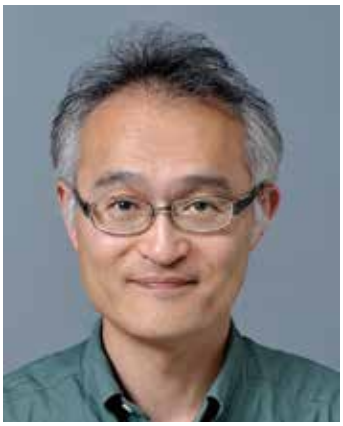


Project Leader **Haruo Okado** Neural Development Project

Brain Development and Maintenance:

Various factors control differentiation of neural stem cells and survival of the resulting neurons and aberrancy of these processes are involved in the incidences of intellectual disability and age-related brain disorders and brain tumors.
We aim to elucidate the mechanisms of the development and maintenance of brain functions and ultimately to develop methods for prevention and treatment of intractable cranial nerve diseases.

Various gene-targeted mice

in utero electroporation

"We are studying the effects of various genetic and environmental factors on the molecular mechanisms of brain development and maintenance, with the ultimate goal of developing new treatments mental diseases."

Laboratory Members

Hirai S, Hotta K, and Okado H. (2018) "Developmental Roles and Evolutionary Significance of AMPA-Type Glutamate Receptors." ***Bioessays.*** 2018 2018 Sep;40(9):e1800028.

Hirai S, Hotta K, Kubo Y, Nishino A, Okabe S, Okamura Y, and Okado H. (2017) "AMPA glutamate receptors are required for sensory-organ formation and morphogenesis in the basal chordate." ***Proc. Natl. Acad. Sci. USA.*** 114: 3939-3944.

Nakajima K, Hirai S, Morio T, and Okado H. (2015) "Benzodiazepines induce sequelae in immature mice with inflammation-induced status epilepticus." ***Epilepsy & Behavior*** 52: 180-186.

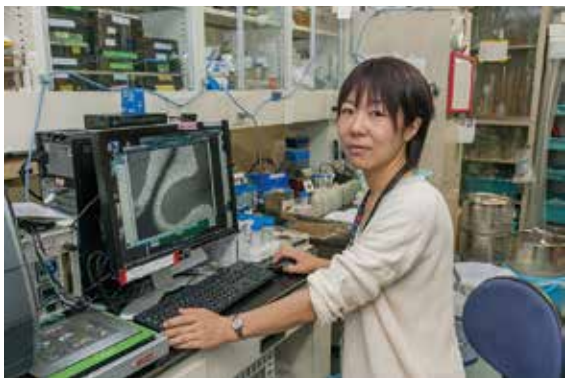
Ohtaka-Maruyama C, Hirai S, Miwa A, Heng JI, Shitara H, Ishii R, Taya C, Kawano H, Kasai M, Nakajima K, and Okado H. (2013) "RP58 regulates the multipolar-bipolar transition of newborn neurons in the developing cerebral cortex." ***Cell Rep.*** 3: 458-471.

Hirai S, Miwa A, Ohtaka-Maruyama C, Kasai M, Okabe S, Hata Y, and Okado H. (2012) "RP58 controls neuron and astrocyte differentiation by downregulating the expression of Id1-4 genes in the developing cortex." ***EMBO J.*** 31: 1190-1202.

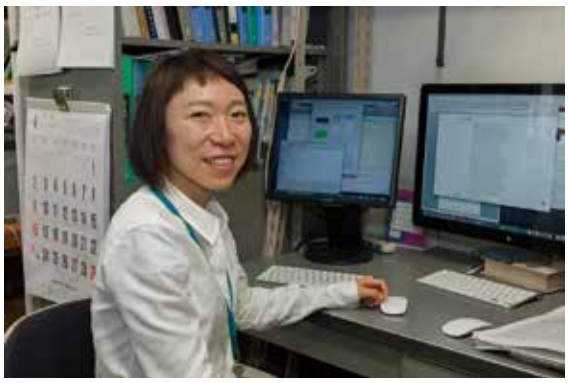
Ohtaka-Maruyama C, Hirai S, Miwa A, Takahashi A, and Okado H. (2012) "The 5'-flanking region of the RP58 coding sequence shows prominent promoter activity in multipolar cells in the sub- ventricular zone during corticogenesis." ***Neuroscience*** 201: 67-84.

Okado H, Ohtaka-Maruyama C, Sugitani Y, Fukuda Y, Ishida R, Hirai S, Miwa A, Takahashi A, Aoki K, Mochida K, Suzuki O, Honda T, Nakajima K, Ogawa M, Terashima T, Matsuda J, Kawano H, and Kasai M. (2009) "Transcriptional repressor RP58 is crucial for cell-division patterning and neuronal survival in the developing cortex." ***Dev. Biol.*** 331: 140-151.

Neural Development



Shinobu Hirai



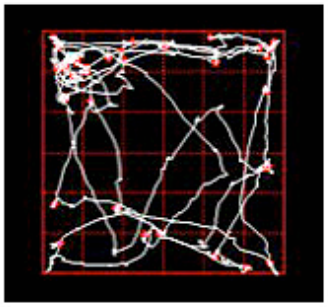
Tomoko Tanaka

Our major projects include

1) **Understanding the mechanisms of transcription repressor, RP58, for brain development and maintenance.**

2) **Exploitation of the nutritional environmental factors to manipulate brain development and functions.**

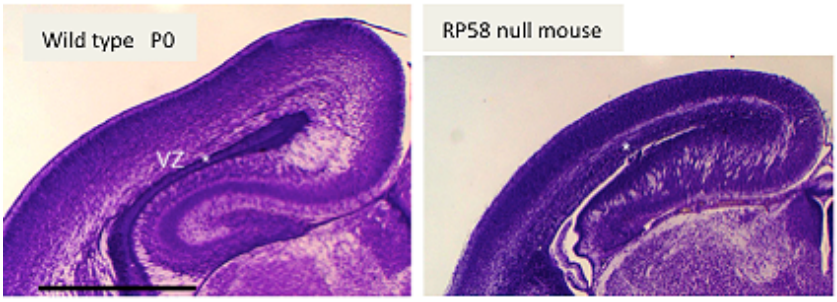
3) **Understanding the roles of environmental factors in development and ageing of brain functions.**



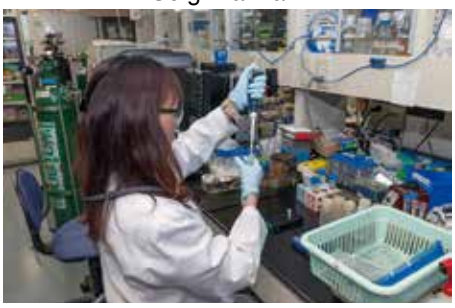
Locomotion, anxiety, memory, and sociality of mice are evaluated using the tracking system. Neuronal activity can be analyzed *in vivo* system.

Yoshie Matsumoto

Seigi Kanzaki



RP58 is required for development of cerebral cortex. The cell-cycle exit of progenitor cells, neuronal radial migration and maturation of cortical neurons are impaired in RP58-deficient mice.



Tomoko Fukuoka

Neural Development