RECONSTRUCTING GENE REGULATORY NETWORKS DURING iPSC REPROGRAMMING AND X CHROMOSOME REACTIVATION

Irene Talon[1]#, Adrian Janiszewski[1]#, Bart Theeuwes[1], Natalie De Geest[1], Greet Bervoets[2], Juan Song[1], Suresh Poovathingal[3], Thomas Lefevre[4], Thierry Voet[4], Stein Aerts[3 5], Jean-Christophe Marine[2], Florian Rambow[2], Vincent Pasque[1]

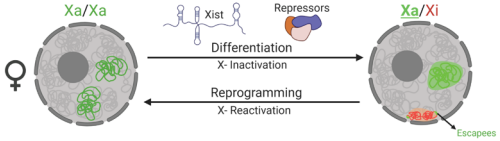
[1] KU Leuven – University of Leuven, Department of Development and Regeneration, Leuven, Belgium.
[2] Laboratory for Molecular Cancer Biology, VIB Center for Cancer Biology, VIB, Leuven, Belgium; Laboratory for Molecular Cancer Biology, Department of Oncology, KU Leuven, Leuven, Belgium.
[3] VIB-KU Leuven Center for Brain & Disease Research, Leuven, Belgium.
[4] Laboratory of Reproductive Genomics, Centre for Human Genetics, KU Leuven, Leuven, Belgium.
[5] KU Leuven, Department of Human Genetics KU Leuven, Leuven, Belgium.
# equal contribution

irene.talon@kuleuven.be
Twitter: @IreneTalon

1. BACKGROUND

The formation and reversal of heterochromatin is central to the establishment of stable cell identity and epigenetic memory during development.

X Chromosome dosage compensation in females cells (XX) is a paradigm to study epigenetics, gene regulation, 3D chromatin organization and lncRNA biology.

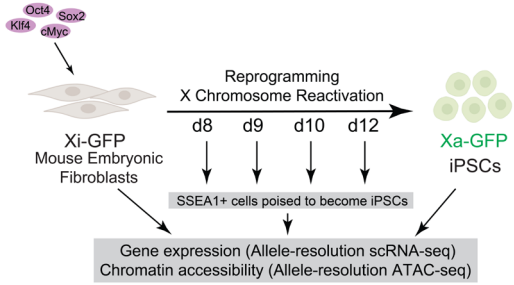


X Chromosome Inactivation (XCI) compensates gene dosage between female (XX) and male (XY) cells.

X Chromosome Reactivation (XCR) occurs in mouse and human development, in germline formation and during the reprogramming of somatic cells to induced pluripotency.

HOW IS DOSAGE COMPENSATION REGULATED DURING X CHROMOSOME REACTIVATION?

2. METHODS



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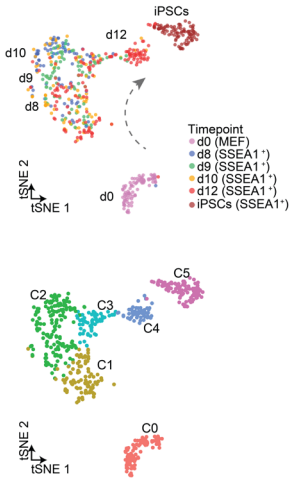
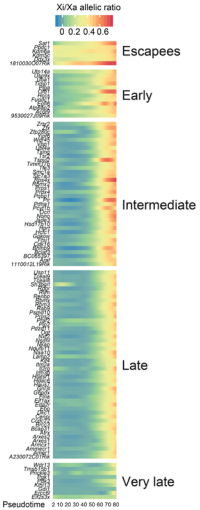
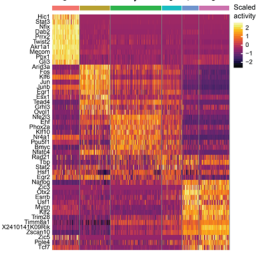
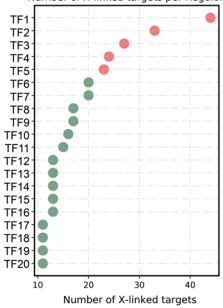
3. TRANSCRIPTIONAL KINETICS OF XCR AT SINGLE CELL RESOLUTION





4. RECONSTRUCTION OF GENE REGULATORY NETWORKS DURING REPROGRAMMING TO PREDICT DRIVERS OF XCR





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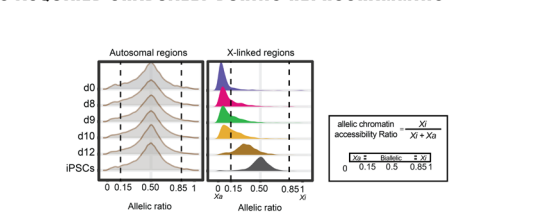
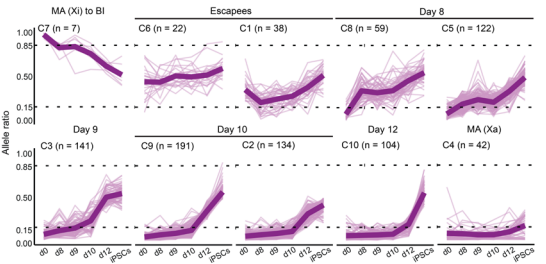
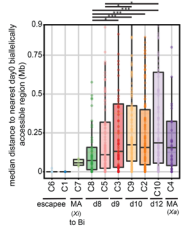
5. CHROMATIN ACCESSIBILITY ON THE INACTIVE X CHROMOSOME IS ACQUIRED GRADUALLY DURING REPROGRAMMING

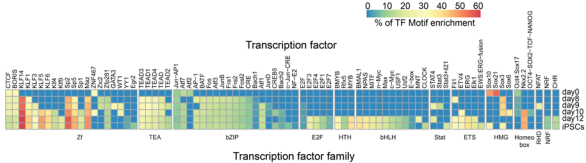




6. CHROMATIN REGIONS THAT OPEN EARLY ARE CLOSER TO BIALLELICALLY OPENED (ESCAPEES) REGIONS IN FIBROBLASTS



7. CHROMATIN REGIONS THAT BECOME ACCESSIBLE AT DIFFERENT TIMES ARE ENRICHED IN DISTINCT SETS OF TF MOTIFS



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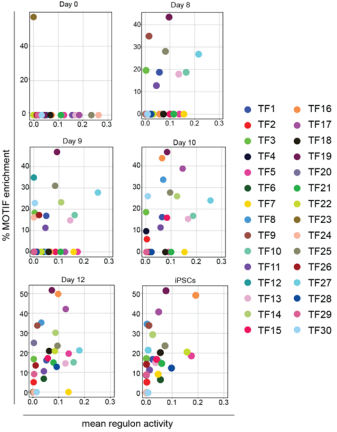
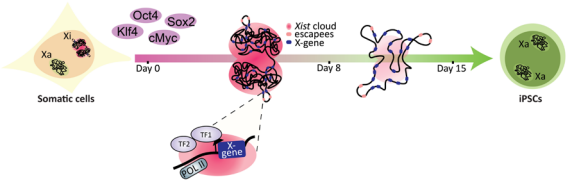
8. ACQUISITION OF CHROMATIN ACCESSIBILITY IS LINKED TO DYNAMIC RECONFIGURATION OF REGULATORY NETWORKS DURING REPROGRAMMING



9. TRANSCRIPTION FACTORS MIGHT DIRECTLY TARGET X-LINKED GENES FOR REACTIVATION



Our results demonstrate how gradual acquisition of a new gene regulatory network during reprogramming of cellular identity is linked with dynamic induction of chromatin accessibility and overcomes stable chromatin silencing on the inactive X chromosome.