Conférence

Centre de recherche du CHU de Québec-Université Laval

CHU de Québec Université Laval
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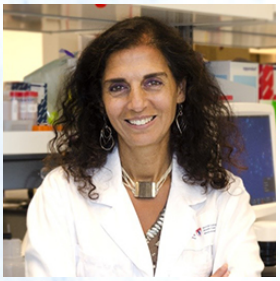

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Invitée par le Comité étudiant regroupement cancer

Date : 21 août 2019

Heure : 11 h

Lieu : Amphithéâtre CRCEO / L'Hôtel-Dieu de Québec
6, rue McMahon
Québec (QC)

Titre : «The Peter Pan Syndrome: stalled development at the root of oncohistone tumorigenesis»

AXE ONCOLOGIE

Childhood brain tumours have suspected prenatal origins. We showed that H3K27M in gliomas impairs the production and the spread of the repressive H3K27me3 mark from PRC2 high-affinity sites. Neither the recruitment of PRC2 to its nucleation sites nor the deposition of the H3K27me3 mark in the proximity of those sites was affected by the mutation. However, our findings indicate that as the marks cannot spread to establish the proper silencing landscape, further lineage specification, a major role of PRC2, is not possible, and the cell is stalled in an early epigenetic and progenitor state, indefinitely multiplying without being able to further differentiate.To identify vulnerable developmental states, we generated a single-cell transcriptome atlas of >44,000 cells from embryonal pons and forebrain, two major tumour locations. We derived signatures for 119 distinct cell populations and defined regional cellular diversity and differentiation dynamics. Projection of bulk tumour transcriptomes onto this dataset shows that WNT medulloblastomas match the rhombic lip-derived mossy fiber neuronal lineage, embryonal tumours with multilayered rosettes fully recapitulate a cortical neuronal lineage, while atypical teratoid-rhabdoid tumours originate outside of the neuro-ectoderm while diffuse intrinsic pontine gliomas resemble a pontine astrocytic progenitor and differentiate upon removal of driver mutation H3K27M. Importantly, single-cell tumour profiles reveal highly defined cell hierarchies mirroring transcriptional programs of the corresponding normal lineages. We identify impaired differentiation of specific neural progenitors as a common mechanism underlying these pediatric cancers and provide a rational framework for future modeling and therapeutic interventions.

Note :
Prière d'aviser vos étudiants gradués et stagiaires postdoctoraux afin d'avoir la participation de tous.

Visioconférence CHUL (E00320, code porte 3200*)