Chromatin interactions in trans are associated with stochastic selection for monoallelic gene activation

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Virus Infection Induces NF-kappaB-dependent interchromosomal associations mediating monoallelic IFN-beta gene expression.

Apostolou E, Thanos D.
Cell, 134(1):85-96. (2008) doi: 10.1016/j.cell.2008.05.052.

Abstract:

The nucleus is an ordered three-dimensional entity, and organization of the genome within the nuclear space might have implications for orchestrating gene expression. Recent technological developments have revealed that chromatin is folded into loops bringing distal regulatory elements into intimate contact with the genes that they regulate. Although long-range chromatin interactions have been observed mostly in *cis* along the same chromosome (Schoenfelder et al., 2010), they can also occur in *trans* between different chromosomes. Interestingly, some reports showed that interactions in *trans* are associated with stochastic selection for gene activation (Apostolou and Thanos, 2008; Lomvardas et al., 2006; Noordermeer et al., 2011).

In this journal club, I will introduce about transcriptional activation of *IFN-β* gene via interchromosomal interaction. Transcriptional activation of the *IFN-β* by virus infection requires the cooperative assembly of an enhanceosome. The stochastic and monoallelic expression of the *IFN-β* gene depends on interchromosomal associations with three identified distinct genetic loci that could mediate binding of the limiting transcription factor NF-kB to the *IFN-β* enhancer, thus triggering enhanceosome assembly and activation of transcription from this allele. The probability of a cell to express *IFN-β* is dramatically increased when the cell is transfected with any of these loci. The secreted IFN-β protein induces high-level expression of the enhanceosome factor IRF-7, which in turn promotes enhanceosome assembly and *IFN-β* transcription from the remaining alleles and in other initially nonexpressing cells. Thus, the *IFN-β* enhancer functions in a nonlinear fashion by working as a signal amplifier.

References:

1. Lomvardas et al., *Cell*, 126(2):403-13, 2006
2. Noordermeer et al., *Nat Cell Biol*. 13(8):944-51, 2011
3. Schoenfelder et al., *Nat Genet*. 42(1):53-61, 2010