**Toward a better understanding of long term brain consequences of Preterm Birth**

**Background:** Preterm birth (<37 of 41 weeks’ gestation) represents 15 million births every year. As the surviving population of children born prematurely ages, new deficits appear over the years, which are directly linked to the status of individuals at the time of their birth (gestational age, birth weight, and inflammatory status). A growing body of evidence shows that the effects on the brain continue for many weeks or even years afterward, increasing the risk of further neurological damages and neurodevelopmental disorders (NDD). Preterm birth induces white matter and gray matter lesions grouped together under the term Encephalopathy of Prematurity (EoP). At the heart of EoP is the reactivity of the glial cells, both executioners (microglial cells) and victims (oligodendrocytes cells) of maternal-fetal infections/inflammations linked to prematurity (40 % of spontaneous preterm birth). Evidence demonstrated that long after initial reactivity, glial cells are keener to react exaggeratedly to a second inflammatory stimuli, most probably through cellular priming.

**Results:** Our hypothesis is that microglial cells engaged in an inflammatory path do not contributeto the formation of the mature cerebral connectivity network as they should, leading to NDD. Microglia primed by perinatal inflammation could increase the healthy age-related inflammation state leading also in long term to an early pathological brain aging. This study is based on a mouse model of perinatal inflammation responsible for EoP-like lesions. We demonstrated early behavioral and brain connectivity deficits relevant to NDD-like by the inflamed microglia. Moreover, using similar approached months after the acute inflammatory hit, we observed a decreased of brain functions associated with a long-term re-activation of microglia.

**Conclusion:** Research focused on cellular reactions that occur in the hours or days after an injury has failed to produce an effective therapeutic for EoP. We demonstrated that there is a tertiary phase of EoP. We aim to change this “acute inflammation phase” focus by illustrating the potential of normalizing long-term persisting glial dysfunction to improve brain structure and health. With this knowledge, we can develop targeted therapies to improve neurodevelopmental outcomes that can be implemented during adulthood.