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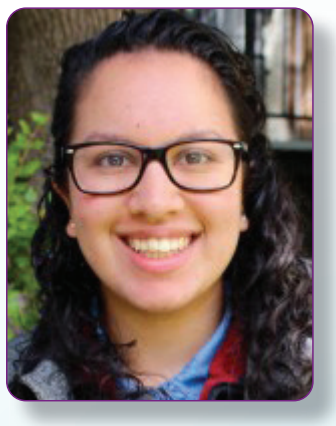

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nature genetics

Stalled developmental programs at the root of pediatric brain tumors

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This paper reveals that several types of highly aggressive and, ultimately, fatal pediatric brain tumors originate during brain development. The genetic event that triggers the disease happens in the very earliest phases of cellular development, most likely prenatal. This is known as the Peter Pan Syndrome as these cells are stuck in time, and their inability to age is what causes the tumors. The challenge is now to identify how best to unlock these cells and promote their differentiation, allowing for normal processes to take over.

Stalled development of progenitor cells in the pons and forebrain, where a large proportion of high-grade embryonal and pediatric tumors emerge, is responsible for several childhood brain cancers. Rather than developing normally, the cells' progress is arrested and they transform into malignancies. But they retain many features of the original cells, and the team of bioinformaticians and clinician-scientists were able to pinpoint the tumor origins among the hundreds of different cell types present in the brain. Applying sophisticated single cell sequencing techniques and large-scale data analysis, researchers compiled the first comprehensive profile of the normal prenatal pons, a major structure on the upper part of the brainstem that controls breathing, as well as sensations including hearing, taste, and balance. They created an atlas of more than 65,000 individual cells and defined the developmental dynamics for 191 distinct cell populations. They then mapped patient samples to this atlas, and identified the origins of WNT medulloblastomas, embryonal tumors with multilayered rosettes (ETMRs), and high grade gliomas (HGGs).

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