Where injured nerve cells heal their bones

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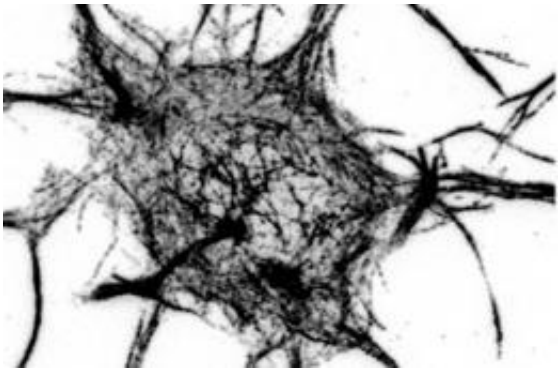

It was long assumed that microtubules can only form from a central point in the cell, the centrosome. The image shows that the microtubules (dark lines) can also form in other areas in mature neurons with inactive centrosomes. Image: Max Planck Institute of Neurobiology/Stiess & Bradke

(PhysOrg.com) -- Microtubules are small protein tubes that give cells their structure and enable both their growth and division. It was assumed up to now that microtubules are formed by the centrosome, a cell organelle localised near the nucleus.

Scientists at the Max Planck Institute of Neurobiology in Martinsried and the Max Planck Institute of Molecular Cellular Biology and Genetics in Dresden have now succeeded in demonstrating that mature neurons of the central nervous system no longer have an active centrosome and that new microtubules can form in these cells independently of the centrosome. Their findings contradict the accepted scientific school of thought as to the origin of microtubules, and also reveal that an essential

regeneration process also exists in mature neurons of the brain and spinal cord. (*Science*, January 8, 2010)

Cells are the building blocks of all living organisms. A large number of different cell types and forms exist that are adapted to the widely varying tasks they perform. These range from almost spherical yeast cells to neurons with thousands of branched projections or dendrites. The existence of these different cell forms is enabled by the cytoskeleton, which gives the cells stability and structure. The cytoskeleton consists of small protein tubes, the microtubules, which can be extended or shortened as required. Therefore a cell can grow or form an extension and retract again, for example. Cell division would also be impossible without the stabilising effect and guidance of the microtubules.

According to the hitherto accepted school of thought, microtubules form, at the centrosome, a structure located near the nucleus, which is also referred to as the microtubule-organising centre. Because of its role in cell division and in microtubule formation, the centrosome is also of great interest to neurobiologists. As a rule, mature neurons cannot divide and do not regrow in the brain and spinal cord following injury. Could this be due to the fact that the centrosome loses its function in these neurons?

This is the question that scientists from the Max Planck Institute of Neurobiology in Martinsried investigated together with their colleagues from the Max Planck Institute of Cellular Biology and Genetics in Dresden and the Erasmus Medical Center in Rotterdam. As the researchers have now reported in the scientific journal Science, the centrosome in mature neurons is, in fact, inactive. Division in these neurons should be extremely difficult in the absence of an active centrosome.

This being established, the next question was obvious: Is the inactive

centrosome also a reason why neurons in the brain and spinal cord do not regrow after injury? The Martinsried-based neurobiologists only succeeded in demonstrating recently that the microtubules at the end of an injured neuron become completely mixed up. According to the traditional view, new microtubules would have to be "added" by the centrosome, which, of course, is not possible if the centrosome is inactive.

To answer this question, the Max Planck scientists in Martinsried and Dresden used cell cultures to examine the sites where microtubules form in neurons. To this end, they dissected the protein tubes into their individual components and then observed their new development in the cells. As expected, in young neurons the microtubules mainly emerged at the centrosome. However, this was not the only location: individual microtubules also formed at completely different sites in the cell body. "The real sensation only became evident when we examined mature neurons," reports Michael Stiess of his research. New microtubules also formed in these cells and, moreover, all over the cell and not only at the centrosome.

The findings refute the accepted doctrine that microtubules are formed from the centrosome. This also has consequences for the regeneration of nerve cells, as it would appear that microtubules can be formed directly at an injured neuronal extension and do not require complex transportation from the cell body. Another discovery made by the scientists is also important here: the locally-formed microtubules are sufficient to allow a neuron to mature. Thus, even young neurons continued to grow although the scientists had removed their centrosomes using a special laser. "This means that one of the basic preconditions for the regeneration of neurons should also be available in the brain and spinal cord," notes Frank Bradke, the head of the study, with enthusiasm. It is now necessary to discover how this development of microtubules and the regrowth of injured neurons can be triggered in the living

organism.

More information: Michael Stiess, Nicola Maghelli, Lukas C. Kapitein, Susana Gomis-Rüth, Michaela Wilsch-Bräuninger, Casper C. Hoogenraad, Iva M. Tolić-Nørrelykke, Frank Bradke, Axon Extension Occurs Independently of Centrosomal Microtubule Nucleation, *Science*, January 8th, 2010

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