Supplementary information

A responsive cascade drug delivery scaffold adapted to the therapeutic time window for peripheral nerve injury repair

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Fig. S1. Size distribution of PLGA nanoparticles prepared under different ultrasonication intensity and duration.
**Fig. S2.** The photograph of calcium cross-linked alginate hydrogel loaded with VB$_{12}$ (pink) and NGF.
Fig. S3. (A) The photograph of calcium cross-linked alginate hydrogel with 1%, 2.5%, and 5% concentration of alginate. (B) The stress-strain curve of each concentration of hydrogel. (C) Rheological characterizations of alginate hydrogels with different concentration.
Fig. S4. A. The result of FTIR test of alginate, alginate + VB$_{12}$, alginate + VB$_{12}$ +NGF, NGF and VB$_{12}$. B. TG-DSC test of alginate, alginate + VB$_{12}$, alginate + VB$_{12}$ +NGF.
Fig. S5. Three-dimensional cytoskeleton (red) and DAPI (blue) staining photographs of PC12 cells cultured on TCP and UCDS with 1%, 2.5% and 5% concentration of hydrogel.
Fig. S6. Statistical data of the pore diameter of the ultrasound-responsive calcium cross-linked alginate hydrogel with no stimulation, 0.1W/cm², 0.5W/cm² and 1W/cm² intensity of stimulation.
Fig. S7. The statistical data of the single release amount of VB$_{12}$ and NGF in the first three days under different intensities of ultrasonic stimulation.
Fig. S8. Results of the representative photo and quantitative analysis of live/dead assay (n = 3) of different groups.
Fig. S9. Representative images of cytoskeleton staining of PC12 cells of RCDDS + 0.1W/cm² US, RCDDS + 0.8W/cm² US and RCDDS + 1W/cm² US.
Fig. S10. Blood routine examination results of neutrophil and monocytes of the rats in five different groups (normal, model, blank scaffold, RCDDS and RCDDS + tun-US) at day 1, 3, 5 and 7 after nerve injury (n = 3).
Fig. S11. Representative CMAP waveform of the rats from $\text{AH}_{\text{VB12}} + \text{US}$ group and $\text{NP-MS-AH}_{\text{NGF}} + \text{US}$ group, RCDDS groups and RCDDS + US group.