SÉMINAIRES ET CONFÉRENCES

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"Safeguarding Pluripotency under Genomic Stress: The Role of Transcription-Replication Conflict Resolution"

Embryonic stem cells (ESCs) must balance rapid proliferation and faithful maintenance of cell identity. This unique cell cycle structure, characterized by high replication rates and a short G1 phase, raises a fundamental question: how do ESCs cope with the inevitable collisions between replication and transcription? Such transcription–replication conflicts (TRCs) are well-known sources of genomic instability, yet their contribution to stem cell biology has remained poorly understood. Our recent findings demonstrate that transcription and replication are unusually uncoordinated in mouse ESCs compared to somatic cells. Strikingly, despite this high "genomic traffic," ESCs experience only modest levels of conflict, suggesting the presence of powerful mechanisms that mitigate TRC-associated stress. Through a focused genetic screen, we identify the RNA:DNA helicase Aquarius as a key factor that preserves transcription–replication coordination and, in doing so, safeguards pluripotent identity. Loss of Aquarius disrupts replication dynamics, triggers DNA damage, and promotes stem cell differentiation, linking TRC resolution to the maintenance of cell fate. Together, these results reveal TRCs as a hidden vulnerability of pluripotent cells, but also as a potential lever for controlling cell identity.

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Zoom

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