dS6K*) as a signalling molecule which when mutated, slows growth and reduces cell size and thereby body size. In order to analyse the function of *dS6K*, Montagne and colleagues isolated flies with null mutations in the *dS6K* gene. They found that the mutant files were delayed in development and were severely reduced in body size (around 60% reduction in body weight and 30% reduction in cell size in homozygous female flies). However, all the body parts were affected to the same extent, implying that proportions were preserved. The latter observation is in accord with recent results showing that the overall form of an organism can be influenced by a competition for developmental resources between different body parts (Nijhout and Emlen 1998). After examining the wings and eyes Montagne *et al* (1999) arrived at the conclusion that the mini-flies were made up of cells which were reduced in size. The total number of cells in the body remained more or less the same. The smaller cell size could have come about because the cells were dividing earlier than usual or because the flies were emerging from developmental delay without complet-