Factor that predicts long survival in brain tumors

August 30 2019, by Dr. Manel Esteller

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The discoveries in the cellular and molecular biology of cancer, the development of drugs against specific genetic mutations, and the emergence of immunotherapy are allowing the cure or improvement of

the quality of life and life expectancy of patients with tumors. However, gliomas still resist these encouraging trends.

Gliomas, brain tumors that are not born from neurons but from glial cells , represent a sad exception. The mortality of brain cancer is around 85 percent within two years after diagnosis. It is, therefore, an area of intense biomedical research.

The group of Dr. Manel Esteller, director of the Josep Carreras Research Institute, ICREA Researcher and professor at the University of Barcelona, has published this finding in the journal *Acta Neuropathologica*. The research describes an epigenetic lesion as a marker of brain tumors with good prognosis, and 15 percent of cases that will have prolonged survival.

"We began the study looking for genes with regulatory functions of genome expression that lost their activity in cancer. We identified a particular gene called NSUN5 of which we knew almost nothing about its function. What surprised us most from the beginning was that its alteration, among the many types of tumors of the human body, was almost exclusive to gliomas, a type of brain cancer. We investigated it in laboratory cells and experimental models. When we got to analyze its impact on patients with glioma, we realized the importance of the finding. The epigenetic lesion of NSUN5, independently of other biomarkers, predicted that minority percentage of patients who would do well. It was astonishing, since most of the time, we discover factors that indicate tumors that will go bad," says Dr. Esteller.

"Mechanically, it seems that by the evolutionary selection, a brain tumor that is about to become extinct ends up causing the alteration of NSUN5. Then, NSUN5 'freezes,' as if standing in time, so that cancer progresses less and survival lengthens. Microenvironment factors surrounding the glioma such as lack of oxygen and lack of local nutrients contribute to

induce NSUN5's inactivation. This process allows the tumor not to die, but grow so little that the patient shows a good prognosis. Therefore, we now have a marker that allows us to predict the 15 percent of cases with good clinical course. Furthermore, it would be exceptional to convert 85 percent of the remaining cases into patients who, 'touching' the NSUN5 gene, also had extended survival. We still don't know how to do it, but it deserves to be investigated carefully," concludes Dr. Esteller.

More information: Maxime Janin et al. Epigenetic loss of RNA-methyltransferase NSUN5 in glioma targets ribosomes to drive a stress adaptive translational program, *Acta Neuropathologica* (2019). DOI: 10.1007/s00401-019-02062-4

Provided by University of Barcelona