

Project Leader **Yoshitaka Tatebayashi** Affective Disorders Research Project

Our Goal is to Decipher the Neurobiological Bases of Affective Disorders.

Major depressive disorder (MDD) and bipolar disorder (BD), collectively known as affective disorders, are essentially relapsing and remitting disorders of affect with nearly full recovery between episodes. We use human postmortem brains of these disorders and animal and cell culture models to identify the processes in which stress or aging causes changes in brain to induce these disorders. A major focus of our work is stress-induced or age-related changes in cellular structure, especially that of oligodendrocyte lineage cells and lipid, within the brain's mood circuitry. We are also interested in the biological relationship between affective disorders and dementias such as Alzheimer's disease.

“Our human postmortem brain studies reveal oligodendroglial reductions and myelindependent fatty acid abnormalities in the frontopolar cortex in affective disorders.”

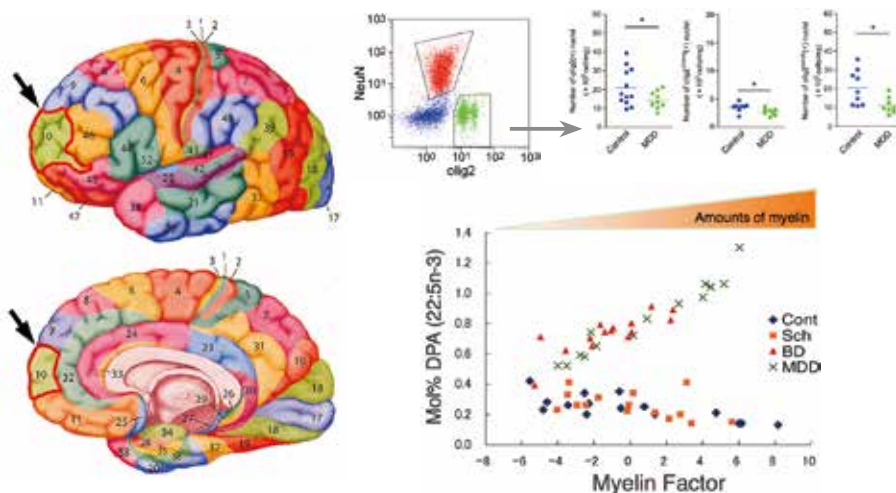
Bauer M, (64 co-authors), Tatebayashi Y et al. (2014) “Relationship between sunlight and the age of onset of bipolar disorder: an international multisite study.” *J. Affect. Disord.* 167:104-111.

Nihonmatsu-Kikuchi N, Hayashi Y, Yu XJ, and Tatebayashi Y. (2013) “Depression and Alzheimer's disease: novel postmortem brain studies reveal a possible common mechanism.” *J. Alzheimers Dis.* 37: 11-21.

Tatebayashi Y, Nihonmatsu-Kikuchi N, Hayashi Y, Yu XJ, Soma M, and Ikeda K. (2012) “Abnormal fatty acid composition in the frontopolar cortex of patients with affective disorders.” *Transl. Psychiatry* 2:e204.

Hayashi Y, Nihonmatsu-Kikuchi N, Hisanaga S, Yu XJ, and Tatebayashi Y. (2012) “Neuropathological similarities and differences between schizophrenia and bipolar disorder: a flow cytometric postmortem brain study.” *PLoS One.* 7: e33019.

Hayashi Y, Nihonmatsu-Kikuchi N, Yu XJ, Ishimoto K, Hisanaga SI, and Tatebayashi Y. (2011) “A novel, rapid, quantitative cell-counting method reveals oligodendroglial reduction in the frontopolar cortex in major depressive disorder.” *Mol. Psychiatry.* 16: 1155-1158.



The exact functions of the human frontopolar cortex (BA10) remain enigmatic. Given that the BA10 is thought to be the most evolutionarily recent expansion of the primate prefrontal cortex, its function may uniquely reflect human adaptations in the context of selecting and updating models of reward contingency in dynamic environments. As adulthood cortical myelination is an essential process for the establishment of efficient neuronal signaling networks, any abnormalities in this process may have important roles in the pathophysiology of affective disorders.

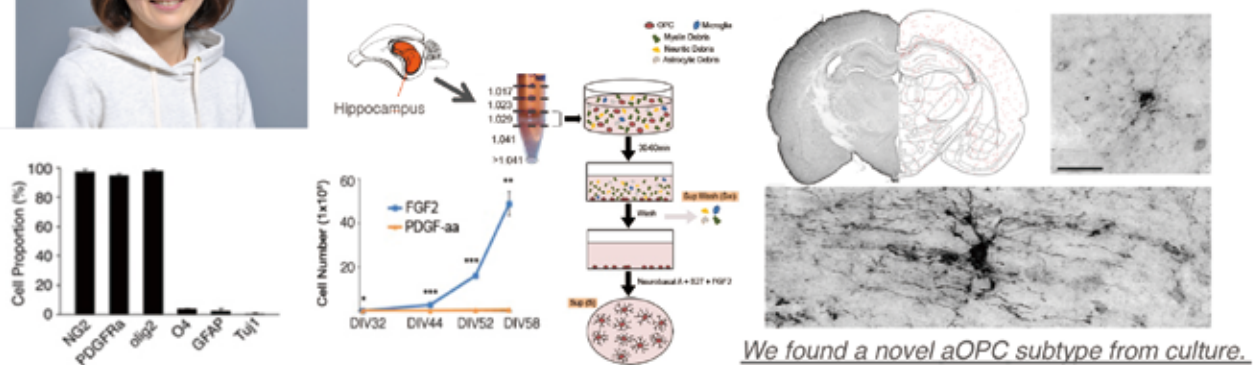
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“Better understanding of these phenomena will provide important insights to facilitate the more effective diagnosis, treatment and prevention of affective disorders.”

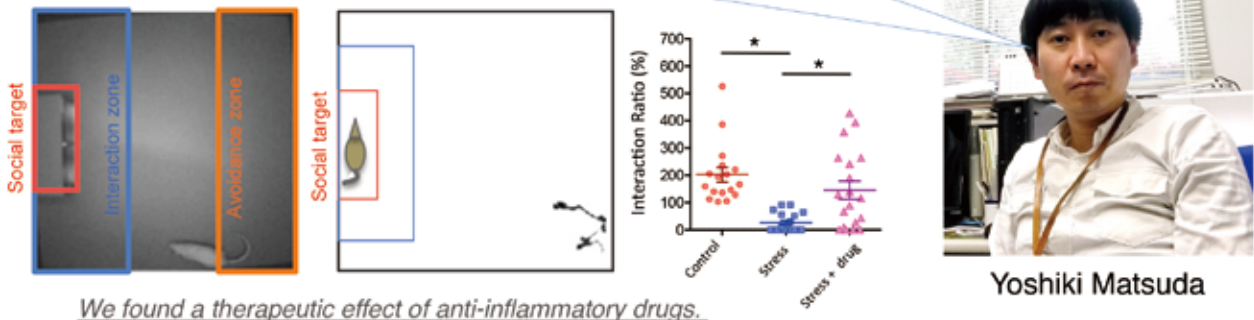
Naomi Nihonmatsu-Kikuchi



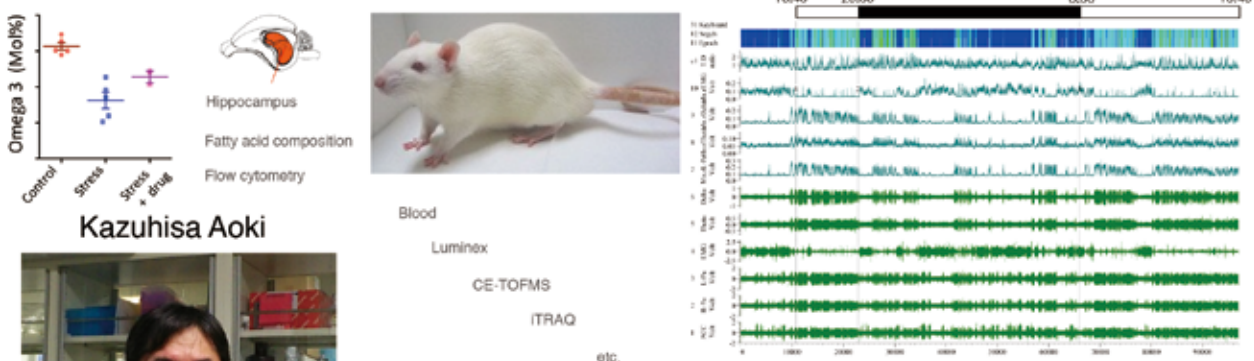
We purify and culture adult oligodendrocyte progenitor cells (aOPCs) from adult mammalian brains to understand their roles in the pathogenesis of affective disorders.



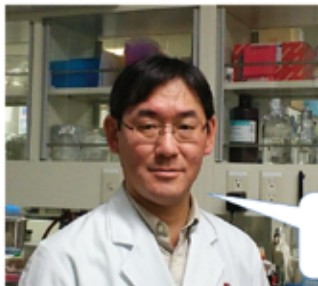
Our animal model clearly indicates essential roles of inflammation in the pathophysiology of depression. Chronic stress induces changes not only in behavior but also in electrophysiology and cellular structure.



Yoshiki Matsuda



Kazuhisa Aoki



We are conducting detailed omics analyses of our animal models to discover novel biomarkers for depression.

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