Nature Reviews Molecular Cell Biology | Published online 22 Aug 2016; doi:10.1038/nrm.2016.112

NUCLEAR ORGANIZATION

Keeping X chromosomes quiet

The long non-coding RNA Xist (X-inactive-specific transcript), which initiates X chromosome inactivation, was recently shown to interact with the lamin B receptor (LBR). Chen *et al*. now reveal that this interaction recruits the X chromosome to the nuclear lamina to enable its inactivation.

Initial experiments showed that a LBR-binding site (LBS) within Xist interacts with LBR, and that this interaction is required for the Xist-mediated silencing of X chromosome genes. In LBR knockdown cells and in cells harbouring Xist lacking the LBS (ΔLBS), silencing was restored by expressing LBR and Xist mutants engineered to interact.

Next, the authors showed that Xist colocalized with the lamina protein lamin B1 following the induction of Xist expression in wild-type cells, but that they were >20-fold further apart in cells in which Xist–LBR interactions were abolished. Targeting Xist to the lamina by engineering its interaction with lamin B1 rescued the Xist silencing defect in ΔLBS cells. Thus, Xist–LBR interactions recruit the X chromosome to the nuclear lamina to enable Xist-mediated gene silencing.

Lara Crow/NPG

In the absence of LBR, Xist RNA and gene silencing did not spread to actively transcribed genes on the X chromosome, owing to increased distance between the Xist compartment and the genes in question; this could be rescued by tethering ΔLBS to the lamina.

The authors propose a model in which Xist, as a result of its interaction with LBR, "shapes the 3-dimensional nuclear structure of the inactive X chromosome to spread to active genes and silence chromosome-wide transcription."

Katharine H. Wrighton

ORIGINAL ARTICLE Chen, C.-K. *et al.* Xist recruits the X chromosome to the nuclear lamina to enable chromosome-wide silencing. *Science* http://dx.doi.org/10.1126/science.aae0047 (2016)