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Purines are essential molecules for the synthesis of DNA, RNA, and energy metabolism, and implicated in various cellular functions. There are two pathways for purine synthesis in mammals: de novo pathway and salvage pathway. Although the balance between these pathways is presumed to be critical for normal brain development, the spatiotemporal regulation of these purine synthesis pathways in the central nervous system remains unknown. Here, we investigated the functional significance of purine synthesis enzymes during mammalian brain development. Developmental immunoblot analysis of mice brains revealed that the enzymes which catalyze de novo purine synthesis are abundant in the early embryonic stage and downregulated toward the postnatal and adult stage. Conversely, the expression level of the enzyme of salvage pathway exhibited the exact opposite behavior. During adult stage, the immunoreactivities of each enzyme were found in different regions speculating that the driving balance of two pathways is essential for proper neuronal development. Functional analysis of the two purine synthesis pathways was performed in pregnant mice and in primary cultured neural stem and progenitor cells (NSPCs) using drugs that selectively inhibit the de novo or salvage pathways. In both in vivo and in vitro, inhibitor for de novo purine pathway significantly decreased the proliferative potential in primary cultured NSPCs, whereas salvage inhibitor had a weak effect. These results indicate that the de novo pathway is predominant during neuronal development. Our findings will contribute to better understanding of neurological diseases caused by abnormalities in purine metabolism. https://mbsj2022.gakkai.online/presentations/2553/abstract

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