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発表題目（※学会発表の場合のみ記載）	**Brain development is regulated by the cooperation of two purine synthetic pathways** 脳発生は二つのプリン合成経路の協調によって制御される

発表の概要と成果（抄録を公開している URL がある場合、「概要・成果」を記載した上で、URL を末尾に記してください。また、抄録 PDF は別途ご提出ください。なお、抄録 PDF は Web 上には公開されません。）

Purines nucleotides are essential building blocks for the synthesis of DNA, RNA, and the energy metabolism (ATP and GTP), and implicated in various cellular signaling pathways (cyclic AMP and cyclic GMP). In mammals, purine level is regulated by the cooperation of two purine synthetic pathways: de novo and salvage pathway. Impairment in purine metabolism leads to various neurological diseases such as Lesch-Nyhan syndrome. In the developing central nervous system (CNS), the de novo purine synthetic pathway is presumed to be primarily utilized because neural stem/progenitor cells (NSPCs) require large amounts of purines for abundant proliferation and neuron production. However, it is not fully understood how these purine synthetic pathways are utilized differently in the developing CNS. In this study, we revealed that the spatiotemporal regulation of two purine synthetic pathways is essential for proper brain development. The five main findings indicated in this study are as follows. (i) There is a shift of utilization for purine metabolic pathways during brain development, with a greater reliance on the de novo pathway in the embryonic stages and a greater reliance on the salvage pathway in the postnatal and adult stages. (ii) While cerebrum NSPCs mainly utilize de novo pathway, cerebellum NSPCs requires both de novo and salvage pathways. (iii) The sensitivity and the demand of purines produced by the de novo pathway are stronger from the posterior to the anterior axis on early embryonic cerebral cortex. (iv) Inhibition of de novo purine synthetic pathway causes suppressing the proliferation of NSPCs and radial migration of newborn neurons in the developing cerebral cortex. (v) Inhibition of de novo pathway downregulated mTORC1/S6K/S6 signaling pathway, resulting brain malformation which deficit the frontal cortex and ganglionic eminence were formed in the region where forebrain originally located. These findings indicate that strict spatiotemporal regulation of purine synthetic pathways in cooperation with mTORC1 signaling are crucial for the normal brain development. Our findings will contribute to better understanding of neurological diseases caused by abnormalities in purine metabolism.