Division of Organogenesis

Brain Morphogenesis

In pursuit of the mystery and complexity of brain development Unveiling the mechanisms underlying the creation of the "control tower" of the organism

A map for brain formation is determined in the early stages of embryogenesis.
Based on this map, the various domains in the brain are formed, and eventually each domain comes to have distinct and specific characters and functions.
Dr. Kenji Shimamura's research sheds light on the sophisticated and dynamic mechanisms underlying the formation of our high-functioning brains.

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Profile

Born in 1965, in Hyogo prefecture.
Graduated with a Bachelor' s degree from the Faculty of Science, Kyoto University, then went on to complete Master' s and Doctoral degrees at the Graduate School of Science at the same university. Holds a Ph.D.
In 1994, he took up a position as a research fellow at the Department of Psychiatry, University of California, San Francisco in the United States.
In 1997, he moved back to Japan to become a senior assistant professor at the Department of Neurobiology, Graduate School of Medicine, The University of Tokyo.
In 2002, he became a professor at the Institute of Molecular Embryology and Genetics, Kumamoto University.

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Searching for the mechanisms determining the properties and destination of neurons and the architectures of each brain tissue according to the map of the brain

The mechanisms by which our brains, highly functioning "control towers" that determine our every activity, are formed remain deeply mysterious and to be understood. Yet this puzzles is exactly what Dr. Kenji Shimamura busies himself with in his research, focusing in particular on how and where neurons are formed, as well as how the various areas of the brain come to develop according to the data setting out the map of the brain.

The neural plate appears at a very early stage in embryogenesis, and is made up of epithelial cells, the stem cells of the central nervous system. It is here, on this sheet of cells, that the map of the brain has been imprinted. "The behavior of neurons is determined by the instructions found in this map; first, the areas of the brain such as the cerebrum and the cerebellum are formed. Research has already revealed the basic principles by which the brain map is imprinted onto this brain primordium, the neural plate, and the mechanism by which different neurons with distinct characteristics are generated according to the position in the brain," says Dr. Shimamura. There is still much we do not know, however, for example how each area goes about forming the structure required of it by the brain map.

Processes to control proliferation and differentiation and to create differences in tissue architecture.

Neural stem cells divide rapidly, and the outcome of division varies: in some cases, both daughter cells arising from division will have the same characteristics as the parent cell (proliferation); in other cases, one cell will be identical to the parent cell (self replication) while the other becomes a neuron (differentiation); in still others, both daughter cells will be neurons. This principle applies to every area of the brain, but the numbers of neurons and neural stem cells produced, and the ratio between them, varies according to position in the brain. This balance is also affected by the stage of development. "We believe there must be mechanisms regulating the balance between neuron production and neural stem cell proliferation according to position and developmental stage," states Dr. Shimamura. One possible mechanism, he suggests, is based on the contact between parent and daughter cells: daughter cells that have become neurons release the contact quickly away from the parent cell, allowing that cell to continue to differentiate rapidly, while those daughter cells that retain the contact with the parent prevent the parent cell from differentiating, prompting it instead to proliferate. His research seeks to verify this hypothesis, in which daughter cells regulate the differentiation and proliferation of parent cells.

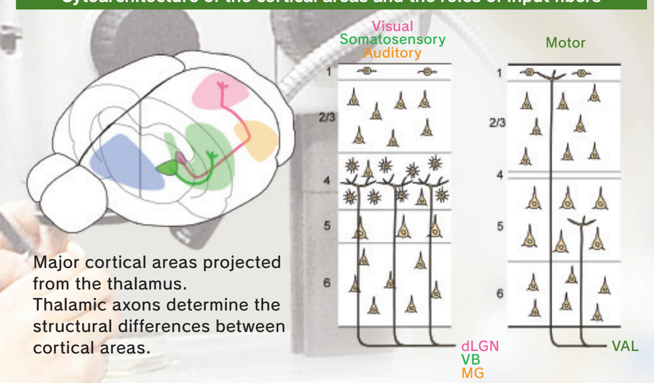
Next, neurons move away from their birthplace and move toward their destination, building brain tissue in the process. Dr. Shimamura speculates that the pace of neuron production must be linked in some way to differences in the internal structures formed after the neurons have moved position. "The neurons start to build up, thickening the walls of the brain, but while in some areas neurons will stack up in layers, in others the neurons form exquisite clusters. The basic mechanism of neuron production remains the same, yet differences emerge in the tissue they form; we believe that quantitative and temporal changes in the basic mechanism are behind these differences." This would suggest that, for example, in one position in the brain, the formation of a large volume of neurons in a short time results in cluster-like tissue, while in another position, the pace of production is slower, allowing the neurons to gradually form sheets over time. Dr. Shimamura continues to press forward with his examination of this assumed mechanism.

Towards the mysteries of evolution: the mechanism of cerebral neocortex formation

The cerebral neocortex, which contains a number of significant regions including the motor, language, visual, and auditory cortices, is made up of six layers. We already know that these layers differ in structure and thickness throughout the various cortices. "So although we know how the cortices are determined, we don't yet know why different structures are formed. Sensory information is transmitted to the neocortex, via the neural fibers derived from thalamic nuclei. What we think is that, at this point, something within the neural fibers may control the formation of layer structure of the target cortical areas".

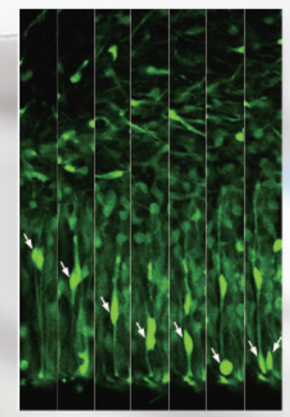
This cerebral neocortex is only observed in mammals, including humans; it does not appear to be present in other vertebrates, including birds and reptiles. By investigating the mechanisms that cause tissue morphology to change according to brain region, Dr. Shimamura hopes to be able to clarify the mechanisms by which different brain structures among the vertebrate species. "I would like to further our understanding of brain morphogenesis, in the hope of advancing our understanding of the mysteries of brain evolution".

Cytoarchitecture of the cortical areas and the roles of input fibers

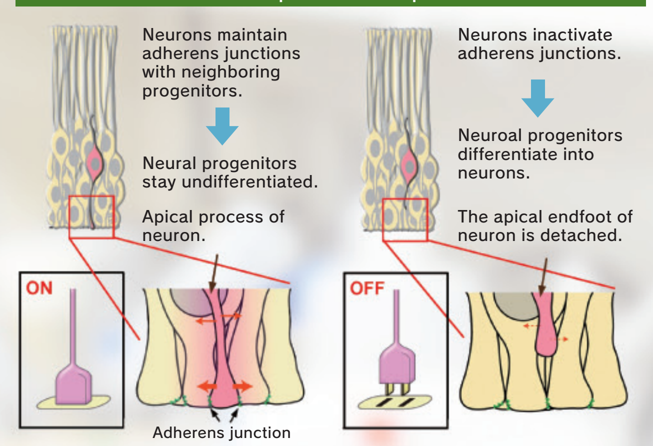


Major cortical areas projected from the thalamus. Thalamic axons determine the structural differences between cortical areas.

Time-lapse observations of neural stem cells



Control of the pace of neuron production



Teaching Staff

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The developmental processes by which the brain forms, starting with a single homogenous sheet of neuroepithelia, is truly mysterious. My research looks at the building processes seen in brain formation, which I examine using mouse and chicken embryos. Through my research, I hope to share the joy of witnessing the formation of life with many people. How are our brains made? How have they evolved? I look forward to hearing from students who are willing to tackle these questions with me!