Neuro-Regeneration for the Next Generation

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As medicine and technology continue to advance, so does human life expectancy. The result of increased life expectancy is the multitude of neurodegenerative disorders that result directly from an ageing brain, which like all biological organisms, will experience physical and chemical changes over time. Eventually, it will be challenging for the organism to repair the damage on its own.

One of the most tragic neurodegenerative diseases is Alzheimer’s disease, characterised by the loss of synapses and general quantity of neurons (Whitehouse, Price et al. 2004). Whilst the disease itself has been extensively studied over the past hundred years, scientists have only managed to temporarily improve the symptoms without coming up with a permanent solution. This is likely due to the combination of challenges that present themselves when attempting to combat this disease: Firstly, there is limited technology that has been developed to diagnose the disease-- the initial onset is often mistaken as standard age-related changes. Secondly, current technology can only diagnose with an 85% accuracy rate and this diagnosis often comes at a very late stage, during which the patient has already suffered for an extended period of time (Knopman, D. S., 2001).

Since the central nervous system (CNS) has little capacity for self-regeneration, it is necessary to supplement the CNS with man-made technology so that patients with Alzheimer’s disease may live both long and interactive lives. Within the field of nanotechnology, scientists...
have begun developing nanomedicine made of nanoparticles that are able to cross the blood brain barrier (BBB), a selective semi-permeable barrier that separates circulating blood from the brain’s extracellular fluid. The nanoparticles are disguised with surface proteins to resemble molecules that the BBB normally allows passage to, and they would then be able to perform predefined tasks as soon as they cross the barrier. As significant as this advancement may be, current nanotechnology can only be applied to medicine and so far, there are only symptom-relieving medicines such as Rivastigmine, an acetylcholinesterase inhibitor which happens to be a candidate for nano-mediated drug delivery (Wilson. B. et al., 2008). Whilst nanomedical technology continues to develop, it is also necessary to find more solutions for Alzheimer’s that directly targets the problem, which is the degeneration of neural circuitry.

One of the potential solutions involves the use of nano-scaffolding for on-site neural tissue regrowth. This particular method includes the use of peptide amphiphile molecules, which are peptide-based molecules with a hydrophobic head group that acts as a ligand for cell surface receptors, and a hydrophilic tail (see in Figure 1).

Figure 1. Self-assembling peptide forming a nanofiber. (Ferrante, E. (2013). “Researchers to Harness the Power of Molecular Self-Assembly.”)
These molecules are genetically engineered to self assemble into a network of nanofiber scaffolds when in the presence of particular physiological ionic conditions. Most recently, researchers explored the isoleucine-lysine-valine-alanine-valine (IKVAV) peptide sequence, which is known to promote growth and development of neurites, the projections from a neuronal cell body. When these peptides encountered the appropriate conditions, the nanofibers formed a gel-like substance with the ability to trap neural progenitor cells that resulted from a combination of the peptide amphiphile solution and cell culture suspensions in vitro. Encapsulated neural progenitor cells show faster rates of growth and more robust development into mature neuronal phenotypes in comparison to control groups (Hartgerink, J. D., et al, 2002). Following the success of these cell cultures, the hope is that peptide amphiphile solutions can be injected into patients with donor cells to have the nanofiber network form on site of the brain. This nanofiber network would hopefully provide cellular signaling to both donor and host cells to aid in neural circuitry regeneration for diseases such as Alzheimer’s.

Another application of nanotechnology within the field of clinical neurobiology involves the use of carbon nanotubes as structural support to neurons (Matsumoto, K., et al. 2010). Carbon nanotubes can be engineered as biocompatible scaffold platforms that are able to promote neuronal regeneration across areas of the nervous system that need repair—these scaffolds should not induce any type of immune system response. In addition, carbon nanotubes inherently share similar structure and possess analogous dimensions to neuronal cytoskeletons—The carbon nanotubes’ cylindrical morphology resembles neuronal dendrites with regards to the nanotubes’ surface-to-volume ratio. Carbon nanotubes also possess high conductivity, which would help with neuronal interactions at the molecular level, thus improving communication between existing neurons (Gilmore, et al., 2008).
To address the issue of governing neurite elongation, which is the direction of desired dendritic growth, researchers have combined microlithography and chemical vapour deposition techniques to fabricate substrates made of multi-walled carbon nanotubes arranged in geometrically patterned substrates. The resulting scaffolds were used as growth substrates to guide hippocampal cell neurite growth. The results showed neurite growth, which followed the edges of the patterned substrate, showing the ways in which carbon nanotubes can, in fact, direct neurite elongation. (Mattson, M. P., et al, 2000). Eventually, these scaffolds may be applied on the surface of the brain’s cortex.
Figure 1. Patterned carbon nanotube substrates are able to direct neurite outgrowth.

A, SEM micrograph showing neuronal line cells cultured on a patterned vertical carbon nanotube substrate (left). The magnified image (right) shows neurites selectively growing along carbon nanotube arrays (Fabbro, A., Prato, M., Ballerini, L. 2013).

B, Dissociated hippocampal neurons cultured on a carbon nanotube-patterned substrate at 7 days in vitro (a), on a carbon nanotube-only, non-patterned substrate at 7 days in vitro (b), and on a carbon nanotube-patterned substrate at 14 days in vitro (magnification of the highlighted region is in (d), in which one typical elongating neurite is highlighted in pink. Image (c) shows the area of the plate that is being viewed and magnified. (Fabbro, A., Prato, M., Ballerini, L. 2013).
If nanomedicine to deliver drugs across the BBB, nano-scaffolding, and carbon nanotube-powered electrical stimulation were combined, it is possible that various neurodegenerative diseases could be terminated in the near future. It’s important to note the ways in which these nanotechnologies may cause severe side effects, such as unwanted cytotoxicity. Currently, this hybrid system has not yet been tested on humans. However, if these nanotechnologies passed through clinical trials and were found to be safe to use on people, the applications that this technology would have are boundless.

The most humanitarian use of nanotechnology on the neurobiological system would be to treat those who are severely memory-impaired, such as injured soldiers who often experience both mental and physical trauma (Jaffe., et al., 2009). Mental disorders such as Post Traumatic Stress Disorder and depression are common amongst combat veterans and one of the symptoms of such disorders is short-term memory loss. If nanotechnology treat Alzheimer’s by repairing CNS damage using neuroregeneration techniques, the same type of technology could be administered to soldiers who suffer similar symptoms. Perhaps this nanotechnology can also be used to treat recovering drug addicts who suffer from memory loss and other neurological diseases.

In today’s society, people are not only looking to cure existing problems, but also seek biological enhancements. By creating new neural circuitry in those who do not need therapy, it is possible that these new synapses will be able to aid humanity in expediting normal learning and memory processes (Jason, Miller, 2012). However, we must first establish adequate technology for medicinal purposes. Thankfully, the evidence provided by studies creating hybrid systems of nanotechnology and neuroclinical biology seems to be a promising beginning.
References


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