# Preventing the spread of repression

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Scientists at the Friedrich Miescher Institute for Biomedical Research have identified a novel and unexpected regulatory activity of RNA at the edge of inactive chromosomal regions. In their publication in *Nature Structural and Molecular Biology* they showed that non-protein coding RNAs demarcate active and inactive chromosomal regions by evicting the proteins necessary for the spreading of repressive chromatin marks.

It was one of the bigger surprises of the human genome project: Even though the human genome is about 30 times bigger than the one of the roundworm C. elegans, it contains only one third more protein-coding genes than that of the simple worm. This was a shock to those who up until then quantified the complexity of an organism through the numbers of genes, and scientists had to turn their attention to the 98% of the human genome that does not code for proteins.

Since then it has become evident that vast DNA regions not only regulate gene expression and organize the architecture of the chromosomes but also contain the templates for non-coding RNAs such as tRNA, rRNA or microRNA. While the function of some of these RNAs, for example in protein synthesis and RNA processing, has been known for a while, the functional relevance for most of the other non-coding RNAs that have been catalogued remain elusive.

Marc Bühler and his team at the Friedrich Miescher Institute for Biomedical Research have now discovered a so far unknown activity of non-coding RNAs. They have identified and functionally characterized a novel class of non-coding RNAs, named "Borderline", which prevent the

spreading of heterochromatin, a type of chromatin that is well known to repress gene activity. Spreading of heterochromatin can lead to the silencing of tumor suppressor genes and can thus contribute to malignancy if not properly controlled. Their results have been published online in the journal *Nature Structural and Molecular Biology*.

Borderline RNA is produced at the boundary between actively transcribed, loose chromatin and tightly packed heterochromatin regions. These long non-coding RNAs are further processed into smaller brdrRNAs and counteract the spreading of heterochromatin through interaction with HP1, a protein that recognizes H3K9 methylation marks on chromatin and helps spread heterochromatin regions through its interactions with methylating enzymes. Upon RNA binding HP1 dissociates from the chromatin template. "That non-coding RNAs function as guide molecules is a recurring theme", said Bühler. "We could now show that the opposite takes place too. Borderline RNA counteracts the association of proteins with chromatin."

Notably, the FMI scientists showed that the Borderline type of RNA is truly non-coding as the mere synthesis of RNA independent of its sequence is sufficient to impair the spreading of heterochromatin. "Borderline RNAs are produced where they are needed to counteract the encroachment of heterochromatin into neighboring regions", said Bühler. "This is an unexpected regulatory activity in demarcating active and inactive chromosomal regions and it may well be that these mechanisms play a role in several organisms."

**More information:** Keller, C. et al. (2013) Noncoding RNAs prevent spreading of a repressive histone mark. *Nat Struct Mol Biol* 20:994-1000. www.nature.com/nsmb/journal/v2 … /full/nsmb.2619.html

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