P44 – **Effects of microbiota modulation on tumor microenvironment in glioma**

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Glioblastoma multiforme (GBM) is a CNS tumor with a poor prognosis. One of the main reason of its recurrence is the presence of a tumor microenvironment that hampers the tumor suppressive functions of innate and adaptive immune cells, compromising their pro inflammatory, anti- tumor activity (1). GBM secretes immunosuppressive factors responsible for the recruitment of cellular elements like microglia and perivascular macrophages, that account up to about 30 % of total tumor mass, whose presence negatively correlates with patient's survival (2,3). The panel of GBM infiltrating immune cells comprises leukocytes, like tumor infiltrating lymphocytes, but also Treg and natural killer (NK) cells (4-6). NK cells, once activated, might have direct cytolytic activity against cancer cells and are currently seen as a key weapon in the success of dendritic cell vaccination strategy (7). Microglia phenotype is also deeply influenced by gut-resident microbes (8), and an unbalanced composition of host microbiota is now recognized as a key element that impairs the host metabolism and the immune system, playing important role not only in systemic diseases, but also modulating several brain functions (9,10). The main objective of the present study is the identification of molecular and cellular targets that could revert the vicious cycle occurring among brain tumor cells, microglia and infiltrating immune cells that, creating an immunosuppressive environment, restrains the host response against malignant glioma. At this aim, wild type mice or murine syngeneic glioma models (GL261 murine glioma cells in C57Bl6 mice) have been treated with cocktails of not orally absorbable antibiotics to induce dysbiosis and analyzed for central/peripheral immune cell activation and glioma growth. Preliminary results we obtained already indicate that it is possible to modulate brain microenvironment inducing a dysbiotic state by two-week antibiotic treatment and that this affects tumor brain microenvironment and growth.

References

1. Xie Q et al. Neuro Oncol. 2014 Dec;16(12):1575-84.
2. Okada M et al. Int J Oncol. 2009 Jun;34(6):1621-7.
3. Ooi YC et al. Clin Neurol Neurosurg. 2014 Apr; 119:125-32.
4. Dunn GP et al. Cancer Immun. 2007 Aug 13;7:12.
5. Lowther DE, Hafler DA Regulatory. Immunol Rev. 2012 Jul;248(1):156-69.
6. Kmiecik J et al. Oncoimmunology. 2014 Jan 1;3(1):e27185.
7. Lion E et al. Oncologist. 2012;17(10):1256-70. doi: 10.1634/theoncologist.2011-0122.
8. Erny D et al. Nat Neurosci. 2015 Jul;18(7):965-77.
9. Bull MJ, Plummer NT. Integr Med (Encinitas) 2014; 13:17–22
10. Frohlich EE et al. Brain Behav Immun 2016; 56: 140–55