An antioxidative biodegradable hydrogel with electroconductive, self-healing, and anti-inflammatory properties for treating Parkinson's disease

Student: Junpeng Xu (4th Year, Ph.D. candidate)
Supervisor: Prof. Shan-hui Hsu
Institute of Polymer Science and Engineering, National Taiwan University, Taipei, Taiwan, ROC

Introduction Parkinson's disease (PD) is a common neurodegenerative disease. Challenges remain in developing hydrogel as injectable brain implants to reverse PD symptoms. Herein, a modified gold nano-crosslinker (~30 nm) was developed and used to crosslink chitosan effectively for preparation of a bioactive self-healing hydrogel with 34G (~80 um) needle injectability. The bioactive hydrogel owned strong anti-inflammatory and antioxidative capabilities to rescue inflamed neural stem cells and promoted their proliferation and differentiation toward neurons in vitro. In vivo studies demonstrated that the bioactive hydrogel improved the motor function of PD rats and alleviated the irregular discharge of nerve cells in the subthalamic nucleus. Histology revealed that the hydrogel alone significantly increased the density of tyrosine hydroxylase positive neurons and fibers as well as reduced inflammation, with a high efficacy similar to drug-loaded hydrogel. The bioactive hydrogel serves as a promising biomaterial for developing novel strategies to treat PD.

Results

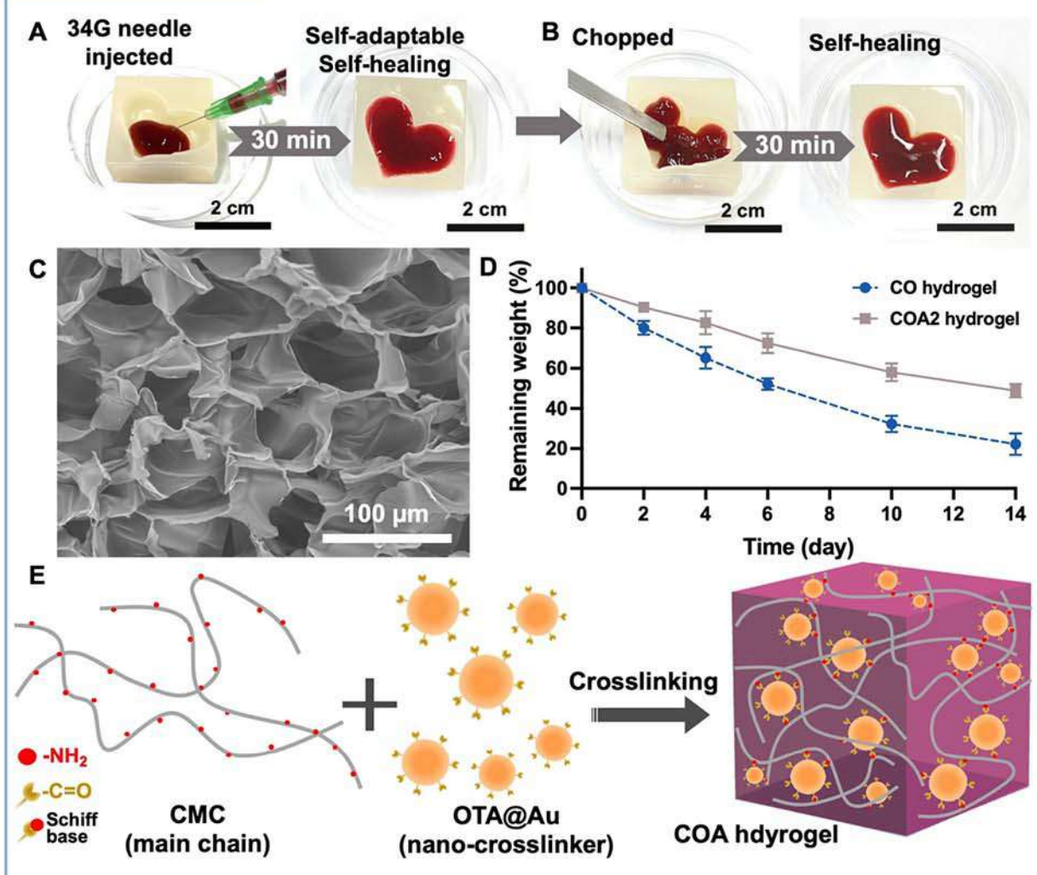

Fig. 1 Preparation and morphology of the self-healing hydrogels. (A&B) The hydrogel can be injected through 34-gauge needle. The self-healing and self-adaption properties were verified. (C) The SEM image for the cross-section of the hydrogel. (D) In vitro degradation profiles. (E) Schematic diagram for the possible gelation mechanism of COA hydrogels.

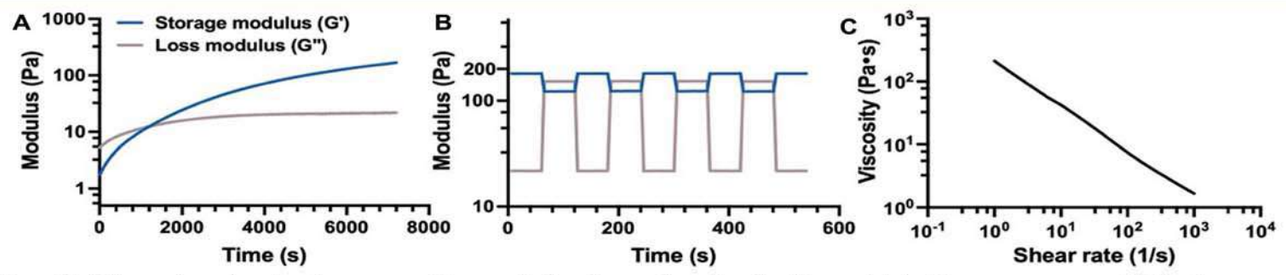

Fig. 2 The rheological properties of hydrogels, including (A) time sweep, (B) damage-healing cycle, and (C) shear thinning property.

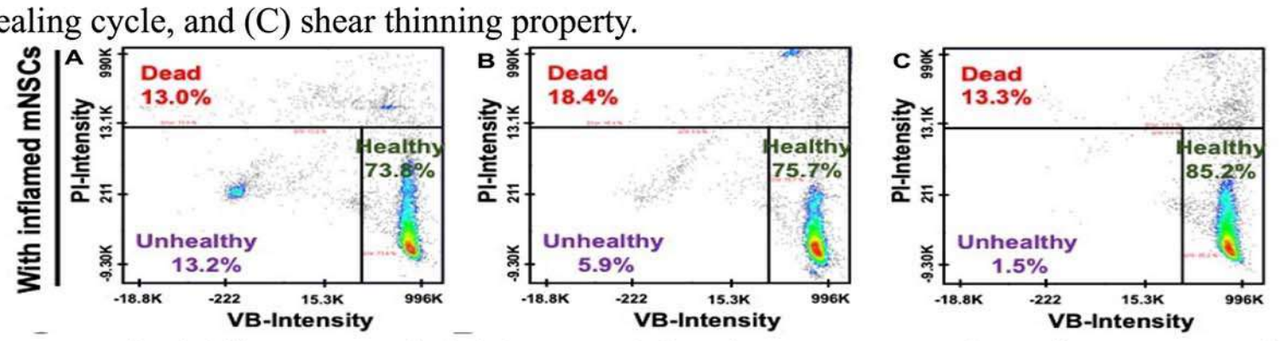

Fig. 3 Cell viability tests. Vitabright-48 staining in response to the cell treatment with encapsulation by the (B) control and (C) target hydrogel compared to the single cells (A).

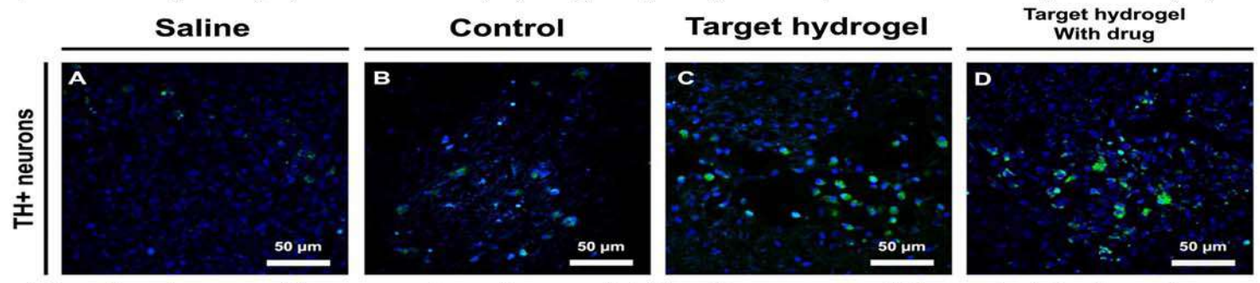

Fig. 4 In vivo immunofluorescent analyses of (A) saline group, (B) control hydrogel group, (C) target hydrogel group, and (D) target hydrogel with drug group for the expression of tyrosine hydroxylase positive (TH+) dopaminergic neurons in the substantia nigra pars compacta.

Conclusion New modified gold nanoparticles with aldehyde groups as efficient nano-crosslinkers were synthesized and characterized. Bioactive self-healing hydrogels made of chitosan and gold nano-crosslinker had proper modulus and conductivity. Neural stem cells showed better proliferation in hydrogel versus non-Au-containing hydrogel, and inclined to differentiate towards neurons expressing the specific marker protein. The hydrogel was antioxidative and anti-inflammatory and rescued ~90% of inflamed neural stem cells in vitro. The biocompatibility and therapeutic efficacy of the injectable hydrogel as brain implants were confirmed in vivo by the PD rat model. The hydrogel implant effectively alleviated the irregular discharge of nerve cells in the intracerebral projection area, promoted the recovery of motor function, and reduced the histological neurodegeneration in PD rats, which was as effective as the drug-loaded hydrogel. These findings support the use of bioactive and conductive hydrogel alone as a promising biomaterial implant for neuroprotection and PD therapy instead of merely a cell/drug carrier.