

Dynamic transcriptional control of neural stem cells

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Place: Lecture room 2, Medical Education & Library Building 3F
医学教育図書棟3階 第2講義室

*This seminar will be held in a face-to-face./今回のセミナーは対面形式で開催されます。

Abstract

Neural stem cells (NSCs) actively proliferate and generate neurons and glial cells (active state) in the embryonic brain while they are mostly dormant (quiescent state) in the adult brain. The expression dynamics of the transcriptional repressor Hes1 are different between active and quiescent NSCs. In active NSCs, Hes1 expression autonomously oscillates by negative feedback and periodically represses the expression of its target genes such as the proneural gene Ascl1/Mash1, thereby driving their oscillations. By contrast, in quiescent NSCs, Hes1 expression is up-regulated, thereby continuously suppressing the proneural gene expression. Furthermore, when Ascl1 oscillation is induced in quiescent NSCs, these NSCs are efficiently activated, producing new neurons continuously. Thus, Hes1 oscillation and the resultant Ascl1 oscillation regulate the active state of NSCs, while high levels of Hes1 and the resultant suppression of Ascl1 promote their quiescent state. We next searched for the upstream gene set that can activate Ascl1 oscillation in aged NSCs and found that inducing Plagl2 and anti-Dyrk1a (iPaD) can efficiently rejuvenate aged dormant NSCs so that these NSCs are frequently activated to produce new neurons, leading to improved cognition. Thus, aging of NSCs can be reversed to induce functional neurogenesis continuously, offering a way to treat age-related neurological disorders.

◆ Inviter: Prof. MATSUOKA Masao (Hematology, Rheumatology and Infectious Disease)

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