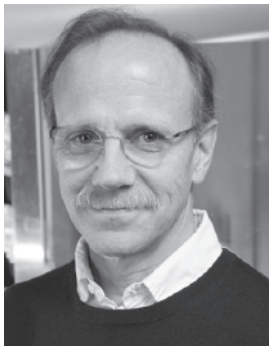
再生サイエンスフロンティアレクチャー

Neural Plasticity and Neuronal Diversity in the Adult Mammalian Brain



Fred Harrison Gage

Laboratory of Genetics, The Salk Institute for Biological Studies

The first part of the talk will focus on evidence supporting the birth and maturation of new neurons in the adult dentate gyrus of the hippocampus in the mammalian brain. The mechanism by which the cells integrate and become functional will be discussed. In addition, the potential functional significance for adult neurogenesis in the context of the normal function of the hippocampus will be discussed. In the second part of the talk I will focus on the recent finding that LINE-1 (Long Interspersed Nucleotide Elements-1 or L1) retroelements are active in somatic neuronal progenitor cells (NPCs) providing an additional mechanism for neuronal diversification. Together with their mutated relatives, retroelement sequences constitute 45% of the mammalian genome with L1 elements alone representing 20%. The fact that L1 can retrotranspose in a defined window of neuronal differentiation, changing the genetic information in single neurons in an arbitrary fashion, allows the brain to develop in distinctly different ways. This characteristic of variety and flexibility may contribute to the uniqueness of an individual brain. However, the molecular mechanism that regulates L1 expression in NPCs is not completely understood. L1s are likely silenced in neural stem cells due to Sox2-mediated transcription repression. Down-regulation of *Sox2* accompanies chromatin modifications, such as DNA de-methylation and histone acetylation, which in turn may trigger neuronal differentiation. The characterization of somatic neuronal diversification will not only be relevant for the understanding of brain complexity and neuronal organization in mammals, but may also shed light on the differences in cognitive abilities.

【略歴】

[Current position]

Adler Professor, Laboratory of Genetics, The Salk Institute for Biological Studies (1995-)
Adjunct Professor, Department of Neurosciences, University of California, San Diego (1988 -)

[Education]

1972 B.S. - University of Florida, Gainesville, FL
1975 M.S. - Johns Hopkins University, Baltimore, MD
1976 Ph.D. - Johns Hopkins University, Baltimore, MD

[Positions Held]

9/74-6/76 NIMH Predoctoral Fellow, The Johns Hopkins University
9/76-6/80 Assistant/Associate Professor, Texas Christian University
6/81-6/85 Associate Professor, Dept. of Histology, University of Lund, Lund, Sweden
6/85-6/88 Associate Professor, Dept. of Neurosciences, University of California, San Diego

[Summary of Research Interests]

Dr. Gage's work concentrates on the adult central nervous system and unexpected plasticity and adaptability to environmental stimulation that remains throughout the life of all mammals. In addition, his studies focus on the cellular, molecular, as well as environmental influences that regulate neurogenesis in the adult.