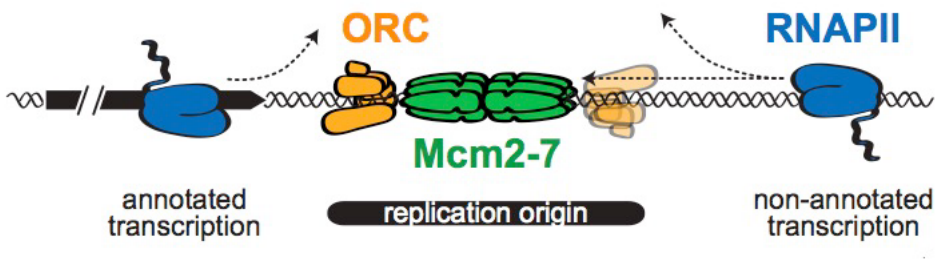
When Transcription Meets Replication

Conflicting activities necessary for the expression, the maintenance and the propagation of genomes need to be coordinated. Just like one's liberty to swing fists ends where another's nose begins, coordination is achieved through a tight control of where and when directly opposed activities take place. In a study published recently in eLife, researchers are now showing, in the yeast *Saccharomyces cerevisiae*, that replication factors generally "protect" sites where replication initiates by terminating incoming transcription, and that the low levels of transcription that enter origins of replication affect their firing efficiency.

The notion of transcription-replication conflicts comes from the realization that both DNA and RNA polymerases read DNA filaments 3' to 5'. RNA polymerases transcribing genomes that concomitantly undergo replication may therefore collide with replisomes. Such collisions may result in DNA breakage and should be avoided. Also, translocation may interfere with the binding of replication factors to DNA, which may antagonize the initiation of replication and should also be prevented. As transiently shutting-down all transcription would likely challenge the general fitness of the organism, it has been proposed that cells evolved pathways either to mediate transcription-replication conflicts, and/or to mutually exclude transcription and replication activities.

Replication initiates on genomes from highly specialized zones coined "replication origins" that are generally localized outside of genic regions. However, a lot of transcription occurs outside of genes (the so-called pervasive transcription) and invades regions that were thought not to be transcribed. Acting as a mechanism counteracting pervasive transcription, DNA-bound proteins can "roadblock" RNAPIIs, i.e. physically impede their progression. This article reports the genome-wide impact of pervasive transcription on the function of yeast replication origins. It shows that, once RNAPIIs reach origin borders, replication factors bound to chromatin roadblock them, generally "protecting" regions where replication originates from invading transcription. Importantly, however, protection is not watertight, which allows some transcription to pass by. This low level of transcription is important for origin function, which is therefore one of the factors that define when and how efficiently origins fire.



Legend. Replication origins are “protected” in yeast from incoming RNA polymerases (blue) whose transcription is terminated by a roadblock mechanism. The low levels of transcription that enter origins affect their function.

To know more. Candelli, T., Gros, J. and Libri, D. Pervasive transcription fine-tunes replication origin activity. eLife. 2018 Dec 17;7.

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