Role of amino-terminal region of MSL1 in recruiting of dosage compensation complex of Drosophila melanogaster

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The dosage compensation complex (DCC) provides equivalent level of X chromosome transcription between females and males by approximately doubling upregulation of the transcription level of single male X chromosome. DCC specifically recognizes X chromosome in males but this mechanism remains unclear.

DCC consists of five proteins, MSL1, MSL2, MSL3, MOF, and MLE, and includes two noncoding RNAs, *roX1* (3.7 kb) and *roX2* (0.6 kb), which perform partially redundant functions. Proteins MSL1, MSL3, MOF, and MLE are also present in females and are involved in the regulation of gene expression independent of dosage compensation. As the MSL2 protein is specific for males, it is believed that the MSL2 protein has a key role in the specific binding of DCC to the X chromosome of males. The MSL1 protein functions as a flexible framework for the assembly of DCC. The N-terminal coil-coiled domain provides homodimerization of the MSL1 protein and interaction with the N-terminal RING domain of the MSL2 protein. The C-terminal end of MSL1 is responsible for recruiting of MSL3 and MOF in DCC.

Here we have tested role of the N-terminal region of MSL1 in specific recruitment of DCC to the X chromosome in males. Using yeast two-hybrid assay, we mapped two regions, 1-15 aa and 41-65 aa, in MSL1 that interact with many zinc-finger transcription factors. We expressed several MSL1 variants carrying different deletions in the N-terminal region. As a result, deletion of any of the regions (1-15 aa or 41-65 aa) led to male lethality suggesting critical role of these regions of MSL1 in activity of DCC. In accordance, we did not observe binding of DCC to polytene chromosomes in mutant males or females expressed MSL2 protein ectopically. These results suggest that specific interaction of zinc-finger proteins with MSL1 is critical for recruitment of DCC to the X chromosome in males. The work was supported by RSF grant № 21-14-00211.