Potential biomarker discovered to allow more precise classification of malignant brain tumours in children

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Potential biomarker discovered to allow more precise classification of malignant brain tumours in children. Credit: Medical University of Vienna

After leukaemia, primary tumours of the brain and spinal cord are the

second commonest cancers in childhood and adolescence. The presence of the enzyme telomerase characterises a particularly malignant subgroup of cerebellar ependymomas and, in addition to the known markers, could provide information that allows a more accurate prognosis and hence also choice of treatment. This was shown by a study conducted at MedUni Vienna and Vienna General Hospital within the framework of the Comprehensive Cancer Center (CCC) and in collaboration with the German Cancer Research Center in Heidelberg. The study has now been published in leading journal Nero-Oncology.

Ependymomas are the third commonest central nervous system tumours in children. They are often highly aggressive within this age-group and the prognosis for patients is poor. In Austria, nine children a year are diagnosed with this type of tumour. The current treatment is surgical removal followed by radiotherapy and chemotherapy.

Many subtypes – one name

The most recent research has shown that ependymomas are not an homogenous type of tumour but can be divided into several subgroups, based on their molecular biological characteristics. These subgroups all have different prognoses and therefore probably also require different treatment.

Enzyme stimulates tumour growth

The new study by Johannes Gojo, junior doctor and researcher at the Department of Pediatrics and Adolescent Medicine of MedUni Vienna and Vienna General Hospital and member of the CCC, investigated whether the enzyme telomerase could be used as a biomarker for ependymomas. Says Gojo: "We were able to show that telomerase was primarily reactivated in tumours that exhibit a particularly aggressive

course. This means that, despite surgical removal and subsequent radiotherapy and chemotherapy, the tumour recurred." The scientists suspect that this will enable them to identify patients who would benefit from more intensive treatment. Conversely, patients with less aggressive tumours could be spared chemotherapy. This would mean a huge improvement in quality-of-life for those affected. Says Gojo: "Thus, together with other parameters, the presence of telomerase could be a big help in deciding on the course of treatment. It therefore represents a highly promising biomarker. However, before we can use the concept clinically, it needs to be validated in further studies."

The study team were also able to gain initial insights into the mechanisms that lead to reactivation of telomerase.

Telomeres determine lifetime

"Human cells are mortal. This means that their lifetime is not determined by the clock or the calendar but by their ability to divide: the longer the so-called telomeres, the more often the cells are able to divide," explains Walter Berger, Deputy Head of the Institute of Cancer Research at MedUni Vienna, member of the CCC and joint corresponding author of the study, alongside Christine Haberler of the Institute of Neurology.

Telomeres are "caps" on the end of chromosomes, which protect the chromosomes from breaking and hence "fraying", as it were, which would result in cell damage. The telomeres shorten with each cell division. If the telomeres are too short or if the cell loses the ability to produce telomerase, it initiates cell death and dies. The enzyme telomerase can preserve telomeres or at least can restore them to their original length. Many tumours have the ability to reactivate telomerase, which then facilitates unrestricted growth.

The results of the study have now been published in *Neuro-Oncology*, one of the leading specialist journals in this field. Appearing in the same issue was an expert commentary from two international experts, who rated the paper as highly relevant.

More information: Johannes Gojo et al. Telomerase activation in posterior fossa group A ependymomas is associated with dismal prognosis and chromosome 1q gain, *Neuro-Oncology* (2017). DOI: 10.1093/neuonc/nox027

Michal Zapotocky et al. Can telomerase activity be unleashed to refine prognosis within ependymoma subgroups?, *Neuro-Oncology* (2017). DOI: 10.1093/neuonc/nox059

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