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Microglia polarization: A common paradigm spanning from neuro-oncology to infectious diseases

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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. In this paradigm, the inhibition of mTOR shifts polarization of glioma-activated microglial cells towards the M1 phenotype, thus preventing the induction of a M2 status that would promote tumor growth. Investigations are currently underway on 54 surgical specimens of glioblastoma multiforme to confirm the influence of brain tumors on microglia polarization. An apparently unrelated line of research in our lab was addressed to investigate the effects of antiretroviral drugs exposure on microglia cultures, seeking for putative mechanisms of neurotoxicity. We found that certain NNRTIs and PIs increased NO production thorough a mechanism independent from iNOS induction. Rather, these agents increased the availability of the iNOS substrate L-arginine by blocking arginase, a well-established marker of M2 polarization. Thus, the investigation of microglia polarization markers turns out to be a common background linking studies on the most different patho-physiological conditions involving the CNS.

Biography

Pierluigi Navarra is full Professor of Pharmacology at the Catholic University Medical School in Rome. He has published more than 180 full papers listed in PubMed.

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