# Nurturing developing neurons: How microglia contribute to brain development by interacting with newborn neurons

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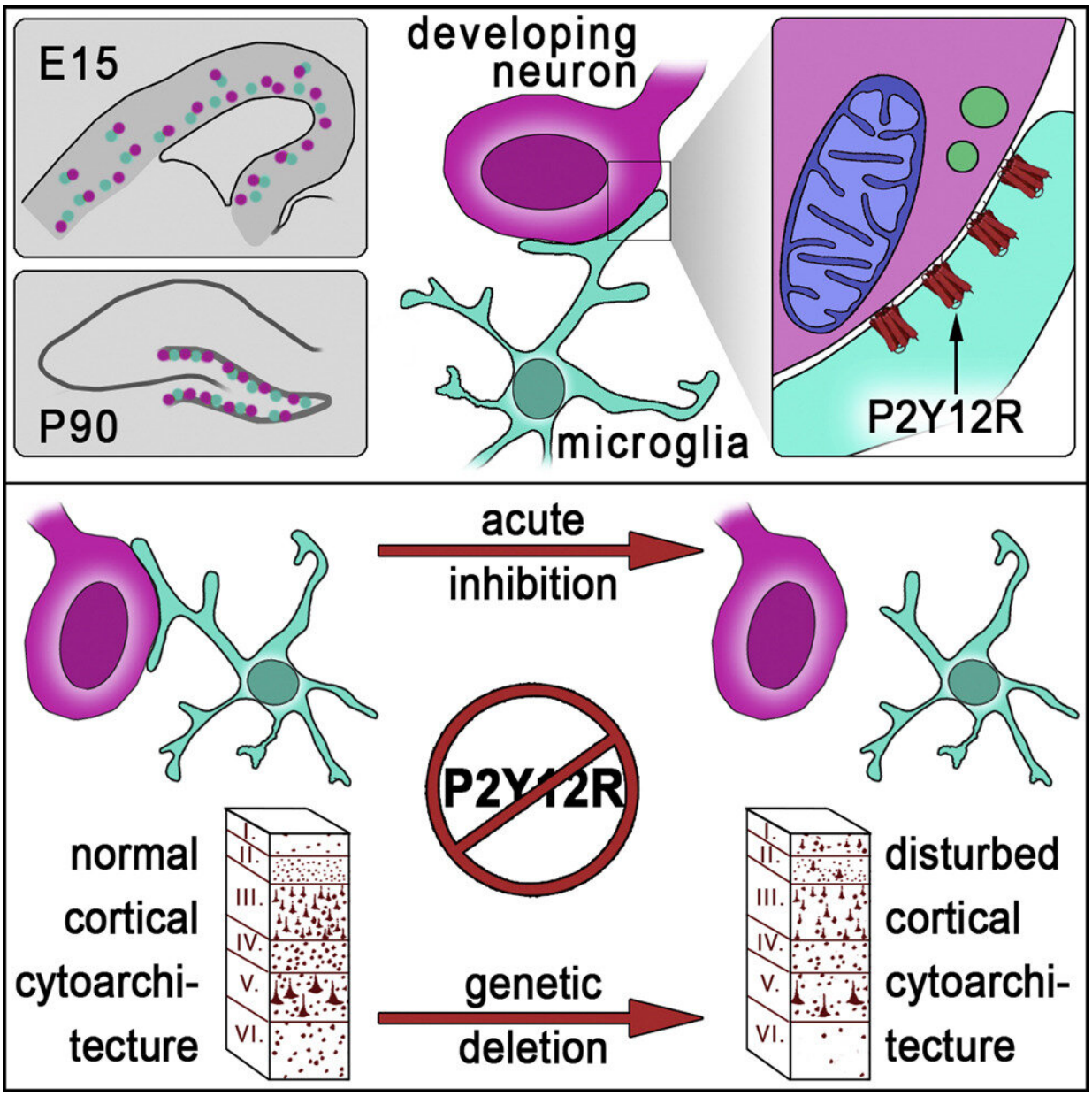


Graphical abstract. Credit: *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111369

The Laboratory of Neuroimmunology of the Institute of Experimental Medicine, Budapest (IEM), Hungary, led by Ádám Dénes, describes the presence of a direct interaction site between microglial cells and the cell body of developing neurons, and reveals its role during brain development. The discovery may be of importance for developmental disorders affecting the nervous system.

The study presenting the results of the research was published in *Cell Reports*.

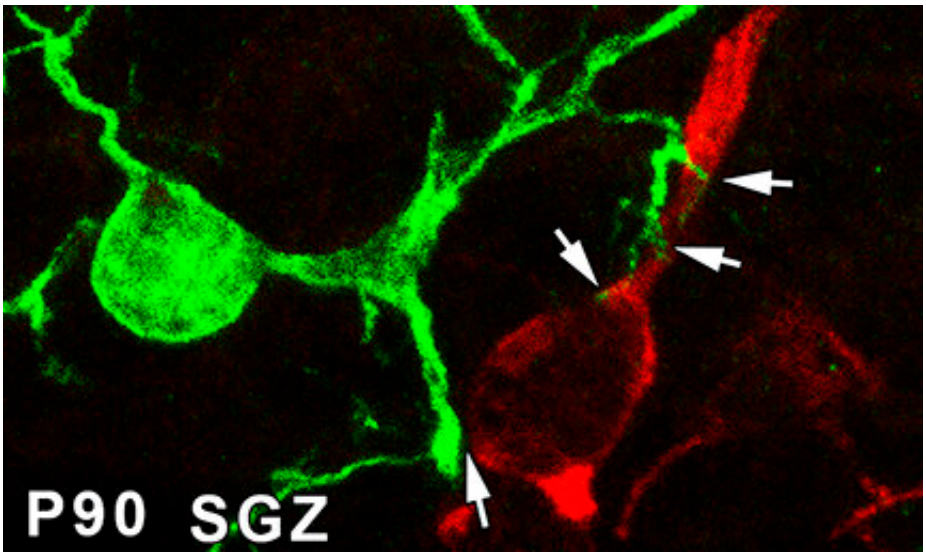
The scientific community knows microglia as the main immune cell of the central nervous system and as the main regulator of inflammatory processes in the brain. The role of inflammatory processes and microglia is also increasingly recognized in neurodevelopmental disorders.

The investigation of the role of microglia in physiological and pathological conditions has become a dynamically developing research field in recent years. The research group has accumulated a significant amount of knowledge in the field of microglia-neuron cell communication, and several of their publications on this subject have received international attention.

They have discovered a novel form of communication established by direct contacts between microglia and the cell body of nerve cells, named somatic microglia-neuron junctions, and revealed the role of these specialized contact sites in microglia-mediated protection of

injured neurons.

Although the important role played by microglia during brain development had been suggested by many previous studies, the exact cellular communication pathways enabling microglia to influence the development of neurons and the formation of neural networks in the brain has been unclear.




Microglia (green) contact newborn neurons (red) in mouse hippocampus. Credit: Institute pf Experimental Medicine, EÖTVÖS LORÁND Research Network

In particular, it was not well understood how and through what types of connections developing neurons that have not yet established interaction with other neurons in the absence of synapses may recieve guidance from microglial cells to develop into complex networks in the developing neocortex.

Among the members of Ádám Dénes' research group, Csaba Cserép and his student Dóra Anett Schwarcz played an outstanding role in the implementation of the research program, with further contribution of the

research group of István Katona at IEM.

During their investigations, the researchers used both high-resolution molecular anatomy techniques, combined light and electron microscopy, and ex vivo imaging studies. Using a multifaceted approach, the researchers proved the presence of direct connections between microglia and developing neurons both during embryonic development and after birth.

"The special, dynamically changing anatomical connections between microglia and developing, immature neurons are similar to the previously discovered somatic microglial junctions in many ways, and their special molecular composition and ultrastructure enable microglia to continuously monitor and effectively influence the development and integration of neurons into complex networks," said Csaba Cserép, the first author of the work.

When the researchers inhibited the communication through the key microglial receptors that are highly enriched at these sites, the development of the normal structure of the cerebral cortex was disturbed. Therefore, microglia should be considered an important regulatory cell type of brain development via these special interaction sites and beyond.

"More thorough understanding of microglial mechanisms that are required for the proper development of the brain may help to find novel therapies for neurodevelopmental disorders and other forms of brain diseases that represent an unresolved challenge worldwide," concluded Ádám Dénes group-leader, the last author of the publication.

**More information:** Csaba Cserép et al, Microglial control of neuronal development via somatic purinergic junctions, *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111369

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