NEURO-ONCOLOGY

A molecular staging system for ependymoma

A staging system based on genetic markers could facilitate the stratification and prognostication of intracranial ependymomas, according to research published in the *Journal of Clinical Oncology*. Stefan Pfister, Andrey Korshunov and their colleagues at the German Cancer Research Center, Heidelberg screened a total of 292 patients with ependymoma and identified three subgroups with distinct cytogenetic profiles that correlated with prognosis.

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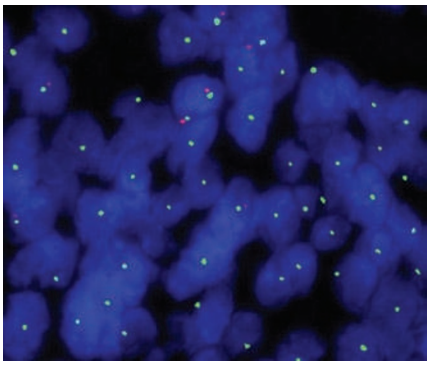
Intracranial ependymoma is one of the most common brain tumors in children and accounts for ≈4% of CNS tumors in adults. "Ependymoma is a challenging tumor in neuro-oncology, since the WHO classification doesn't work for clinical risk stratification, and little is known about its biology," says Pfister. "We probably have the largest uniformly treated and clinically well-documented cohort of ependymoma samples at hand, so we decided to try and find some cytogenetic markers that might be applicable for risk stratification."

The screening cohort consisted of 122 patients, who were investigated at the time of primary diagnosis, before receiving adjuvant therapy. The researchers used array-based comparative genomic hybridization to identify DNA copy-number aberrations in tumor samples from these individuals, and the results were correlated with survival data.

On the basis of their findings, the researchers were able to divide the patients into three distinct subgroups. Gain of chromosome 1q and/or homozygous deletion of the *CDKN2A* gene was associated with anaplastic histology and poor patient survival. Gains of chromosomes 9, 15q and 18 or loss of chromosome 6, on the other hand, were associated with an excellent prognosis. The team also identified an intermediate-risk tumor group, most of which had either a balanced DNA copy-number profile (that is, no detectable chromosomal gains or losses) or a single copy-number aberration.

The candidate prognostic markers identified from the initial screen were validated by means of fluorescence *in situ* hybridization (FISH) in paraffin-embedded ependymoma tissue from a separate cohort of 170 patients. Pfister emphasizes that "FISH is a widely used and robust method to detect DNA copy-number aberrations at relatively low cost with a very high specificity and sensitivity," rendering it very useful for routine application in clinical trials.



Fluorescence *in situ* hybridization analysis of a high-risk ependymoma with homozygous deletion of the *CDKN2A/B* locus (red) and heterozygous loss of the centromeric probe (green). Image provided by Dr Stefan Pfister.

The data obtained from this study indicate that the new molecular staging system has considerably greater predictive power than current systems based on clinical parameters. "The next step will be to validate these findings prospectively in a clinical trial, which we will, hopefully, be able to do in the upcoming European pediatric ependymona trial," says Pfister. The researchers also plan to elucidate the underlying tumor biology in each molecular subgroup, and to develop targeted therapies on the basis of these findings.

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Original article Korshunov, A. *et al.* Molecular staging of intracranial ependymoma in children and adults. *J. Clin. Oncol.* **28**, 3182–3190 (2010)