Supplementary Information

Biotinylated Heparin-binding Peptide Amphiphile

A biotinylated version of the heparin-binding peptide amphiphile (biotinHBPA; Fig. S1) was synthesized for specific labeling of HBPA with streptavidin-conjugated markers based on previous work [1]. A biotinylated lysine purchased from NovaBiochem was coupled to a RINK amide resin (NovaBiochem) using standard fluorenylmethoxycarbonyl (Fmoc) solid phase peptide synthesis. The remainder of the peptide was synthesized and purified using the methods described previously [2].

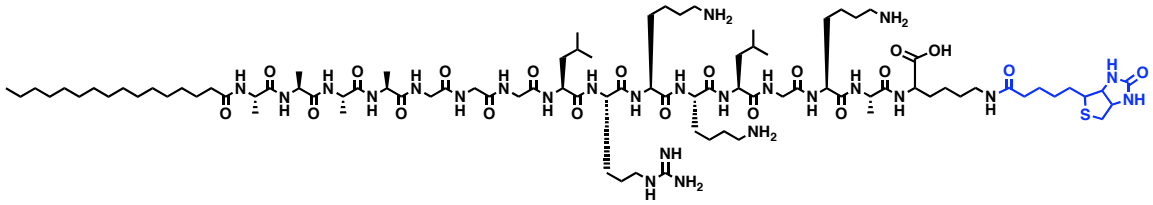

Figure S1. Chemical structure of biotinHBPA with biotin (blue).

Islet Endothelial Cell Sprouting Assay

The non-heparin-binding peptide amphiphile (PA) with the sequence VVAAEE (Fig. S2) was synthesized and purified using methods described previously [3].

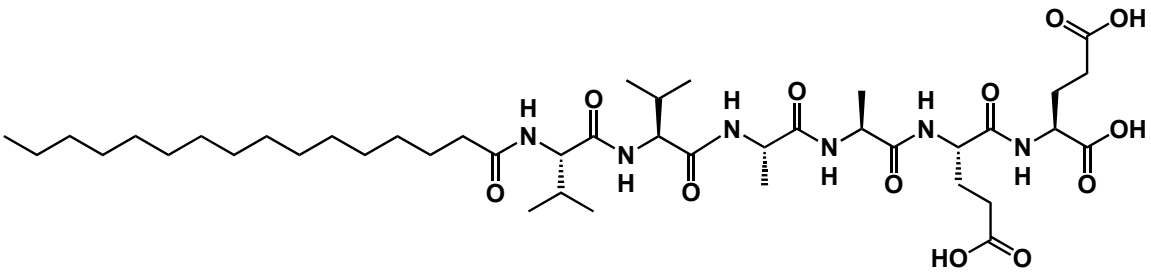

Figure S2. Chemical structure of non-heparin-binding peptide amphiphile with the peptide sequence VVAAEE.

Islets were embedded in the VVAAEE PA hydrogel, which provided a 3D matrix to support sprouting. Islets were stained with Live/Dead™ Viability/Cytotoxicity Kit to visualize sprouts, and sprouts were defined as cord-like, linear cell extensions out of the islet as shown in Fig. S3.

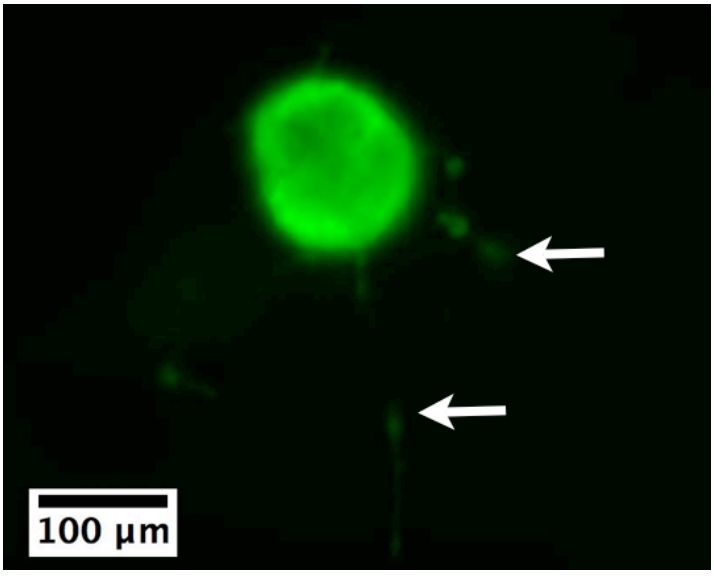

Figure S3. Fluorescence microscopy image of murine islet embedded in the VVAAEE PA hydrogel on Day 1 stained with calcein (green) to visualize

sprouting. Arrows indicate capillary sprouts protruding from the islet into the surrounding matrix.

Cryogenic Transmission Electron Microscopy

HBPA and heparin were reconstituted at 1 mg/mL in water and phosphate buffered saline (PBS; HyClone), respectively. HBPA and heparin were mixed at equal volume then diluted for a final concentration of 0.1 mg/mL each HBPA and heparin. HBPA without heparin was also diluted to 0.1 mg/mL to evaluate nanofiber formation in the absence of heparin. Immediately following dilution, the sample was prepared for cryogenic transmission electroscopy (cryoTEM).

A Vitrobot Mark IV equipped with controlled humidity and temperature was used for plunging samples. A small volume of the HBPA-heparin solution was deposited on a copper TEM grid with holey carbon support film (Electron Microscopy Sciences) and held in place with tweezers mounted to the Vitrobot. The specimen was blotted in 90-95% humidity and plunged into a liquid ethane reservoir that was cooled by liquid nitrogen. The vitrified samples were transferred in liquid nitrogen to a Gatan 626 cryo-holder through a cryo-transfer state and imaged using a JEOL 1230 microscope with an accelerating voltage of 100kV.

We observed HBPA nanofibers at the concentrations used (Fig. S4) with morphologies similar to those previously observed [4]. The addition of growth factors is not expected to affect nanofiber morphology since they are used at

concentrations (100 ng/mL) 1000 times less than the HBPA and heparin concentrations (0.1 mg/mL).

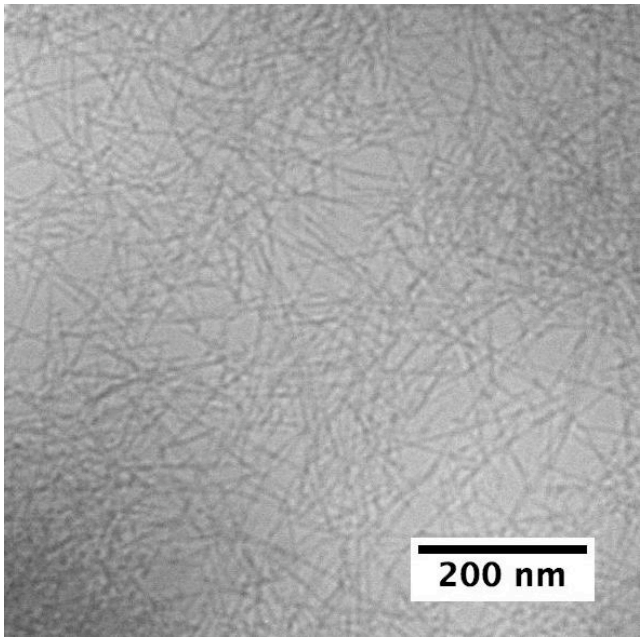

Figure S4. Cryogenic TEM micrograph of HBPA nanofibers formed from 0.1 mg/mL HBPA and 0.1 mg/mL heparin.

Islet viability

Islets immediately after isolation on day 0 were stained using Live/Dead™ Viability/Cytotoxicity Kit and imaged on a Nikon inverted fluorescent microscope.

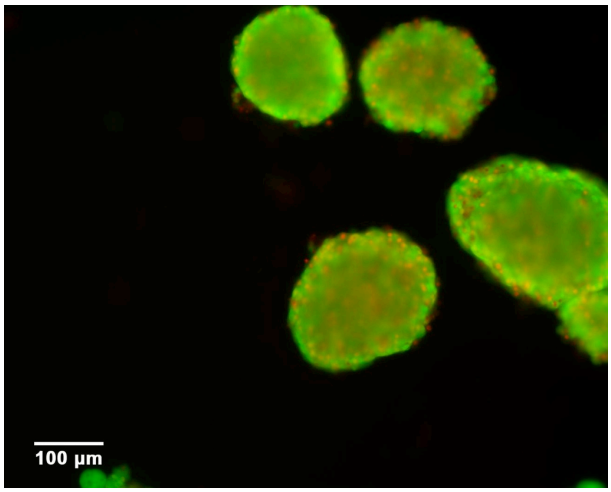

Figure S5. Fluorescence microscopy images of murine islets after isolation on Day 0 showing live (green) and dead (red) cells.

1. Guler MO, Soukasene S, Hulvat JF, Stupp SI. Presentation and recognition of biotin on nanofibers formed by branched peptide amphiphiles. Nano Lett 2005;5(2):249-252.
2. Rajangam K, Arnold MS, Rocco MA, Stupp SI. Peptide amphiphile nanostructure-heparin interactions and their relationship to bioactivity. Biomaterials 2008;29(23):3298-3305.
3. Ghanaati S, Webber MJ, Unger RE, Orth C, Hulvat JF, Kiehna SE, et al. Dynamic in vivo biocompatibility of angiogenic peptide amphiphile nanofibers. Biomaterials 2009;30(31):6202-6212.
4. Rajangam K, Behanna HA, Hui MJ, Han XQ, Hulvat JF, Lomasney JW, et al. Heparin binding nanostructures to promote growth of blood vessels. Nano Lett 2006;6(9):2086-2090.