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# Okayama University research: Rising from the ashes—dead brain cells can be regenerated after traumatic injury

(Okayama, 14 January) **In a recent study published in *Scientific Reports* researchers at Okayama University describe the development of a method to generate neurons from other types of cells to compensate for brain cells lost during injury.**

A stroke is a debilitating neurological condition that arises when there is deprivation of blood to brain cells. It can lead to loss of memory, motor skills, and cognition. Currently, stroke patients are treated by restoring proper blood flow to their neurons. However, these neurons are often dead by the time treatment is given. Replacing dead neurons is therefore an ideal but very difficult strategy to regain loss of brain function. Now, researchers at Okayama University have now developed a method of converting non-neuronal cells in the brain into neurons for this purpose.

Ascl1, Sox2, and NeuroD1 are proteins found within neurons. When they are introduced tactically into ordinary cells, the cells start showing neuron-like properties. The research team led by Professor ABE Koji and Senior Lecturer YAMASHITA Toru designed their studies based on this principle. Small silicon filaments were first inserted into specific blood vessels within the brains of mice. These filaments clogged the vessels and restricted blood flow thereby giving the mice a stroke.

Three days after a stroke was induced, a delivery system comprising a weakened virus was used to inject Ascl1, Sox2, or NeuroD1 into the damaged brain areas. Viral systems usually attack rapidly-diving, younger cells, and not mature cells like neurons. This gave the team tight control over the type of cells the virus would enter and deposit the proteins into. Indeed, it was observed that protective, non-neuronal cells called as glial cells were the ones targeted successfully.

Twenty-one days after the viral injection these glial cells started presenting markers typically found in young neurons. Forty-nine days after the injection these cells had characteristics of mature neurons, including the branching pattern typical to neurons. The injection of Ascl1, Sox2, or NeuroD1 successfully led to the generation of “new” neurons. The researchers also analysed behavioural patterns of these mice to assess their mobility post stroke. However, in spite of brain cell regeneration their movement was not completely restored.

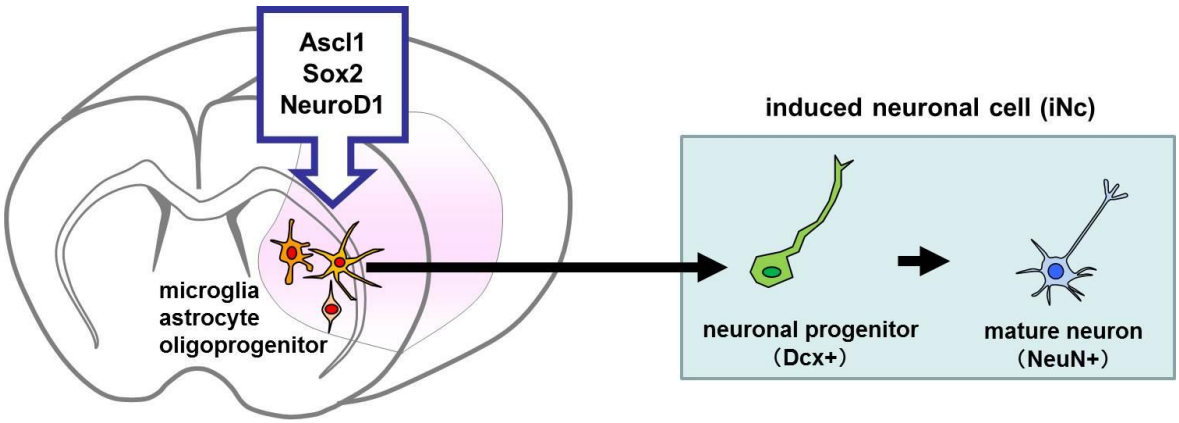
“Taken together, the present study successfully achieved, for the first time, in vivo direct reprogramming by enforced transcriptional factors (Ascl1, Sox2 and NeuroD1) in the post-stroke mouse brain”, conclude the authors. This successful regeneration of brain cells after a

stroke is a step forward in therapy; it remains to be studied whether tweaking this process further can restore neurological function as well.

**Background**

Stroke: A stroke occurs when oxygen supply to the brain cells is cut off. This is usually the result of an occluded blood vessel or uncontrolled bleeding within the brain. Brain cells can die within minutes of such injury. At present, regeneration of neurons in stroke patients has not been conducted successfully and neuroscientists have been at this endeavour for decades.

**Neurons:** Neurons are specialized cells that are the building blocks of the brain. Each function controlled by our brain is being executed by specific types of neurons. Thus, the location and function of neurons determines which neurological function will be hampered by a stroke. Given how indispensable neurons are for our day-to-day functioning, preserving healthy neurons and generating younger ones has been an age-old mystery in medical science. Neurons are protected closely by their neighbours: glial cells.




**Caption**

Somatic cells including intracerebral glial cells can be directly converted into induced neuronal cells (iNc) by enforced specific transcriptional factors. Here, we show in vivo direct reprogramming by enforced transcriptional factors (Ascl1, Sox2 and NeuroD1) in the post-stroke mouse brain. The reprogrammed cells first express neuronal progenitor marker Dcx, then express mature neuronal marker NeuN, accompanied with morphological changes including long processes and synapse-like structures. The present study provides a future novel self-repair strategy for ischemic stroke with beneficial modifications of inducer-suppressor balance.

**Reference**

Toru Yamashita, Jingwei Shang, Yumiko Nakano, Ryuta Morihara, Kota Sato, Mami Takemoto, Nozomi Hishikawa, Yasuyuki Ohta, Koji Abe. In vivo direct reprogramming of glial linage to mature neurons after cerebral ischemia. *Scientific Reports*, (2019) 9:10956.
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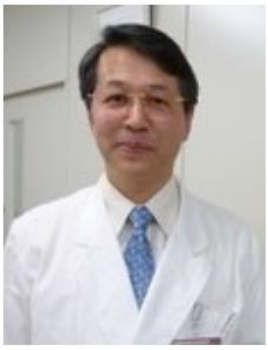

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Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html


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