CDB SEMINAR

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16:00~17:00 A7F Seminar Room

A gene network regulating temporal changes in neural stem cell function.

Summary

Neural stem cells (NSCs) persist throughout life in the central nervous system (CNS). Alterations in NSC activity and function occur to match changing growth and regeneration demands during development and aging. For example, self-renewal capacity and the rate of neurogenesis decline during NSC aging. However, the mechanisms that regulate these temporal changes in NSC function are largely unknown.

We identified a gene network that is coordinated by microRNA let-7b that regulates developmental and age-related changes in NSCs. Let-7b expression increases in NSCs during fetal development and continues to rise through old age. Let-7b heterochronically regulates the expression of multiple downstream genes including Hmga2 and Imp1. We analyzed NSCs in Hmga2 and Imp1 knockout mice, and found that Hmga2 regulates NSC aging in adult mice by inhibiting two tumor suppressors Ink4a and Arf, while Imp1 maintains the undifferentiated state of fetal NSCs by promoting their proliferation and inhibiting their differentiation.

These observations suggest that there is a heterochronic gene network coordinated by the microRNA Let-7b that regulates the expression of multiple downstream genes that control different aspects of NSC function in a temporally specific manner.

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