# Multimodal Tissue Engineering Strategy for Nerve Regeneration

**Xiumei Wang, Ph. D.**
School of Materials Science and Engineering, Tsinghua University

No.1 Qinghuayuan, Haidian District, Beijing 100084, China
Email: wxm@mail.tsinghua.edu.cn | Tel: 86-10-62782966|

**Abstract**
Biomaterials have been widely accepted as artificial regenerative niches for delivering cell-regulatory signals to instruct cell fate and tissue regeneration. Biomaterials are not only simple physical scaffold for cell and growth factors delivery, but display and deliver multimodal cell-regulatory signals to instruct cell fate and tissue regeneration. In our studies, we proposed a multimodal tissue engineering strategy for nerve regeneration, in which bioactive materials possessing multimodal cell-regulatory signals were designed to play a synergistic effect. First, we developed a series of nanofiber hydrogels with angiogenic and neurotrophic activities. The functionalized self-assembling peptide (fSAP) hydrogels were designed and prepared by using some functional short peptides that biomimicked the biological functions of growth factors and extracellular matrix including vascular endothelial growth factor, brain-derived growth factor, nerve growth factor, and extracellular matrix functional fragment IKVAV. Besides, a hierarchically aligned nanofiber fibrin hydrogel (AFG) was prepared using liquid electrospinning technology and molecular self-assembly technology, which has the directional structure and soft stiffness of bionic nerve tissue. The fSAP and AFG could be combined to obtain an interpenetrating network nanofiber hydrogel, and simultaneously deliver biophysical- (directional structure, nanofiber, low elasticity) and biochemical- (growth factor/extracellular matrix functional fragments) regulatory signals. The composite hydrogels synergistically promoted the crosstalk between neuronal cells and vascular endothelial cells in vitro and in vivo. The rat sciatic nerve defect model, the beagle dog spinal cord hemi-section defect model, the rat cerebral cortex defect model, and the cynomolgus monkey spinal cord hemi-section defect model were used to evaluate the function of hydrogel for nerve regeneration and repair. The results showed that AFG can promote the neural differentiation of mesenchymal stem cells better than non-directional fibrin hydrogels and fibrin-modified hard substrates; promote the recruitment and migration of exogenous and endogenous stem cells, and the rapid neurite outgrowth and signal conduction; accelerate the recovery of motor function. The angiogenic/neurotrophic dual-functional hydrogel demonstrated the synergistic effect of multifunctional peptides to better promote the vascularization and nerve tissue regeneration in the injured area. In addition, the synergy between biophysical and biochemical cues can further accelerate nerve regeneration and repair. Related researches show a great promising for biomaterial-based regeneration medicine and clinical translation in nerve repair

**Bio**

Prof. Xiumei Wang is currently a professor at the school of Materials Science and Engineering, Tsinghua University. She obtained her Ph.D. degree in Materials Science and Engineering at Tsinghua University, China, in 2005, and continued her postdoctoral fellow at the University of Rochester and Massachusetts Institute of Technology, MA, USA from 2005 to 2008. She started her professional career in Tsinghua University from 2008. Her researches mainly focus on: 1) Engineering biomaterials to direct the stem cells fate; 2) Designing bioactive hydrogels to promote typical tissue regeneration; 3) Biomimetic bone substitutes for bone regeneration and clinical

translation. She published over 170 SCI papers, filed 19 patents, several books and book chapters. She is the executive member of the Chinese Society for Biomaterials and served the co-Editor-in-Chief of Tissue Engineering Part C-Method and the editorial member of Frontier of Materials Science, Regenerative Biomaterials, Biomaterials Research. She was honored “the State Natural Science Award 2011” by the State Council of the P.R. China, Science and Technology Award of Beijing, Science and Technology Award of Shandong Province, Chinese Medical Science and Technology Awards by the Ministry of Health and the Ministry of Science and Technology of China, 2012 Distinguished Young Scholar of Tsinghua University, and 2013 New Century Excellent Talents by the Ministry of Education of China.