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SETMAR IN GLIOBLASTOMA: SPLICE VARIANTS AND FEEDBACK NETWORK IN CONTROLLING TARGET GENES EXPRESSION

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SETMAR is a chimeric protein, acting as a house-kipping genome guardian in healthy cells. In a recent work [i], we demonstrate that SETMAR expression increases in GBM where different splice variants are produced depending on the stage of the cells: stem cells express a small hyper-stable SETMAR (sm-SETMAR) whereas differentiated cells express a large form known as the "regular" SETMAR enzyme (r-SETMAR). The only difference between both SETMAR proteins originates from the lack of the SET domain on the sm-SETMAR, due to exon-exclusion during pre-mRNA maturation. As a result sm-SETMAR is devoid of any methyl-transferase activity, preventing chromatin modifications and regulations usually assign to r-SETMAR. In contrast, both proteins are still able to promote DNA repair by NHEJ, albeit sm-SETMAR is less effective. Our current works hypothesis that sm-SETMAR may contribute to confer cancer stem cells properties of chimio- and radio-resistance, in addition to alter their normal epigenetic profile. Because SETMAR originates from a mobile genetic element, the human genome contains of thousands of SETMAR DNA binding sites that are in fact fossils of the original transposon. They together constitute a regulatory network. The characterization of target genes differentially regulated by the one or other one of the SETMAR proteins through this network during GBM biogenesis is under progress.

BIOGRAPHY

Corinne Auge Gouillou has completed her PhD at the Pasteur Institute of Paris in 1993 and postdoctoral studies from Tours University. She has been leading her research team for over 15 years and published more than 25 papers in reputed journals. She is very strongly involved in teaching and pedagogy, especially for young students who arrive at the University. She has been serving as a referee for many journals, and led a French network dedicated to mobile DNA.

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