4th Draft

Maternal Immune Activation

and

Neuro-Developmental & Psychiatric Disorders

1. What causes Maternal Immune Activation (MIA)?

2. What is the importance of Microglia and the Embryonic Yolk-Sac?

Fetal brain response to maternal inflammation requires microglia (2024)

Using a rodent **maternal immune** activation (MIA) model in which polyinosinic:polycytidylic acid is injected into pregnant mice, we demonstrate long-lasting transcriptional changes in fetal microglia that persist into postnatal life.

Microglial GPR56 is the molecular target of maternal immune ...(2022)

Maternal inflammation induces immune activation of fetal

The role of **microglia** in early neurodevelopment and the effects of **maternal immune activation**. (2024)

The timing of **immune activation** may interfere with **microglia** functioning during early neurodevelopment, potentially leading to long-term consequences in postnatal life. In this review we will discuss the involvement of **microglia** in brain development du …

3. What Systems of the body does MIA dysregulate?

4. What Cell Types and Cellular Pathways does MIA dysregulate?

5. What is the role of Epigenetics?

Evidence from human and animal studies indicates that **maternal immune activation** programmes the fetal brain and immune system through inflammatory and **epigenetic** mechanisms during key periods of CNS, microglial and immune system development, and colonization of gut microbiota.

Maternal immune activation and neuroinflammation in human ...

Maternal immune activation in rodent models: A systematic review of neurodevelopmental changes in gene expression and **epigenetic** modulation in the offspring brain.

Neurosci Biobehav Rev. 2021

Maternal immune activation (mIA) during pregnancy is hypothesised to disrupt offspring neurodevelopment and predispose offspring to neurodevelopmental disorders such as schizophrenia. ...Across 118 studies, we focus on 88 candidate genes and show replicated c …

Brain methylome remodeling selectively regulates neuronal **activity** genes linking to emotional behaviors in mice exposed to **maternal immune activation**.

Nat Commun. 2023

How early life experience is translated into storable **epigenetic** information leading to behavioral changes remains poorly understood.

Here we found that Zika virus (ZIKV) induced-**maternal immune activation** (MIA) imparts offspring with anxiety- and depr …
Transcriptional and **Epigenetic** Regulation of Microglia in Health and Disease.

Trends Mol Med. 2019

The transcription factor PU.1 plays a key role in regulating several **microglial** functions. Environmental factors such as microbiota, early life stress, and **maternal**

immune activation can dysregulate PU.1 and innate **immune** response. This review d …

6. What Neuro-Developmental Disorders are associated with MIA?

7. What Psychiatric Disorders are associated with MIA?

8. Are there transgenerational aspects of MIA?

9. Are there attempts to reverse MIA?

- Rescue of **maternal immune activation**-induced behavioral abnormalities in adult mouse offspring by pathogen-**activated maternal** T(reg) cells. Xu Z, Zhang X, Chang H, Kong Y, Ni Y, Liu R, Zhang X, Hu Y, Yang Z, Hou M, Mao R, Liu WT, Du Y, Yu S, Wang Z, Ji M, Zhou Z. Nat Neurosci. 2021 Jun;24(6):818830. doi: 10.1038/s41593-021-00837-1. Epub 2021 Apr 15. PMID: 33859437
  Maternal immune activation (MIA) induced by lipopolysaccharides or polyinosinic:polycytidylic acid injections can induce behavioral abnormalities in adult mouse offspring. ...We show that adoptive transfer of regulatory T (T(reg)) cells largely **reversed** …

- Resveratrol ameliorates **maternal immune activation**-associated cognitive impairment in adult male offspring by relieving inflammation and improving synaptic dysfunction.
  Zhang YM, Wei RM, Zhang MY, Zhang KX, Zhang JY, Fang SK, Ge YJ, Kong XY, Chen GH, Li XY. Front Behav Neurosci. 2023 Nov 22;17:1271653. doi: 10.3389/fnbeh.2023.1271653. eCollection 2023. PMID: 38074521 Free PMC article.
  Additionally, the levels of interleukin (IL)-1beta, IL-6, and tumor necrosis factor-alpha (TNF-alpha) were increased while those of SIRT1, BDNF, PSD95, and SYP were decreased in male offspring of LPS-treated **mothers**.
  Treatment with resveratrol **reversed** cognitive im …

Maternal immune activation results in complex microglial transcriptome signature in the adult offspring that is reversed by minocycline treatment

The rebalancing of the immune system at the maternal-fetal interface ameliorates autism-like behavior in adult offspring