Kilpatrick

Insights: Publications

SHAPE reveals transcript-wide interactions, complex structural domains, and protein interactions across the *Xist* lncRNA in living cells

PNAS 113 (37), 10322-10327

SEPTEMBER 13, 2016

The 18-kb *Xist* long noncoding RNA (lncRNA) is essential for X-chromosome inactivation during female eutherian mammalian development. Global structural architecture, cell-induced conformational changes, and protein–RNA interactions within *Xist* are poorly understood. We used selective 2′-hydroxyl acylation analyzed by primer extension and mutational profiling (SHAPE-MaP) to examine these features of *Xist* at single-nucleotide resolution both in living cells and ex vivo. The *Xist* RNA forms complex well-defined secondary structure domains and the cellular environment strongly modulates the RNA structure, via motifs spanning one-half of all *Xist* nucleotides. The *Xist* RNA structure modulates protein interactions in cells via multiple mechanisms. For example, repeat-containing elements adopt accessible and dynamic structures that function as landing pads for protein cofactors. Structured RNA motifs create interaction domains for specific proteins and also sequester other motifs, such that only a subset of potential binding sites forms stable interactions. This work creates a broad quantitative framework for understanding structure–function interrelationships for *Xist* and other lncRNAs in cells.