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Insights: Publications

A 5′ fragment of *Xist* can sequester RNA produced from adjacent genes on chromatin

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Xist requires Repeat-A, a protein-binding module in its first two kilobases (2kb), to repress transcription. We report that when expressed as a standalone transcript in mouse embryonic stem cells (ESCs), the first 2kb of *Xist* (*Xist*-2kb) does not induce transcriptional silencing. Instead, *Xist*-2kb sequesters RNA produced from adjacent genes on chromatin. Sequestration does not spread beyond adjacent genes, requires the same sequence elements in Repeat-A that full-length *Xist* requires to repress transcription and can be induced by lncRNAs with similar sequence composition to *Xist*-2kb. We did not detect sequestration by full-length *Xist*, but we did detect it by mutant forms of *Xist* with attenuated transcriptional silencing capability. *Xist*-2kb associated with SPEN, a Repeat-A binding protein required for *Xist*-induced transcriptional silencing, but SPEN was not necessary for sequestration. Thus, when expressed in mouse ESCs, a 5′ fragment of *Xist* that contains Repeat-A sequesters RNA from adjacent genes on chromatin and associates with the silencing factor SPEN, but it does not induce transcriptional silencing. Instead, *Xist*-induced transcriptional silencing requires synergy between Repeat-A and additional sequence elements in *Xist*. We propose that sequestration is mechanistically related to the Repeat-A dependent stabilization and tethering of *Xist* near actively transcribed regions of chromatin.