



Paris, December 19, 2017

## Press release

---

# Microbiome Influences Brain's Immune Cells in a Sex and Age-dependent manner

**A joint study conducted by Inserm researchers from IBENS (Institute of Biology of the Ecole Normale Supérieure – Inserm/CNRS/ENS) in Paris and researchers from SIgN (Singapore Immunology Network, A\*STAR) in Singapore reveals a hitherto undiscovered impact of microbiota on immune brain cells, occurring from fetal stages. These cells, called microglia, which are known players in brain development and functioning, differentially respond to microbiome perturbations in male or female mice. These results are published in *Cell*.**

Microglia are immune cells that respond to traumatic injury or inflammatory signals to protect the brain, acting as sensors of various environmental signals. In addition to their role as immune sentinels, microglia have also been shown to regulate several steps of brain wiring and functioning. Consistently, microglia dysfunction has been linked with the etiology of several neurodegenerative diseases and neurodevelopmental disorders, including Schizophrenia or Autism Spectrum Disorders. Microglia therefore play major roles in brain circuits and could constitute an entry point for environmental signals.

To test this hypothesis, Morgane Thion and Sonia Garel, Inserm researchers, together with their associates, used a multidisciplinary approach involving germ-free mice, which lack all the microbiome, and adult mice treated with antibiotics, which acutely destroys the gut flora. Through a combination of global genomic analyses and histological studies, researchers have shown that microglia are profoundly affected by microbiota disruption, already from prenatal stages. Strikingly, the impact of the microbiome on microglia depended on the sexual identity and the age: microglia of males were perturbed prenatally whereas those of females were affected in adulthood. This surprising sexual dimorphism echoes the fact that many neurodevelopmental disorders have a higher incidence in men, whereas autoimmune diseases are more prevalent in women.

While the underlying mechanisms and consequences remain to be discovered, this study reveals a key role of microglia at the brain/environment interface and shows that males and females have distinct susceptibilities to microbiome alterations. For the authors,

these elements should be systematically taken into consideration at preclinical and clinical level.

## Source

***“Microbiome influences prenatal and adult microglia in a sex-specific manner”***

**Morgane Sonia Thion<sup>1,15</sup>, Donovan Low<sup>2,15</sup>, Aymeric Silvin<sup>2,16</sup>, Jinmiao Chen<sup>2,16</sup>, Pauline Grisel<sup>1,16</sup>, Jonas Schulte-Schrepping<sup>3</sup>, Ronnie Blecher<sup>4</sup>, Thomas Ulas<sup>3</sup>, Paola Squarzoni<sup>1</sup>, Guillaume Hoeffel<sup>2</sup>, Fanny Coupier<sup>1</sup>, Eleni Siopis<sup>5</sup>, Friederike Sophie David<sup>3</sup>, Claus Scholz<sup>3</sup>, Foo Shihui<sup>2</sup>, Josephine Lum<sup>2</sup>, Arlaine Anne Amoyo<sup>6</sup>, Anis Larbi<sup>2</sup>, Michael Poidinger<sup>2</sup>, Anne Buttgereit<sup>7</sup>, Pierre-Marie Lledo<sup>5</sup>, Melanie Greter<sup>7</sup>, Jerry Kok Yen Chan<sup>8,9</sup>, Ido Amit<sup>4</sup>, Marc Beyer<sup>3,10</sup>, Joachim Ludwig Schultze<sup>3,11</sup>, Andreas Schlitzer<sup>2,12</sup>, Sven Pettersson<sup>11,14</sup>, Florent Ginhoux<sup>2,17,18,\*</sup>, Sonia Garel<sup>1,17,\*</sup>**

<sup>1</sup>Institut de Biologie de l'Ecole normale supérieure (IBENS), Ecole Normale Supérieure, CNRS, INSERM, PSL Research University, 75005 Paris, France

<sup>2</sup>Singapore Immunology Network, Agency for Science, Technology and Research, Singapore, 138648, Singapore

<sup>3</sup>Genomics and Immunoregulation, Life and Medical Sciences (LIMES) Institute, University of Bonn, 53115 Bonn, Germany

<sup>4</sup>Department of Immunology, Weizmann Institute of Science, 76100 Rehovot, Israel

<sup>5</sup>Institut Pasteur, Unité Perception et Mémoire, CNRS, UMR 3571, F-75015 Paris, France

<sup>6</sup>National Cancer Centre, Singapore, 169610, Singapore

<sup>7</sup>Institute of Experimental Immunology, University of Zurich, 8057 Zurich, Switzerland

<sup>8</sup>Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore, 229899, Singapore

<sup>9</sup>KK Research Centre, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore, 229899, Singapore

<sup>10</sup>Molecular Immunology in Neurodegeneration, German Center for Neurodegenerative Diseases (DZNE), 53127 Bonn, Germany

<sup>11</sup>Platform of Single Cell Genomics and Epigenomics at the German Center for Neurodegenerative Diseases and the University of Bonn, 53175 Bonn, Germany

<sup>12</sup>Myeloid Cell Biology, LIMES-Institute, University of Bonn, 53115 Bonn, Germany

<sup>13</sup>Lee Kong Chian School of Medicine and School of Biological Sciences, Nanyang Technological University, Singapore, 639798, Singapore

<sup>14</sup>Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, 17165, Sweden

**Cell, <https://doi.org/10.1016/j.cell.2017.11.042>**

## Researcher contact

### **Sonia Garel**

Inserm Research Director

Institute of Biology of the Ecole Normale Supérieure (IBENS), Ecole Normale Supérieure, Paris

Tel.: +33 (0)6 33 49 48 14

Email: garel@biologie.ens.fr