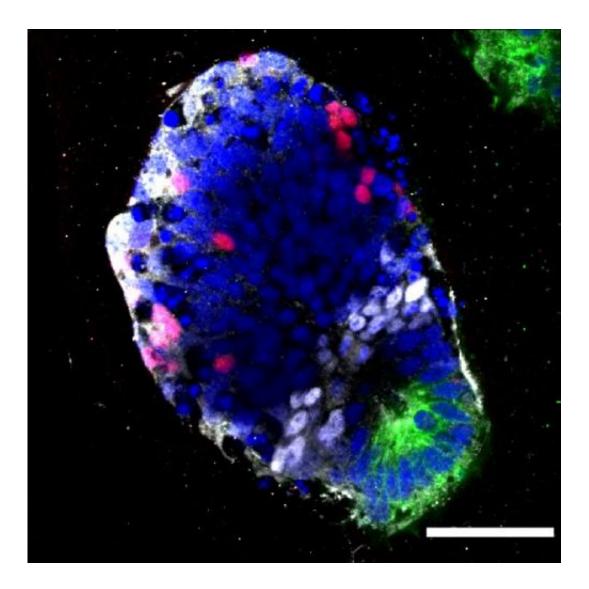


Reconstruction of a patterned piece of spinal cord in 3D culture

October 30 2014



The confocal cross-section of a three-dimensional cyst shows the floor plate (green), which was formed after the addition of retinoic acid. Furthermore, the development of motor neurons (white) as well as interneurons (red) was shown. The Dresden researchers could demonstrate in vitro the typical pattern of an



embryonic spinal cord. Credit: CRTD/Andrea Meinhardt

The central nervous system in vertebrates develops from the neural tube, which is the basis for the differentiation in spinal cord and brain. Professor Elly Tanaka and her research group at the DFG Research Center for Regenerative Therapies Dresden - Cluster of Excellence at the TU Dresden (CRTD) demonstrated for the first time the in vitro growth of a piece of spinal cord in three dimensions from mouse embryonic stem cells. Correct spatial organization of motor neurons, interneurons and dorsal interneurons along the dorsal/ventral axis was observed.

This study has been published online by the American journal *Stem Cell Reports*.

For many years Elly Tanaka and her research group have been studying the regenerative potential of axolotls at the molecular level. The Mexican salamanders have the potential to regenerate their <u>spinal cord</u> and other organs to restore full functionality after injury. Mammals such as humans are not able to regenerate most organs. The restoration of the spinal cord in axolotl occurs in a three dimensional structure similar to an embryonic spinal cord. Due to their positions in the tissue, cells in the regenerated spinal cord know which function to perform in the restored tissue. "In this study we applied the knowledge gained about the regenerative potential in axolotls to a mammal, the mouse" explains Professor Elly Tanaka.

Single mouse <u>embryonic stem cells</u> embedded in a three-dimensional matrix and were grown in neural differentiation medium led to the clonal development of neuroepithelial cysts. These cysts settled in the midbrain and hindbrain along the neural axis. "Our goal, however, was to generate



spinal cord in vitro," says Dr. Andrea Meinhardt, a postdoc at the CRTD. "For this reason we added retinoic acid to the culture medium on the second day of the 3D cell culture." The result not only caused the neural tissue to switch to spinal cord but also induced the formation of a local signaling center for forming all the different cell types of the spinal cord. "For the first time we could hereby reconstruct the structure of a typical embryonic neural tube in vitro," said Andrea Meinhardt.

"With this study we have moved a tiny step closer to turn the idea of constructing a three-dimensional piece of spinal cord for transplantation in humans into reality" says Elly Tanaka.

More information: "3D reconstitution of the patterned neural tube from embryonic stem cells." *Stem Cell Reports* (dx.doi.org/10.1016/j.stemcr.2014.09.020)

Provided by Dresden University of Technology

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