

Study shows R-loops coordinate with SOX2 in regulating reprogramming to pluripotency

June 11 2020, by Liu Jia



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R-loops are unique structures in the cell, composed of RNA–DNA hybrids and a displaced single-stranded DNA, that are commonly found around transcribed genes. However, R-loops are also dynamic and widespread entities that play unclear regulatory and epigenetic roles in the genome.

A recent study, published online in *Science Advances* and by the researchers at the Guangzhou Institutes of Biomedicine and Health (GIBH) of the Chinese Academy of Sciences, has shed light on the activity of R-loops in the [reprogramming](#) of somatic cells to induced [pluripotent stem cells](#) (iPSCs). They revealed that R-loops influence the reprogramming of somatic cells into iPSCs, and disrupting this activity leads to defects in the reprogramming of somatic [cells](#) to iPSCs.

R-loops may act as epigenetic markers by altering transcription factor binding, chromatin modifications, and DNA methylation. The researchers mapped the landscape of R-loops during OSKM (Oct4, Sox2, Klf4, and c-Myc, four [transcription factors](#) in the reprogramming cocktail) mediated somatic cell reprogramming and showed a dynamic association between R-loop formation and dissolution and the process of somatic cell reprogramming.

"Our data indicate that R-loops cause sharp changes at both the early and late stages of reprogramming, but they have transient and subtle changes at the intermediate stage, which shows a similar pattern with chromatin opening, DNA methylation, and [gene expression](#) during reprogramming," said YAO Hongjie, an author of this study from GIBH.

YAO and his colleagues found that some R-loops formed in advance of gene expression, suggesting R-loops are poising genes ready for transcription. Their research revealed that the transcription factor Sox2 (but not any other Yamanaka factor in the reprogramming cocktail) was intimately involved in forming a complex with R-loops.

"It is not only a transcription factor that induces transcription but also an essential regulator that maintains the balance of R-loops, and further promotes reprogramming together with R-loop-resolving factors," said YAO.

More information: Yaoyi Li et al. R-loops coordinate with SOX2 in regulating reprogramming to pluripotency, *Science Advances* (2020).
[DOI: 10.1126/sciadv.aba0777](https://doi.org/10.1126/sciadv.aba0777)

Provided by Chinese Academy of Sciences

Citation: Study shows R-loops coordinate with SOX2 in regulating reprogramming to pluripotency (2020, June 11) retrieved 6 May 2024 from
<https://medicalxpress.com/news/2020-06-r-loops-sox2-reprogramming-pluripotency.html>

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