# Self-Assembling Peptide Nanofiber Scaffold (SAPNS) and Regeneration

Posted on: **October 25, 2006**

**Here is described the creation of a permissive environment for axonal regrowth using a synthetic biological nanomaterial that self assembles *in vivo*, with components that break down into beneficial building blocks and produce no adverse effects on the CNS. This discovery allows for the reconnection of disconnected parts of the CNS after trauma.**

There are several formidable **barriers that must be overcome to achieve axonal regeneration** after injury in the central nervous system (CNS), whether caused by a knife or a stroke. These obstacles are:

- scar tissue formation after tissue injury;
- gaps in nervous tissue formed during phagocytosis of dying cells after injury;
- factors that inhibit axon growth in the mature mammalian CNS;
- failure of many adult neurons to initiate axonal extension.

The reconnection of disconnected parts of the CNS after trauma will be allowed after reducing or overcoming at least the first two obstacles.

The previously undiscovered **treatment in this study used a designed self-assembling peptide** (*part (a) at figure below*) that spontaneously forms nanofibers, creating a scaffold-like tissue-bridging structure. The nanofibers provide a framework for partial reinnervation by axons with regenerative potential in young and adult animals. Because the peptide fibers are nanoscale, there is likely a direct interaction between the peptide scaffold, the extracellular matrix, and the neural tissue on both sides of the lesion. These structures create a scaffold that connects the two faces of the lesion, allowing movement of cells into the scaffold. The peptide scaffold in experiments created a permissive environment for axonal growth while discouraging or preventing the scar formation that normally occurs at an early stage. This material appears to offer a treatment for ameliorating or bypassing tissue disruptions after neuronal damage.

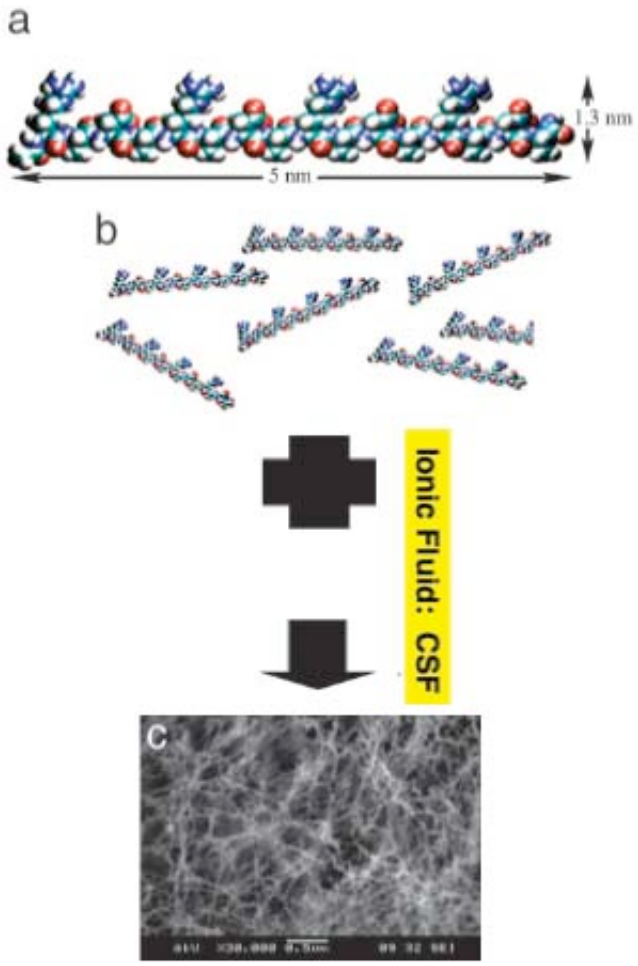
**SAPNSs are synthetic biological materials** formed through the assembly of ionic self-complementary peptides and are designed by using alternating positive and negative L-amino acids that form highly hydrated scaffolds in the presence of physiological concentration salts, like saline, tissue culture media, physiological solutions, or human body fluids such as cerebrospinal fluid (*part*

*(b) at figure below*). The scaffold consists of β-sheet ionic peptide containing 50% charged residues. A number of additional self-assembling peptides have been designed, synthesized, and characterized for salt-facilitated matrix formation.

The **SAPNS consists of interwoven nanofibers** (*part (c) at figure below*), and the individual fibers are ~10 nm in diameter. The nanofiber density correlates with the concentration of peptide solution. This designed peptide nanofiber scaffold provides several **benefits over currently available polymer biomaterials**:

- the peptide scaffold which forms a network of nanofibers that are similar in scale to the native extracellular matrix and therefore provides an *in vivo* environment for cell growth, migration, and differentiation;
- it can be broken down into natural L-amino acids and potentially used by the surrounding tissue, because the majority of the material is excreted in the urine;
- it is synthetic and free of chemical and biological contaminants that typically are present in animal-derived biomaterials such as many collagens;
- it appears to be immunologically inert, thus avoiding the problem of neural tissue rejection.

All of these attributes make it very attractive for using the peptide nanofiber scaffold in both *in vitro* and *in vivo* studies. **Scientific studies show that the SAPNS can support the attachment of a variety of mammalian primary cells in tissue culture.** Additionally, one of the peptide scaffolds, arginine, alanine, aspartate, and alanine (RADA) 16-I (*part (a) at figure below*) supports not only the growth of PC12 cells but also the formation of functional synapses *in vitro* using rat primary hippocampal neurons.




SAPNS repair for the animal brain. **(a)** Molecular model of the RADA16-I molecular building block. **(b)** Molecular model of numerous RADA16-I molecules undergo self assembly to form well ordered nanofibers with the hydrophobic alanine sandwich inside and hydrophilic residues on the outside. **(c)** The SAPNS is examined by using scanning electron microscopy. (Scale bar, 500 nm.)

Thus, RADA-I supports a wide range of neuronal growth and development using both *in vitro* and *in situ* cell culture systems. A tissue gap caused by deep transection of the optic tract in the hamster midbrain and injection of saline can completely block reinnervation of the superior colliculus (SC) by the retina even at young ages [postnatal days (P) 2–9] when the axons typically have more regenerative potential. Saline was used, because it is the standard irritant for most neurosurgical procedures and is considered to be benign in the brain.

Before the use of the SAPNS, scientists demonstrated substantial recovery of visual-orienting behavior in hamsters using a peripheral nerve optic tract bridge model. In one of the models, the optic tract was completely severed at the brachium of the SC, and the reconnection of the optic tract was accomplished with several surgically implanted segments of sciatic nerve taken from one of the animals' legs. However, the use of this model often results in leg disabilities in experimental animals.

In an attempt to facilitate optic tract regeneration with restoration of function, without additional clinical complications, scientists asked whether the SAPNS could create a permissive environment for regeneration in the damaged

tissues as a substitute for sciatic nerve grafts. They examined both short- and long-term effects of injecting a peptide scaffold into the wound site in both young and adult animals using this model. And **it was shown that the SAPNS not only permitted significant axonal growth through the site of the treated lesion, partially restoring the optic tract, but also resulted in the return of functional vision in brachium transected experimental adult animals.** And the use of this biological nanofiber scaffold is an effective approach to facilitate the reconstruction of a continuous tissue substrate after CNS injury.

Source: ***Rutledge G. Ellis-Behnke, Yu-Xiang Liang, Si-Wei You, David K. C. Tay, Shuguang Zhang, Kwok-Fai So, and Gerald E. Schneider*; Nano neuro knitting: Peptide nanofiber scaffold for brain repair and axon regeneration with functional return of vision; *PNAS* March 28, 2006, vol. 103, no. 13, 5054–5059.**

**< Previous |**