

## Supporting Information

# Mimicking Neuroligin-2 Functions in $\beta$ -cells by Functionalized Nanoparticles as a Novel Approach for Antidiabetic Therapy

Anna Munder,<sup>§</sup> Liron L. Israel,<sup>§,‡</sup> Shirin Kahremany,<sup>§</sup> Rina Ben-Shabat-Binyamini,<sup>§,‡</sup> Charles Zhang,<sup>†</sup> Michal Kolitz-Domb,<sup>§,‡</sup> Olga Viskind,<sup>§</sup> Anna Levine,<sup>§</sup> Hanoch Senderowitz,<sup>§</sup> Steven Chessler,<sup>†</sup> Jean-Paul Lellouche,<sup>§,‡,\*</sup> and Arie Gruzman<sup>§\*</sup>

<sup>§</sup>Department of Chemistry, Faculty of Exact Sciences, Bar-Ilan University, Ramat Gan, Israel.

<sup>‡</sup>Nanomaterials Research Center, Institute of Nanotechnology & Advanced Materials (BINA),  
Bar-Ilan University, Ramat Gan, Israel.

<sup>†</sup>Division of Endocrinology, Diabetes & Metabolism, Department of Medicine, University of  
California, Irvine, California, United States.

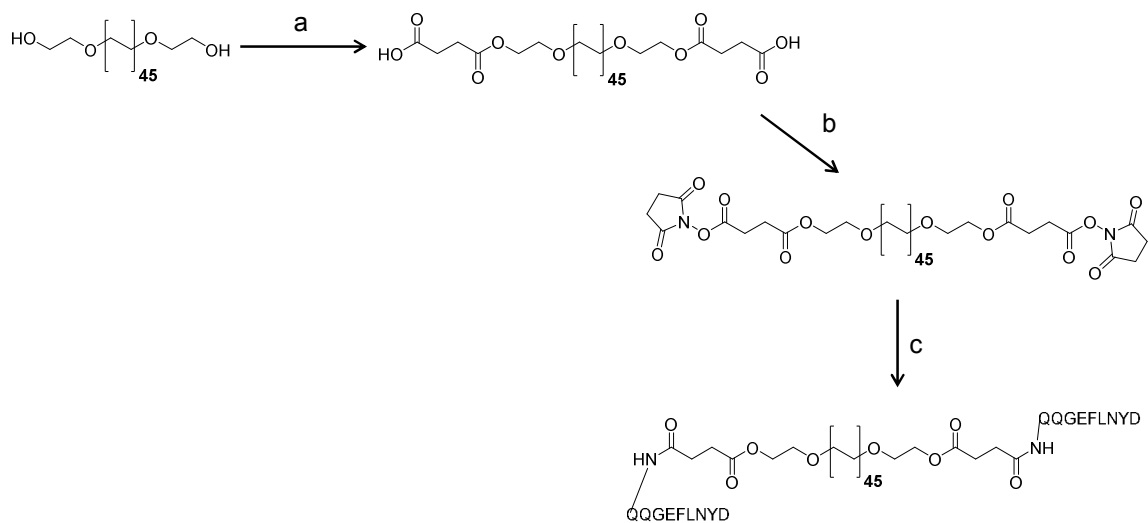
<sup>§</sup>The Scientific Equipment Center, Faculty of Biological Sciences, Bar-Ilan University, Ramat  
Gan, Israel.

\*E-mail: Jean-Paul.M.Lellouche@biu.ac.il,

\*E-mail: gruzmaa@biu.ac.il

1. **Scheme S1.** Synthesis of HSA-112
2. **Figure S1.** Analytical data of synthesized peptides
  - Figure S1a.** HSA-28
  - Figure S1b.** EEIQYSDFN (scrambled peptide)
  - Figure S1c.** SEGNRWSNSTKGLFQRA (CNSP1)
  - Figure S1d.** HSEGLFQRA (CNSP2)
3. **Figure S2.** Analytical data of HSA-112
4. **Figure S3.** Calibration curve of HSA-28
5. **Figure S4.** Evaluation of possible HSA-28P stimulatory effect on proliferation rate of PC-3 and PC-12 cell lines

## 1. Scheme S1. Synthesis of HSA-112

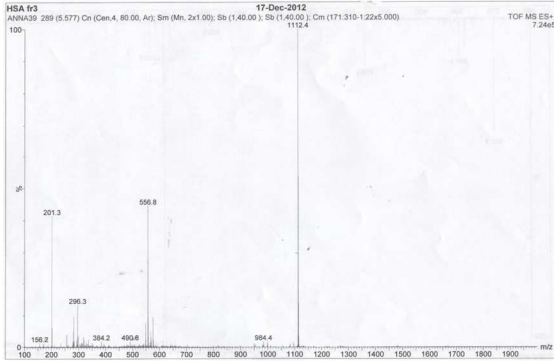


**Reagents and conditions:** (a) succinic anhydride C<sub>4</sub>H<sub>4</sub>O<sub>3</sub>, dry tetrahydrofuran (THF), 3% dry pyridine C<sub>5</sub>H<sub>5</sub>N, nitrogen pressure, 60° C, 24h; (b) N-hydroxysuccinimide C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub>, N,N'-dicyclohexylcarbodiimide (DCC) C<sub>13</sub>H<sub>22</sub>N<sub>2</sub>, dry THF, room temperature, 8h; (c) HSA-28 peptide, solution of 15% NaHCO<sub>3</sub>/dioxane 1:1, room temperature, 48h.

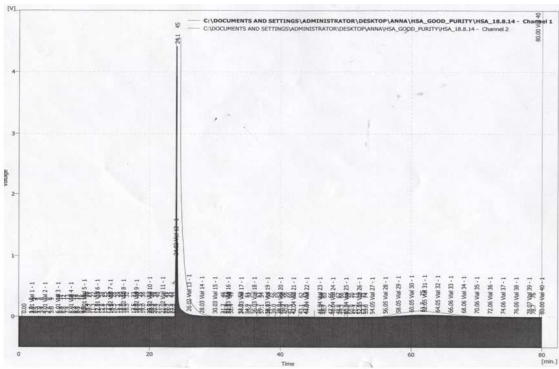
## 2. Figure S1. Analytical data for synthesized peptides

### Figure S1a. HSA-28 ( $MH^+ = 1112.4$ )

Mass spectrum (ESI<sup>+</sup>)



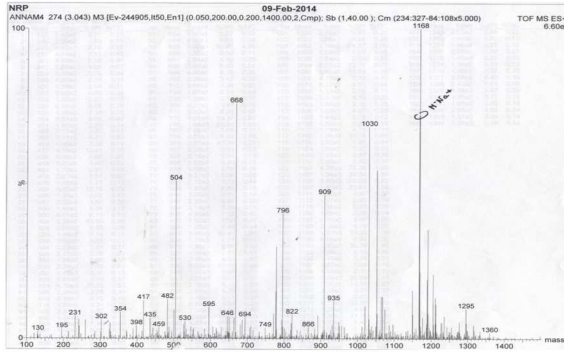
HPLC analysis



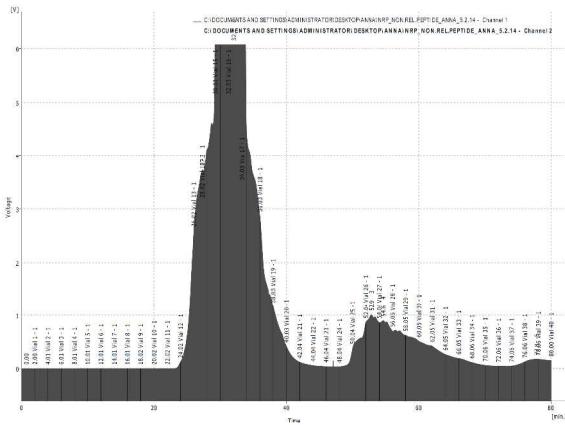
**Figure S1b. EEIQYSDFN (scrambled peptide)**

Mass spectrum (ESI<sup>+</sup>)

EEIQYSDFN (scrambled peptide) (MNa<sup>+</sup>=1168.0)



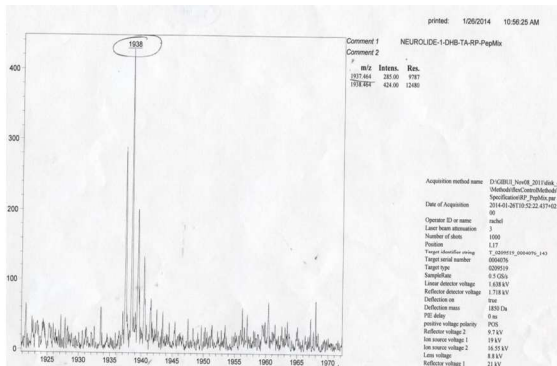
**HPLC analysis**



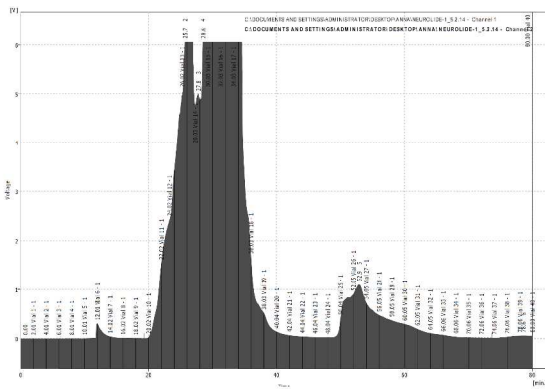
### Figure S1c. SEGNRWSNSTKGLFQRA (CNSP1)

Mass spectrum (MALDI)

SEGNRWSNSTKGLFQRA (CNSP1) ( $MH^+ = 1938.0$ )



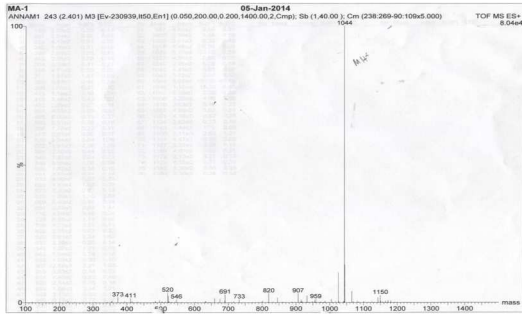
### HPLC analysis



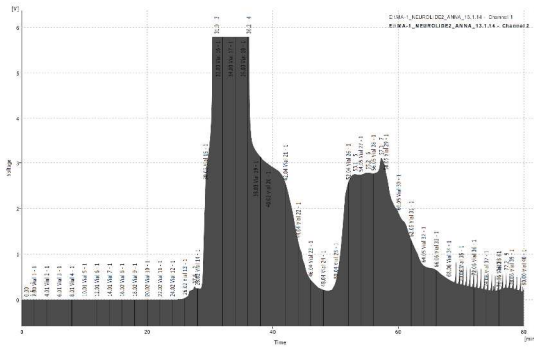
**Figure S1d. HSEGLFQRA (CNSP2)**

Mass spectrum (ESI<sup>+</sup>)

HSEGLFQRA (CNSP2) (MH<sup>+</sup> =1044.0)



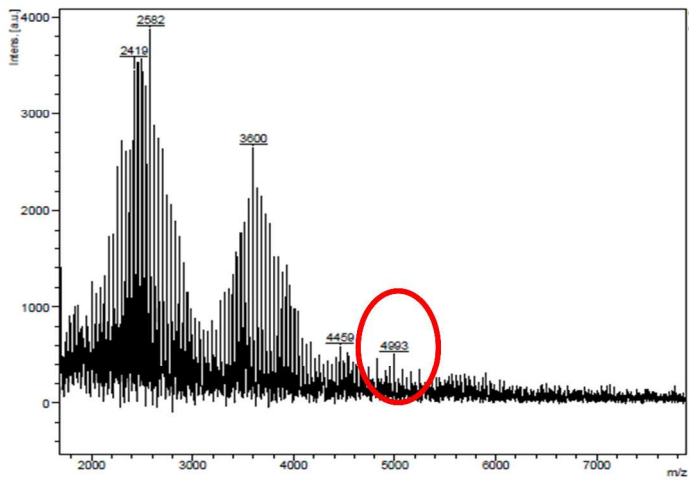
**HPLC analysis**



### 3. Figure S2. Analytical data of HSA-112

Mass spectrum (MALDI)

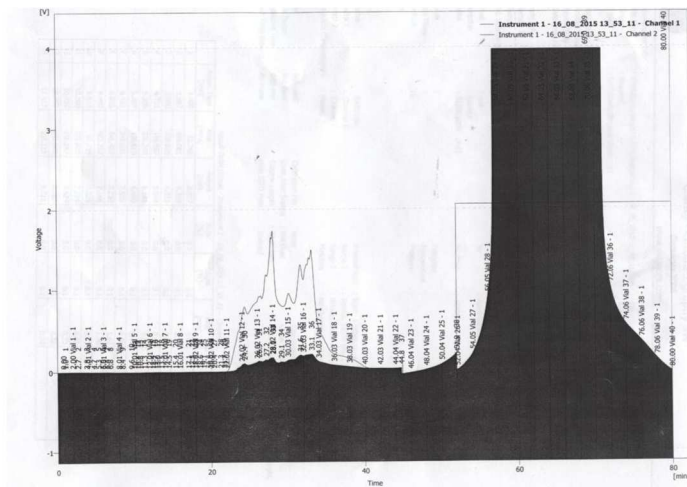
HSA-112 (double substituted by HSA-28 PEG<sub>2000</sub>)(MH<sup>+</sup>≈4993.0)



HPLC analysis

A peak in retention time around 23-38 min is monosubstituted by HSA-28 PEG<sub>2000</sub>

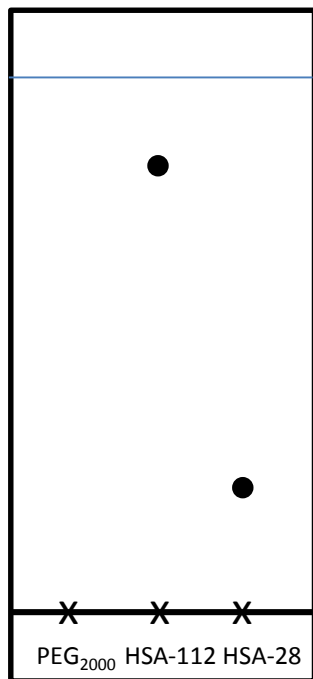
A peak in retention time around 55-70 min is disubstituted by HSA-28 PEG<sub>2000</sub>





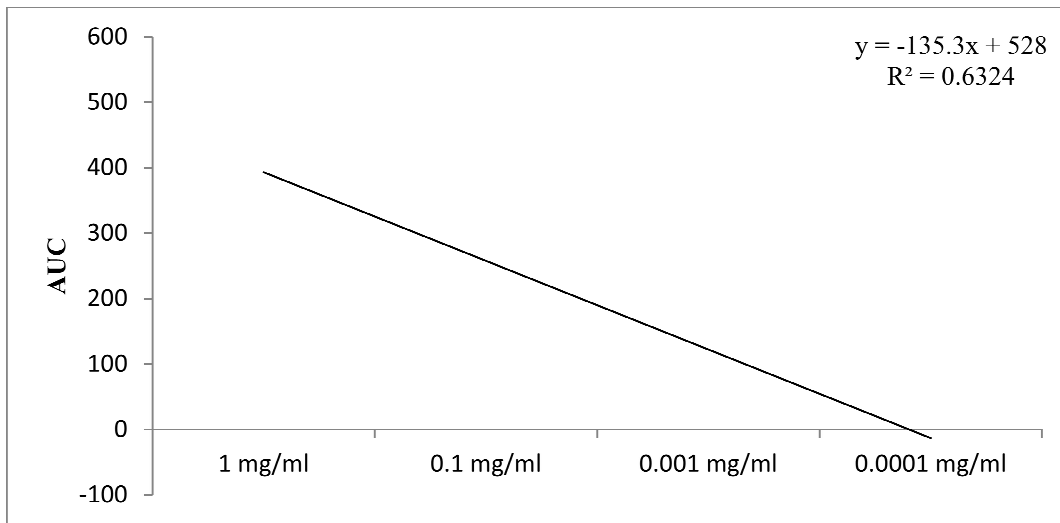
TLC

UV detection

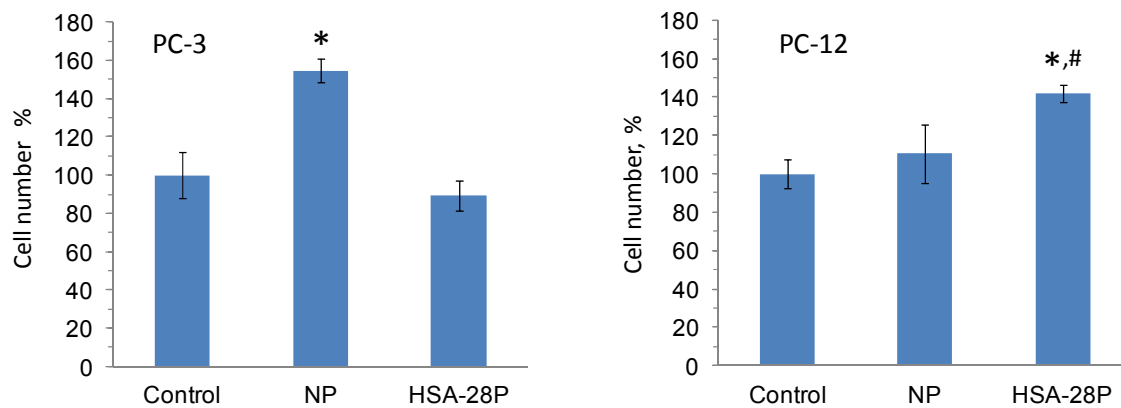


Eluent: Diethylether/Ethanol (80/20)

4. **Figure S3.** Calibration curve of HSA-28



5. **Figure S4**



**Fig. S4.** Evaluation of possible HSA-28P stimulatory effect on proliferation rate of PC-3 and PC-12 cell lines. PC-3 cells or PC-12 cells were incubated for 24h with the medium

supplemented with HSA-28P (2.76 $\mu$ M), or NP (0.76  $\mu$ g/ml). After the incubation time cells were detached by trypsin, colored by trypan blue and counted as described in Methods, n=6. MEAN $\pm$ SE.