

## ◀ Production method of an in vitro neural network ▶

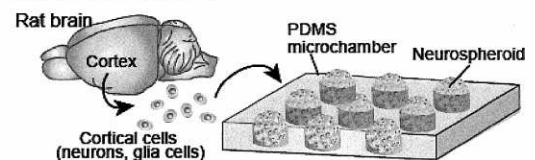
### <Summary of the invention>

A living neural network can be efficiently produced by simply culturing nerve cells, for 1-2 weeks, in spheroids placed in wells of a microchamber; the axons extend from the spheroids and efficiently build a network. These *in vitro* neural networks can easily be transferred onto the brain of a living animal where they can normally perform their functions. Therefore, this technique may be used in the preparation of animal models of neurological disease, such as an animal model for drug screening or for regenerative therapy in neurological disorders.

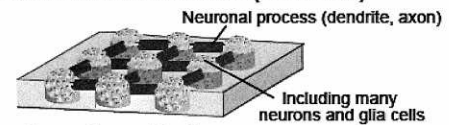
### ! Characteristics

- ◆ The *in vitro* neural network has a rigidity to resist physical impacts and loads because more than ten neurites connect between the spheroids.
- ◆ The resulting neural network can be easily peeled off from the microchamber by using the tip of a pipet or spatula.
- ◆ The neural network can also be folded to form a three-dimensional network.

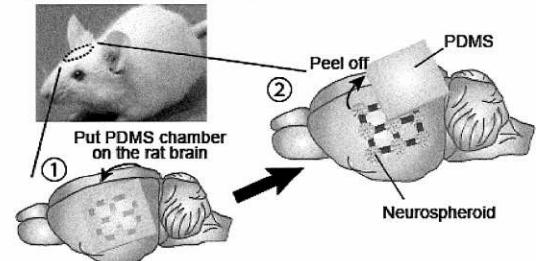
#### 1. Spheroid formation



#### 2. Neuronal network formation (1-2 weeks)



#### 3. Transfer on the rat brain



### ! Examples

◆ The *in vitro* neural network was transferred onto the cerebral cortex of a rat. Anterograde tracers (PHA-L) were transported across synapses into nerve cells of the rat cerebral cortex from the *in vitro* neural network.

⇒ Neurons in the *in vitro* neural network were synaptically connected to neurons of the cerebral cortex of the rat.

◆ A multi-layered neural network was also made by closely attaching two *in vitro* neural networks together and this multi-layered network could easily be transferred onto a cerebral cortex.

### ! Possible applications

- ◆ Developing tools for drug discovery
  - e.g.) An animal model of a neurological disorder can be made by preparing an *in vitro* neural network from nerve cells generated by inducing iPS cells derived from a patient of a neurological disorder to differentiate and then transferring it to an animal brain
- ◆ Regenerative therapy in neurological disorders
  - e.g.) Applicable in regenerative therapy of brain infarction, cerebral hemorrhage, brain contusion, Alzheimer's disease, Parkinson's disease, etc.

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<Notes> Patent Pending (PCT/JP2010/063803)

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