**Supplementary Information**

# Light-guiding hydrogels for cell-based sensing and optogenetic synthesis *in vivo*

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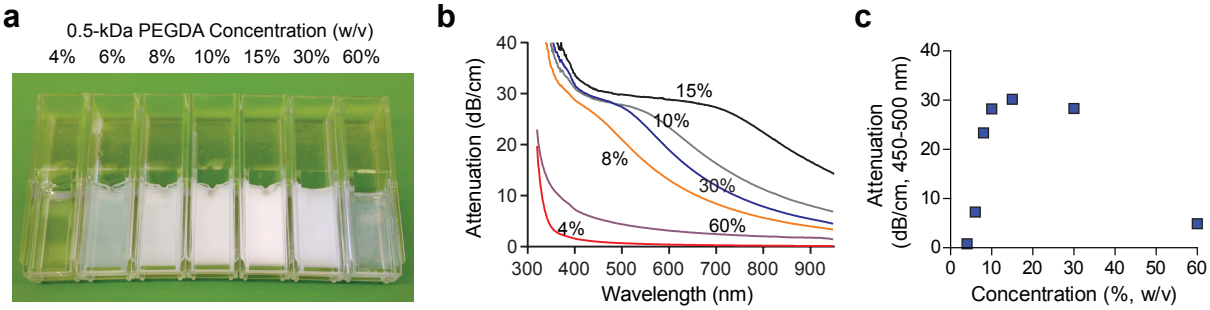
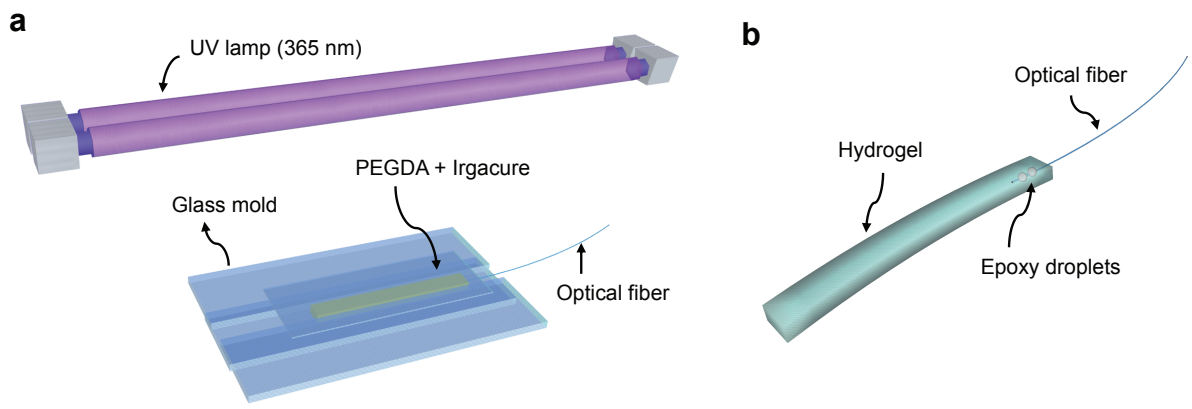
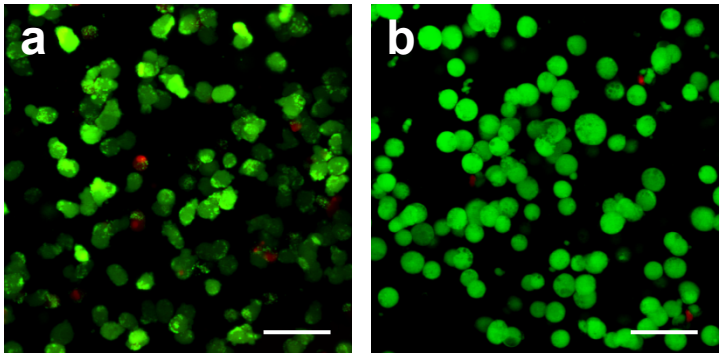


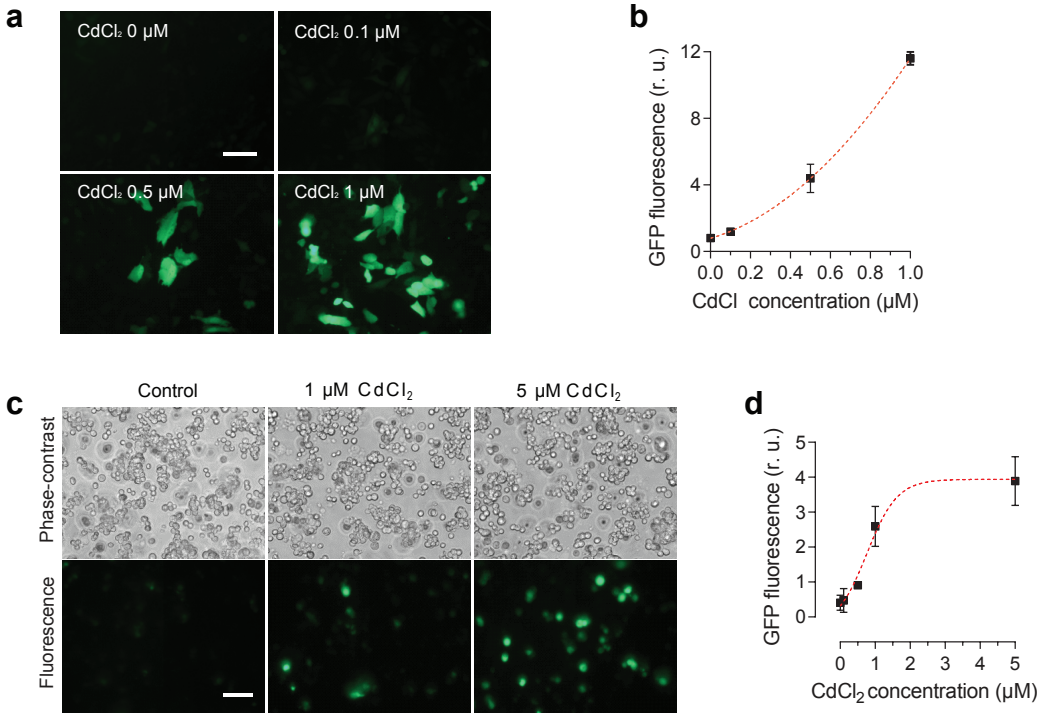

**Supplementary Fig. S1** | Effect of the precursor concentration on optical transparency. (**a**) Photographs of PEG hydrogels at varying concentrations of PEGDA (0.5 kDa) in standard 1-cm-wide cuvettes. (**b**) Optical attenuation spectra. (**c**) Average attenuation coefficients averaged over a spectral range of 450-500 nm.



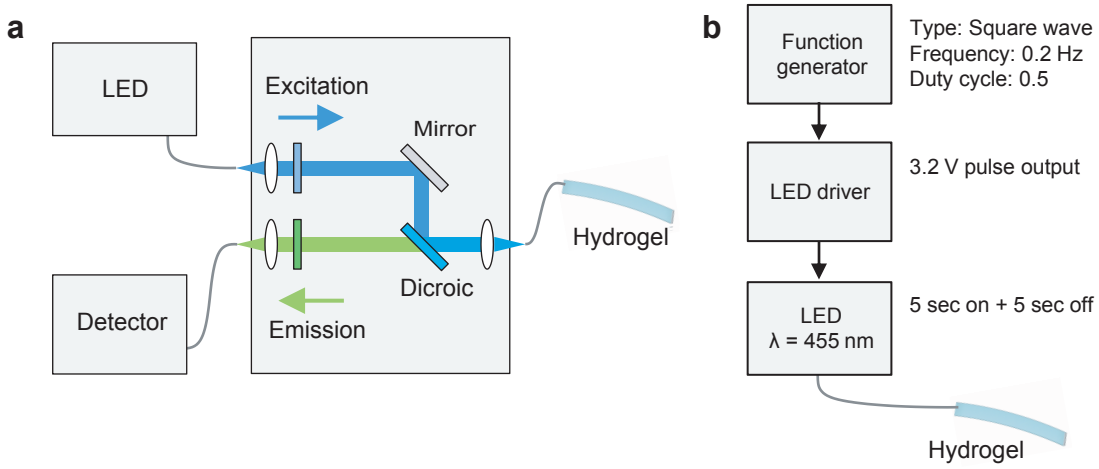

**Supplementary Fig. S2** | Fabrication of a hydrogel optical waveguide. (**a**) Precursor solution containing PEG diacrylates (PEGDA) and photoinitiator (Irgacure) was photo-crosslinked *in situ* in a glass mold. (**b**) Schematic of the fabricated hydrogel optical waveguide.



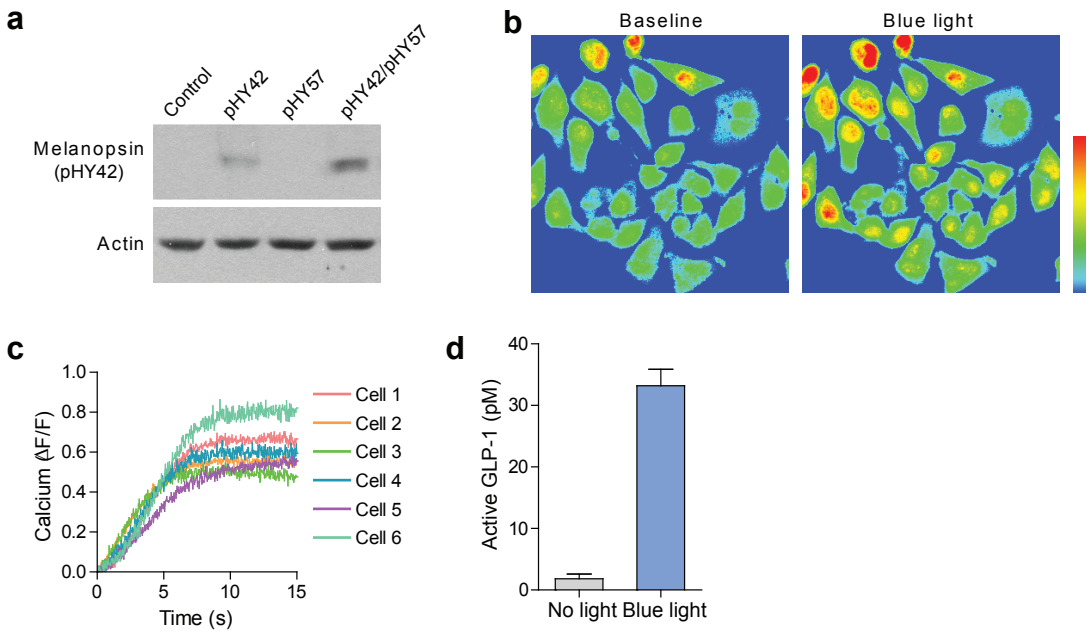

**Supplementary Fig. S3** | Cell viability after hydrogel encapsulation. (**a**) HEK293 human embryonic kidney cell line. (**b**) EL4 mouse T cell line. Cells were encapsulated in PEG hydrogel through photopolymerization and cell viability was tested by staining with calcein AM (green; viable cells) and ethidium homodimer (red; dead cells). In the hydrogels, 96% of the HEK293 cells are live after encapsulation (a), and 97.5% of EL4 cells are live (b). Scale bar, 50 μm.




**Supplementary Fig. S4** | Activation of heat-shock protein (hsp70) gene in response to cadmium ions. (**a**) Fluorescence images of the hsp-70-GFP sensing cells *in vitro*. (**b**) Dose-dependent activation of GFP fluorescence. (c) Phase contrast images and corresponding fluorescence images of the sensing cells in a hydrogel at 24 hours after $CdCl_2$ was added to the medium. (**d**) Dose-dependent activation of GFP signal *in vitro*.




**Supplementary Fig. S5** | Schematic of the experimental setups for sending and receiving light to and from a hydrogel. (**a**) Setup for fluorescence sensing. A fiber-coupled blue LED (λ = 455 nm; excitation) was coupled to the hydrogel through the pigtail fiber and the fluorescence emission (500-550 nm) was collected to a photo-detector. (**b**) Setup for optogenetic therapy. To generate pulsed blue light, a light emitting diode (LED) was driven in a pulsed mode at 0.1 Hz.




**Supplementary Fig. S6** | Stable cell line for light-induced GLP-1 secretion, produced with two plasmids named pHY42 (human melanopsin) and pHY57 (NFAT promoter driven GLP-1 expression). (**a**) Western blot analysis confirming the expression of melanopsin. (**b**) Fluorescence calcium-level images before and after illuminating blue light (10 s). The cells were preloded with a fluorescent calcium indicator. (**c**) Time traces of the calcium signals in various cells. (**d**) The GLP-1 level in the cell media measured by ELISA before and after illuminating blue activation light.

## Supplementary Video S1

A fully awake mouse with a hydrogel (4 mm x 1 mm x 40 mm) implanted in the subcutaneous pocket. Video was taken one day after implantation.