Glioblastoma is the most common primary brain tumour. Despite the introduction of heavy and aggressive treatment, the median survival is 12 to 15 months, linked in particular to almost constant relapses. Glioblastoma stem cells (CSG) are cells within the tumour, capable of self-renewal and differentiation into the cellular sub-populations that make up glioblastoma. The recent data make them considered to have a major role in both the development of these tumors but also and especially in the resistance to the different therapies (chemo and radiotherapy) and therefore in the recurrences. A better understanding of the molecular and cellular mechanisms involved in the characterization of these CSGs, their development and the mechanisms involved in their therapeutic escape is therefore fundamental. To do this, being able to dissect these in vitro mechanisms is a prerequisite and necessary step. Finally, the targeting of therapeutic active ingredients towards CSGs becomes necessary, in addition to conventional treatments, in order in particular to limit toxic side effects on the normal surrounding tissue.

The aim of the proposed project is to understand the effects of this peptide on glioblastoma stem cells.

Main milestones of the thesis (approximately 12 lines):
Major stages of the thesis (approx. 12 lines):
Based on these preliminary results of glioblastoma (CSG) or gliosphere stem cell models, the objectives are to characterize Cscs, understand their resistance mechanism(s) and determine the effects of a peptide (NFL-TBS.40-63) recently isolated by the laboratory. The research programme will be carried out along two axes:
1: the determination of molecular characteristics (expression or suppression of gene(s) or protein(s) by RT-PCR, western-blots, FACS, etc.) and cellular (proliferation, viability, migration, etc.) with particular reference to defining the resistance mechanisms of these CSG, focusing on the processes of hypoxia.
2: determination of the effects of the peptide NFL-TBS.40-63 (dose effect, LD50, proliferation, self-esteem, etc.). We will also study the targeting capabilities of this peptide when adsorbed to the surface of lipid nanocapsules (Lncs) containing TMZ.

Scientific and technical skills required by the candidate (2 lines):
Molecular and cellular biology

3 publications from the team related to the topic (last 5 years):
The NFL-TBS.40-63 peptide targets and kills glioblastoma stem cells derived from human patients and also targets nanocapsules into these cells, Lépinoux-Chambaud C. Eyer J. Int J Pharm. 2019 Jul 20;566:218-228

National and international collaborations:
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