Sonia GAREL
Biens – Institut de biologie de l'Ecole normale supérieure
ENS, Paris – France

Microglia in the early wiring of the neocortex

Prenatal inflammation and dysfunction of microglia, the brain resident macrophages, have both been associated with the etiology of several neuropsychiatric disorders, including schizophrenia and autism spectrum disorders. Consistently, microglia were shown to regulate neurogenesis, synaptic remodeling and maturation at postnatal stages. However, microglia invade the brain during mid-embryogenesis and could thus exert earlier prenatal and perinatal roles during normal and pathological brain wiring. Here we show that embryonic microglia, which display a transient uneven distribution, regulate the wiring of forebrain circuits. By taking advantage of multiple mouse models, including cell-depletion approaches, we found that perturbing microglia activity affects the development of neocortical inhibitory interneurons, which constitute main actors in neuropsychiatric diseases. In particular, absence, prenatal inflammation or functional perturbation of microglia affects the timely positioning of specific subsets of interneurons as well as their subsequent functional integration in the neocortex. We furthermore found that responses of microglia to environmental signals, including the ones from the microbiome, are sexually dimorphic in males and females. This remarkable finding has major implications for our comprehension of sexual biases in the occurrence of microglia-related diseases, such as the prevalence in males of neurodevelopmental disorders. Our work reveals key roles for immune cells during the normal assembly of cortical circuits and provides novel insights onto how microglia dysfunction or immune risks lead to pathological brain wiring.