
Pilocytic astrocytoma of the optic pathway: a tumour deriving from radial glia cells with a specific gene signature.


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Pilocytic astrocytomas are WHO grade I gliomas that occur predominantly in childhood. They share features of both astroglial and oligodendroglial lineages. These tumours affect preferentially the cerebellum (benign clinical course) and the optic pathway, especially the hypothalamo-chiasmatic region (poor prognosis). Understanding the molecular basis responsible for the aggressive behaviour of hypothalamo-chiasmatic pilocytic astrocytomas is a prerequisite to setting up new molecular targeted therapies. We used the microarray technique to compare the transcriptional profiles of five hypothalamo-chiasmatic and six cerebellar pilocytic astrocytomas. Validation of the microarray results and comparison of the tumours with normal developing tissue was done by quantitative real-time PCR and immunohistochemistry. Results demonstrate that cerebellar and hypothalamo-chiasmatic pilocytic astrocytomas are two genetically distinct and topography-dependent entities. Numerous genes upregulated in hypothalamo-chiasmatic pilocytic astrocytomas also increased in the developing chiasm, suggesting that developmental genes mirror the cell of origin whereas migrative, adhesive and proliferative genes reflect infiltrative properties of these tumours. Of particular interest, NOTCH2, a gene expressed in radial glia and involved in gliomagenesis, was upregulated in hypothalamo-chiasmatic pilocytic astrocytomas. In order to find progenitor cells that could give rise to hypothalamo-chiasmatic pilocytic astrocytomas, we performed a morphological study of the hypothalamo-chiasmatic region and identified, in the floor of the third ventricle, a unique population of vimentin- and glial fibrillary acidic protein-positive cells highly suggestive of radial glia cells. Therefore, pilocytic astrocytomas of the hypothalamo-chiasmatic region should be considered as a distinct entity which probably originates from a unique population of cells with radial glia phenotype.

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