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NON-CODING RNA

Structure and function for lncRNAs

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Long non-coding RNAs (lncRNAs) have recently emerged as important regulators of gene expression, but there are few examples for which the relationship between lncRNA structure and function is well understood. A pair of recent studies make important strides towards such an understanding for the roX lncRNAs, which are key players in fruitfly dosage compensation.

In *Drosophila melanogaster*, dosage compensation involves the transcriptional upregulation of genes on the single X chromosome in males to match the expression from the two X chromosomes in females. This upregulation is mediated by the male-specific lethal (MSL) complex, which coats the male X chromosome and brings about histone acetylation, resulting in increased transcription. The MSL complex includes two lncRNAs, roX1 and roX2, which are crucial for its targeting to the X chromosome. However, how roX1 and roX2 are incorporated into the complex and their roles in MSL function have been poorly understood.

Several lines of evidence have previously suggested that the MLE RNA helicase, which is also a component of the MSL complex, is required for the association of the roX lncRNAs with the complex. Now, studies from two sets of authors — Maenner *et al.* and Ilik *et al.* — provide direct biochemical evidence for this. They show that the interaction with MLE involves specific, conserved domains in roX1 and roX2 that contain predicted stem-loop structures. Between them, the roX RNAs contain several of these domains. Both groups confirmed these predicted secondary structures using chemical and enzymatic methods.

Ilik *et al.* showed that both MLE and MSL2 (another protein component of the MSL complex) bind to the roX RNAs through these structures. Maenner and colleagues further showed that MLE activity disrupts roX2 secondary structure in an ATP-dependent manner, and that this causes remodelling of the lncRNA to reveal a binding site for MSL2. This explains how MLE could promote the assembly of the MSL complex. An important feature of the complex is that it initially binds certain high-affinity sites on the X chromosome and then spreads to other regions. Ilik and colleagues propose that the ability of roX lncRNAs to bind both MLE and MSL through multiple sites allows combinatorial binding that enables this spreading.

These findings are important as they have identified specific functional domains in lncRNAs and have elucidated a mechanism of lncRNA functional regulation by a helicase. The scene is set for further detailed mechanistic studies of lncRNA function.

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