Microglia polarization in neuro-oncology

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Although microglia with different phenotypes can co-exist within the same tumor, their activation/function vary with the location in the tumor and/or at different stages of disease. Recently we have investigated microglia polarization in the framework of microglia interactions with primary brain tumors. In a series of in vitro experiments, we have characterized the influence of glioma-soluble factors on microglial function, comparing the effects of media harvested under basal conditions with those of media obtained after inducing a pro-inflammatory activation state in glioma cells. Microglia exposed to basal glioma-derived factors (a condition resembling the early stage of pathology), shows increased M2b polarization status and up-regulation of IL-10 only. At variance, when exposed to activated glioma-derived factors (a condition mimicking the late stage of pathology), microglia presents as a mixture of polarization phenotypes (M1 and M2a/b), with up-regulation of iNOS, Arginase and IL-10 (Lisi et al 2014a). In this paradigm, the inhibition of mTOR polarizes glioma-activated microglial cells towards the M1 phenotype, thus preventing the induction of the M2 status that would promote tumor growth (Lisi et al 2014b). Investigations are currently underway on 42 surgical specimens of human glioblastoma multiforme. To study change in the number, morphology and activity of microglial cells present at center of tumor *versus* microglia present at tumor periphery we compare the number of CD163 (marker of macrophage-microglia phenotype) positive cells. In addition we are investigating iNOS (M1 marker), Arginase (M2 marker) and phospho-mTOR positive cells in both the paradigms (center *vs* periphery).

References

Lisi L, Stigliano E, Lauriola L, Navarra P, Dello Russo C. Proinflammatory-activated glioma cells induce a switch in microglial polarization and activation status, from a predominant M2b phenotype to a mixture of M1 and M2a/B polarized cells. ASN Neuro. 2014 May 8;6(3):171-83. (a)

Lisi L, Laudati E, Navarra P, Dello Russo C. The mTOR kinase inhibitors polarize glioma-activated microglia to express a M1 phenotype. J Neuroinflammation. 2014 Jul 23;11:125. (b)