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Neuronal survival and axonal regrowth obtained in vitro

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While repair of the central nervous system has long been considered impossible, French researchers from Inserm, the CNRS and the UPMC have just developed a strategy that could promote neuronal regeneration after injury. The in vitro studies have just been published in the journal *PLoS ONE.*

Repair of the central nervous system and restoration of voluntary motor activity through axonal re-growth has long been considered impossible in mammals. Over the last decade, numerous attempts proved disappointing overall. The Inserm team led by Alain Privat has recently shown that an essential component interfering with regeneration was due to the activity of astrocytes, feeder cells that surround neurons.

Normally, the primary role of astrocytes is to supply the nutrients necessary for neuronal function. In the event of spinal injury or lesion, astrocytes synthesize two particular proteins (glial fibrillary acidic protein (GFAP) and vimentin), which isolate the damaged neuron to prevent interference with the operation of the central nervous system.

While the protection is initially useful, in the long run it induces formation of impermeable cicatricial tissue around the neuron, thus constituting impenetrable scarring hostile to axonal regeneration and hence to propagation of nervous impulses. In the event of severe injury, the scarring engenders motor paralysis.

On the basis of the initial findings, the researchers pursued a strategy

aimed at developing a therapeutic instrument to block formation of cicatricial tissue. In order to do so, they used gene therapy based on use of interfering RNA. The short RNA sequences, which were made to measure, were inserted into the cytoplasm of cultured astrocytes using a viral therapeutic vector. Once in the cell, the RNA activates mechanisms which block the synthesis of the two proteins secreted by astrocytes and responsible for cicatrix formation. Using that technique, the researchers succeeded in controlling the reaction of astrocytes and when the latter were cultured with neurons, they promoted neuronal survival and triggered axonal growth.

The promising results are now to be validated by in vivo studies. The next stage of the work, currently ongoing, applies the same method to the mouse. The approach may be used in the future in patients having undergone spinal injury.

Source: INSERM (Institut national de la santé et de la recherche médicale)