Role of microglia in neurodevelopmental disorders

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Neurodevelopmental disorders are affecting children worldwide and the number of children affected by Autism Spectrum Disorder (ASD) has grown at an alarming rate, with a current U.S diagnosis of 1 in 68 births. In the absence of a cure, there is an urgent need in developing novel therapies for ASD. Patients suffering from ASD present social deficits and learning disabilities associated with microglia abnormalities, the immune cells of the brain, necessary for an adequate neurodevelopment. Using maternal immune activation (MIA) as a rodent model of ASD, we revealed microglia as a viable therapeutic target. Indeed, we found that pharmacological microglia replacement reversed MIA-induced social and repetitive behaviors abnormalities and neuronal alterations. We then investigated MIA-induced learning deficits and showed that microglial renewal can also normalize learning abilities. In addition, we identified potential microglial gene candidates as MIA-mediators, including Wnt5a. Using ex-vivo technologies we showed that targeting microglial Wnt5a gene can affect neuronal morphology and activity. Finally, we used a transgenic Wnt5a-microglia specific knockdown mouse model and found a promising correction of MIA-induced social deficits by targeting Wnt5a in microglia. Together, we showed that MIAinduced neuronal deficits are linked to microglial alterations, leading to aberrant synaptogenesis and behavioral deficits in offspring. Our research aims to better understand neurodevelopmental disorders and to the development of a new line of treatment beneficial for patients suffering from neurodevelopmental disorders.