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REAPPRAISING THE ROLE OF R-LOOPS IN TRANSCRIPTION-DRIVEN GENOME INSTABILITY

29.APRIL 2025 – 11 AM – LECTURE HALL

R-loops are three-stranded structures that result from the pairing of an RNA molecule to a complementary DNA strand in the context of an intact DNA duplex. R-loop formation is increasingly associated with human pathologies, such as cancer and neurodegenerative diseases. Popular models explain the toxicity of R-loops by their still-hypothetical ability to hinder the progression of replication forks during DNA replication, which would ultimately result in disease-promoting genome instability.

Here we challenge this model using an innovative strategy to rapidly deliver ready-made *Escherichia coli* RNase H1 (RnhA) in live human cells, an enzyme that degrades the RNA moiety of RNA:DNA hybrids. We show that RnhA is enriched in the vicinity of active replication forks and that it rescues replication fork progression in different stress conditions. However, RnhA had no impact on R-loops mapped by several methods, suggesting that the loss of R-loops is unlikely to explain the rescue of replication fork progression by RnhA delivery. Our results reveal the existence of distinct populations of RNA:DNA hybrids that are differently sensitive to RnhA and invites a necessary reappraising the role of R-loops in transcription-driven genome instability.

Invited by : André Verdel

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Allée des Alpes, 38700 La Tronche (tram line B, stop : Grand Sablon)
The seminar is followed by discussions and exchanges with the speaker and a sandwich buffet is offered

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