Fig S1: Food dyes efficiently quench FAM-NP41 bladder fluorescence.
A fluorescent plate reader assay was used to show dose dependent quenching of FAM-NP41 fluorescence. Erythrosine extra bluish (Santa Cruz Biotechnology, Inc.) was the most efficient quencher with > ~80% quenching at 2.5 times dye to fluorescein ratio and > 95% quenching at 5X dye to fluorescein ratio **(A)**. Other food dyes tested included Allura Red and Sunset Yellow. To test for quenching in-vivo we administered, by direct iv injection, 50 mg/kg MW 879.76 (~1.5 µmoles per 25 gm mouse) to mice that had been injected with 150nmoles of FAM-NP41 2 hours prior. This represents approximately a 10 X dye to FAM-NP41 dose. Some bladder fluorescence remained after imaging so additional dye (30 µl, 10 mM Erythrosin extra bluish) was injected directly into the bladder. Images are shown for mouse bladder with no dye quencher **(B)** and addition of Erythrosine extra bluish (intravenous and intra bladder) **(C)** with bladder fluorescence quench to near background level. Dye would likely not be needed if this method was used for human patients as bladder catheterization in patients could be started as FAM-NP41 is administered so bladder fluorescence could be washed out.

Fig S2: TAMRA-NP41 labels autonomic unmyelinated nerve in prostate gland of rat.
Fluorescence image of nerve fascicles (white arrows) around prostate gland in living male Sprague-Dawley rat, imaged 15 min post i.v. injection of 500nmol of NP41-TAMRA **(A)**. Tissue was excised and frozen unfixed for validation of peptide fluorescence signal using confocal imaging **(B)** and immunohistochemistry with an antibody to TAMRA detected with horse radish peroxidase-secondary and diaminobenzidine staining **(C)**. Antibody staining against tyrosine hydroxylase was used to validate presence of autonomic nerves **(D)** no-primary negative control **(E)**.

Fig S3: Screening of human nerve binding peptides identified by phage display.
Topical application of 100µM of human nerve binding peptides FAM-HNP401 **(A)**, FAM-HNP402 **(B)**, FAM-HNP403 **(C)** on serial sections of fresh-viable **human** sural nerve (upper row) and **human** temporalis muscle (lower row). For comparison topical application of 100µM of carboxy-FAM **(D)** and peptide screened for binding to mouse nerve NP41-FAM **(E)**. H&E of staining of nerve and muscle **(F)**. All fluorescence images acquired on Lumar microscope at 34X magnification with a 2s exposure and levelled equally for comparison.

Fig S4: Screening of human nerve binding peptides identified by phage display.

Topical application of 100μM of human nerve binding peptides FAM-HNP401 **(A)**, FAM-HNP402 **(B)**, FAM-HNP403 **(C)** on serial sections of fresh-viable **human** ansa cervicalis nerve (upper row) and **human** great auricular nerve (lower row) from the neck of two different patients. For comparison topical application of 100μM of carboxy-FAM **(D)** and peptide screened for binding to mouse nerve NP41-FAM **(E)**. All fluorescence images acquired on Lumar microscope at 34X magnification with a 2s exposure and levelled equally for comparison.

Fig S5: Differential binding of nerve binding peptides to human and mouse tissue.
Determination of optimal dose response by topical application of FAM-HNP401 on human laryngeal nerve sections at final concentration of 375 μM **(A)**, 100 μM **(B)**, 50 μM **(C)**, 10 μM **(D)** and 1 μM **(E)**, imaged with confocal microscopy with identical parameters and levelled equally for comparison. ** brightened 2 fold for viewing. Nerve to muscle contrast at high concentration of 375 μM for FAM-NP41 (**F** and **G**) and FAM-HNP401 (**H** and **I**) imaged on confocal microscopy and levelled for direct comparison. Mouse facial nerve (red arrows) with surrounding muscle treated with 375 μM **(J)**, 100 μM **(K)** of FAM-NP41 or 375 μM **(L)**, 100 μM **(M)** of FAM-HNP401. Images in bottom row acquired on Lumar imaging scope with identical parameters and are comparable. FAM-HNP401 shows high binding of muscle in mouse tissue with poor contrast compared to FAM-NP41. High resolution confocal image of low concentration of FAM-HNP401 (10 μM) on human nerve shows binding of peptide to non-axonal structural components of nerve **(N)**.

Fig S6: Autofluorescence of human nerve tissue.
Topical application of 100μM FAM-HNP401 **(A)** or buffer only **(B)** on 10μm sections of unfixed human sural nerve followed by imaging using confocal microscopy under identical acquisition parameters for direct comparison. Images were levelled equally using Image J followed by a 16 fold brightening of **(B)** for viewing.

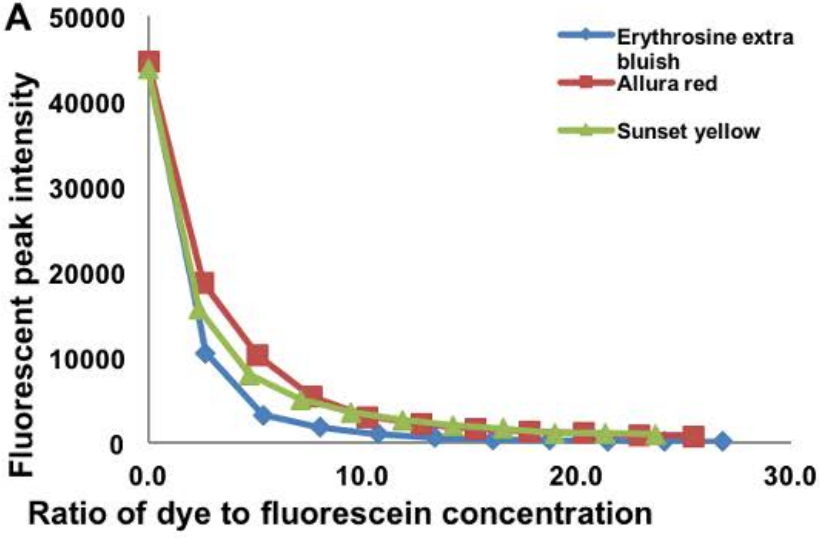
Fig S7: Mass spectroscopy analysis of urine samples from mice injected with nerve binding peptides.
Fragmented ion peaks from Cysteine-FAM collected from the urine of mice that were injected with FAM-HNP401 indicating peptide is metabolized **(A)**. Similar results were obtained with mice injected with FAM-NP41 **(B)**. However, mouse injected with FAM-dNP41, where peptides is made with d-amino acids, is detectable in the urine and is not metabolized **(C)**.

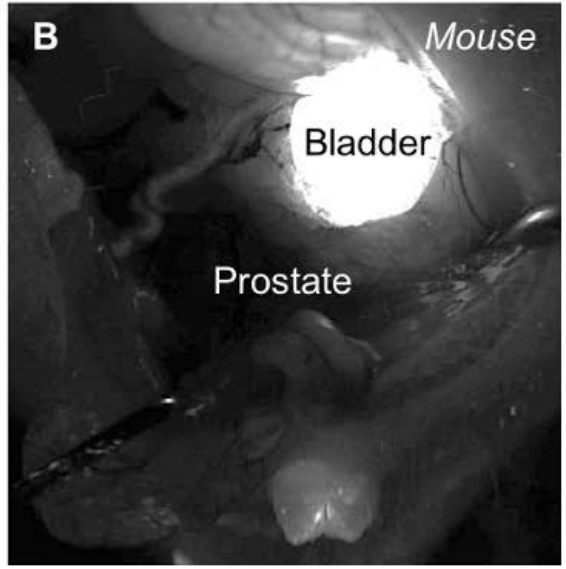
Fig S8: Stability of peptides in ex-vivo human plasma and cerebrospinal fluid from rats. FAM-HNP401 peptide detected at 5min **(A)** and 2hours **(B)** after incubation at 37^{o}C in human plasma in at a dose of 53.2 mg/kg or 2µmole. An equal volume of 1:1 acetonitirile: water with 2% acetic acid is added to precipitate the protein matter, supernatant is extracted for analysis by LC-MS on a C18 reverse phase column with gradient of 9:1 H2O+0.05%TFA: Acetonitrile+0.05%TFA to 1:9 H2O+0.05%TFA: Acetonitrile+0.05%TFA in 20min. Detector channel of 450nm shows FAM-HNP401. The peptide remain intact at 2hours post incubation with x% of the composition at 5min post incubation with human plasma. FAM-NP41 peptide detected at 5min **(C)** and 2hours **(D)** after incubation at 37^{o}C in human plasma in at a dose of 53.2 mg/kg or 2µmole, followed by LC-MS analysis with method described above. Similar to our previous result, FAM-NP41 remains intact at 2hours post incubation with x% of the composition at 5min post incubation with human plasma. We also tested FAM-HNP401 **(E)** and FAM-NP41 **(F)** in cerebrospinal spinal fluid from rat at 2 hours after incubation to demonstrate stability of the peptides in circulation.

Fig S9: FAM-HNP401 binds to fresh viable nerve acquired from human prostate gland. Topical application of 100µM FAM-HNP401 **(A)** or FAM-NP41 **(B)** on 10µm sections of unfixed nerves from the prostate gland followed by imaging using confocal microscopy. Immunofluorescence for nerve using neurofilament antibody SMI312 **(C)** on fixed section of nerve from prostate gland and corresponding H&E staining **(D)**. These images are obtained from different patients than those shown in **Fig 5.** of the manuscript.

Table S1: Table of peptide sequences and their abbreviation.

Fig. S1.


A
50000
40000
30000
20000
10000
0
Fluorescent peak intensity
0.0
10.0
20.0
30.0
Ratio of dye to fluorescein concentration
Erythrosine extra bluish
Allura red
Sunset yellow


B
Mouse
Bladder
Prostate

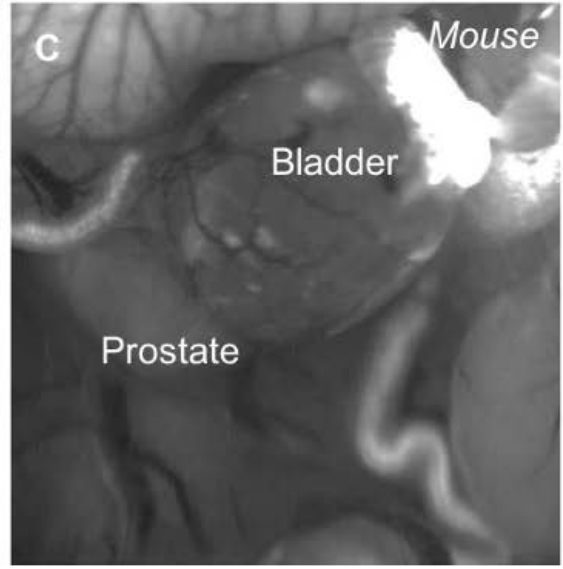

C
Mouse
Bladder
Prostate

Fig. S2.

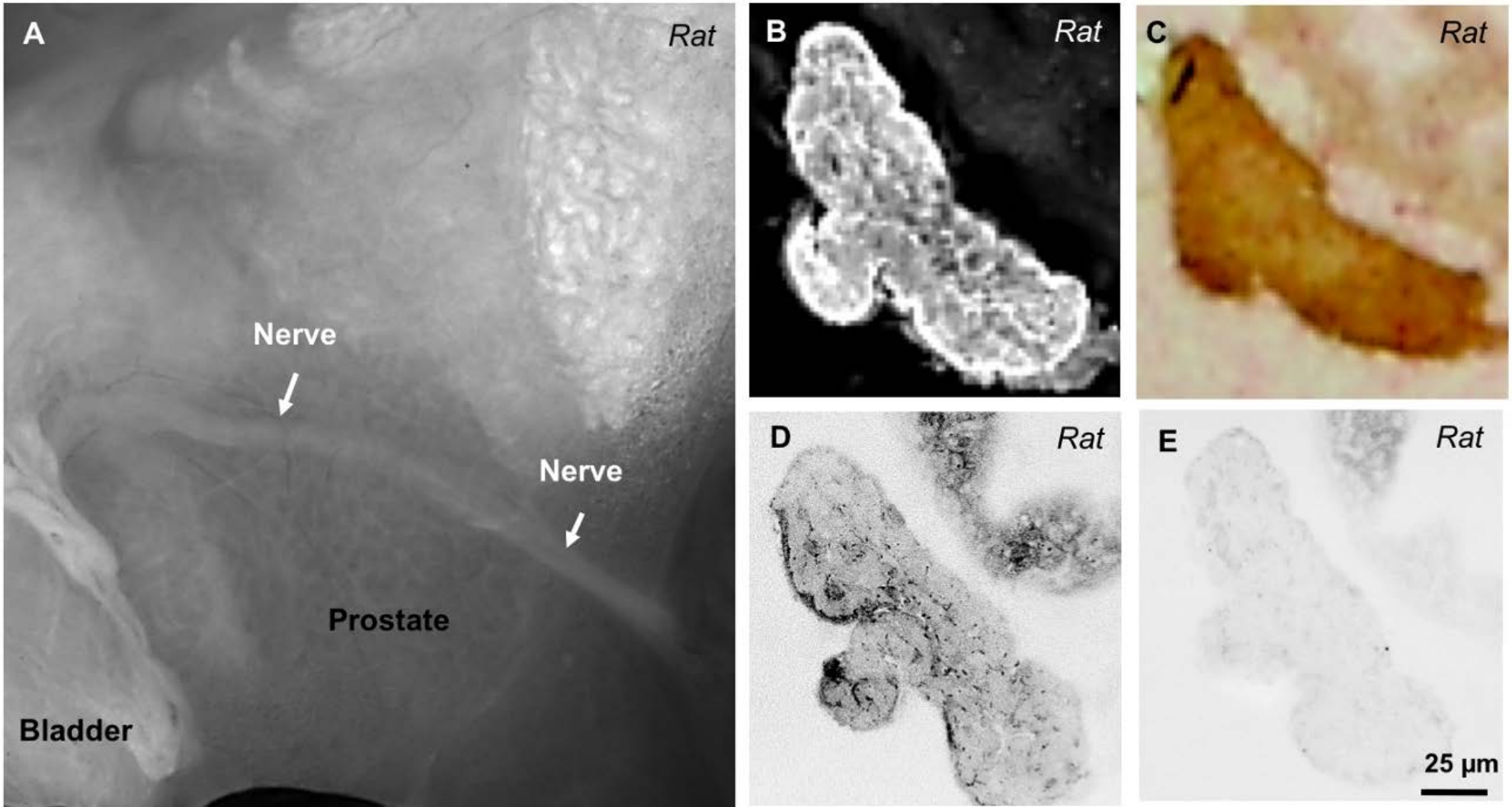


Fig. S3.

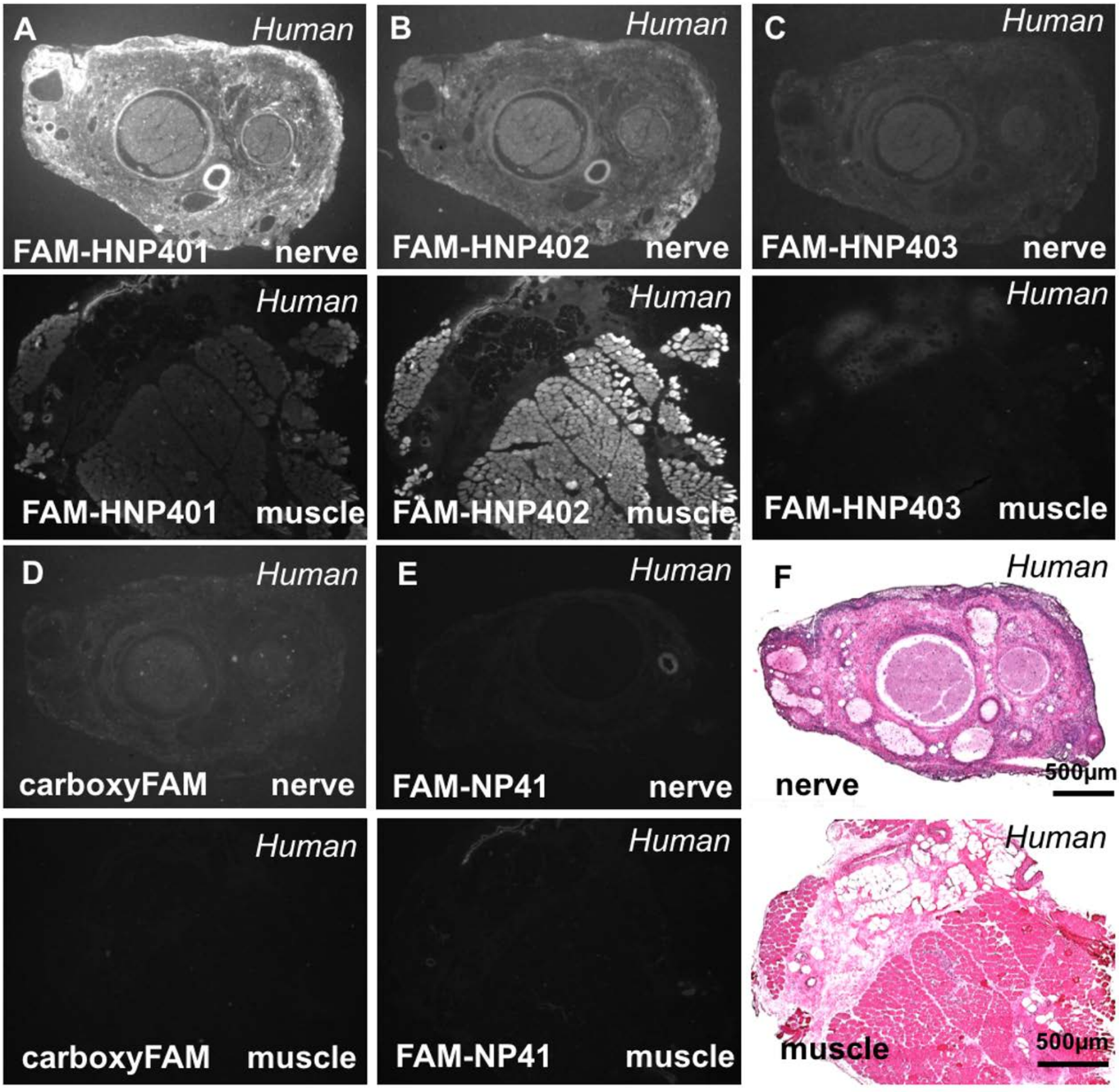

A
Human
FAM-HNP401 nerve
B
Human
FAM-HNP402 nerve
C
Human
FAM-HNP403 nerve
Human
FAM-HNP401 muscle
Human
FAM-HNP402 muscle
Human
FAM-HNP403 muscle
D
Human
carboxyFAM nerve
E
Human
FAM-NP41 nerve
F
Human
nerve
500μm
Human
carboxyFAM muscle
Human
FAM-NP41 muscle
Human
muscle
500μm

Fig. S4.

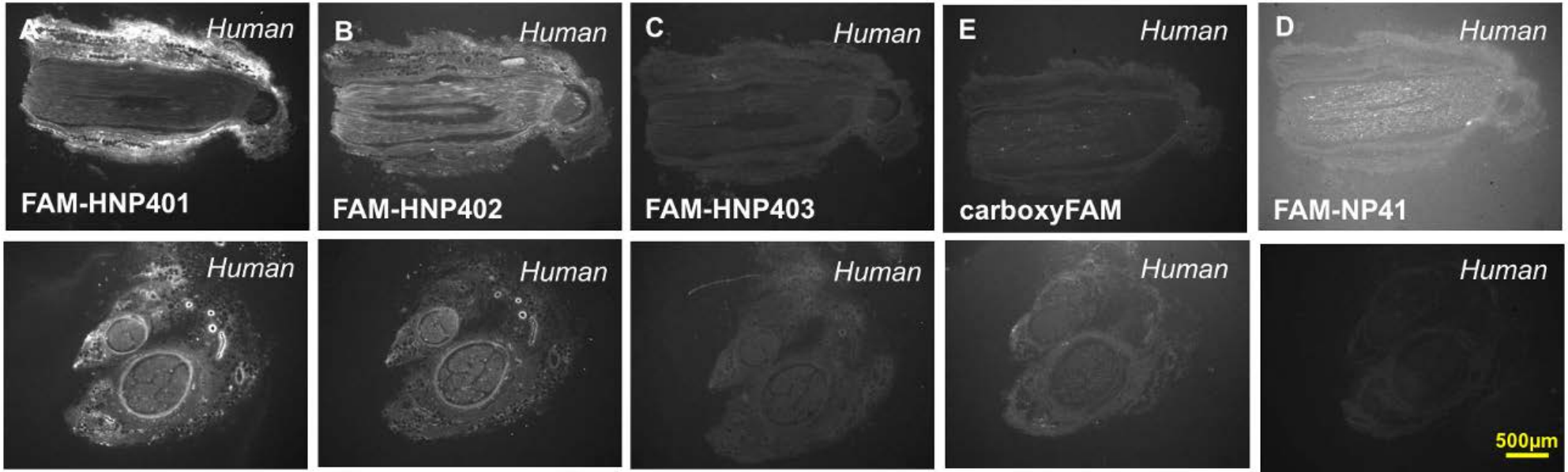
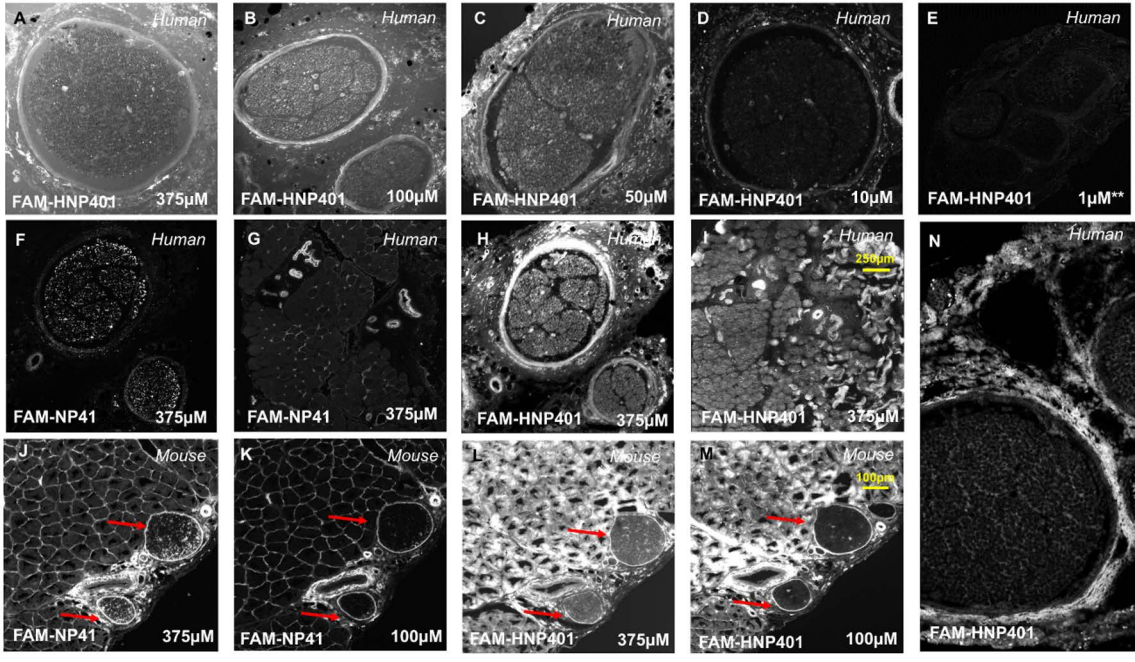

A
Human
FAM-HNP401
B
Human
FAM-HNP402
C
Human
FAM-HNP403
E
Human
carboxyFAM
D
Human
FAM-NP41
Human
Human
Human
Human
Human
500μm

Fig. S5.


A
Human
FAM-HNP401
375μM
B
Human
FAM-HNP401
100μM
C
Human
FAM-HNP401
50μM
D
Human
FAM-HNP401
10μM
E
Human
FAM-HNP401
1μM**
F
Human
FAM-NP41
375μM
G
Human
FAM-NP41
375μM
H
Human
FAM-HNP401
375μM
I
Human
250μm
FAM-HNP401
375μM
N
Human
FAM-HNP401
J
Mouse
FAM-NP41
375μM
K
Mouse
FAM-NP41
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L
Mouse
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375μM
M
Mouse
100μm
FAM-HNP401
100μM

Fig. S6.

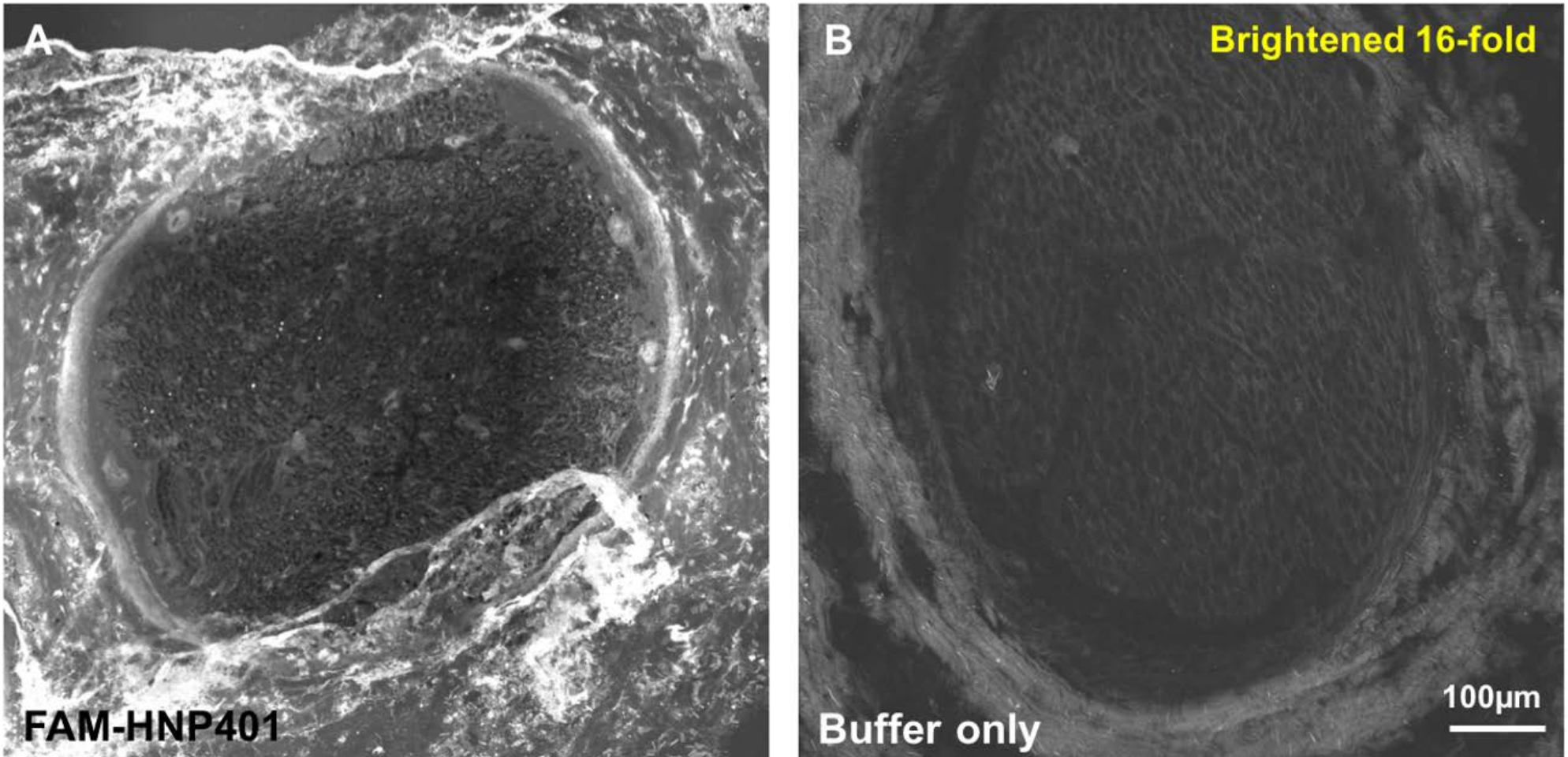


Fig. S7.

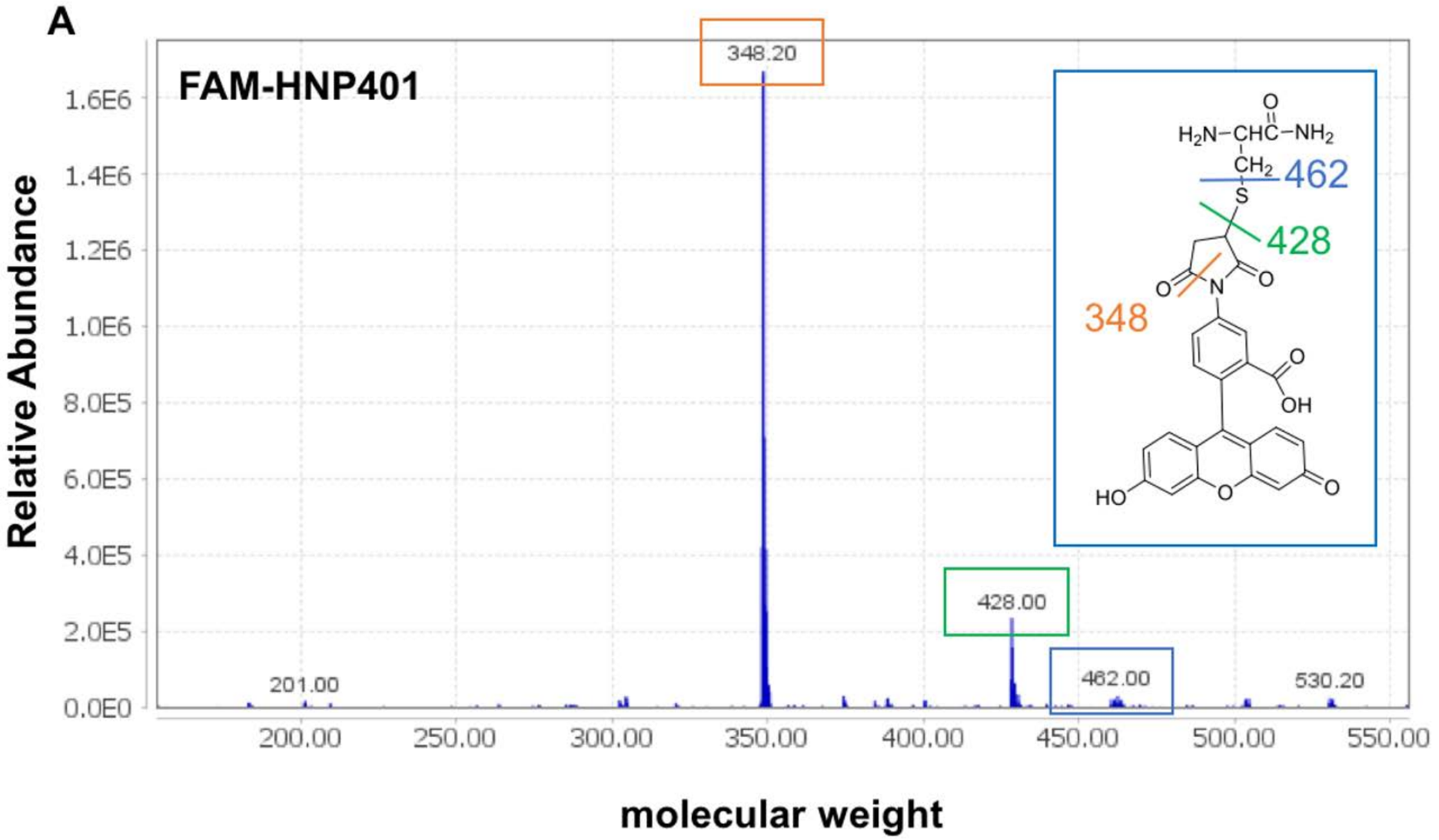
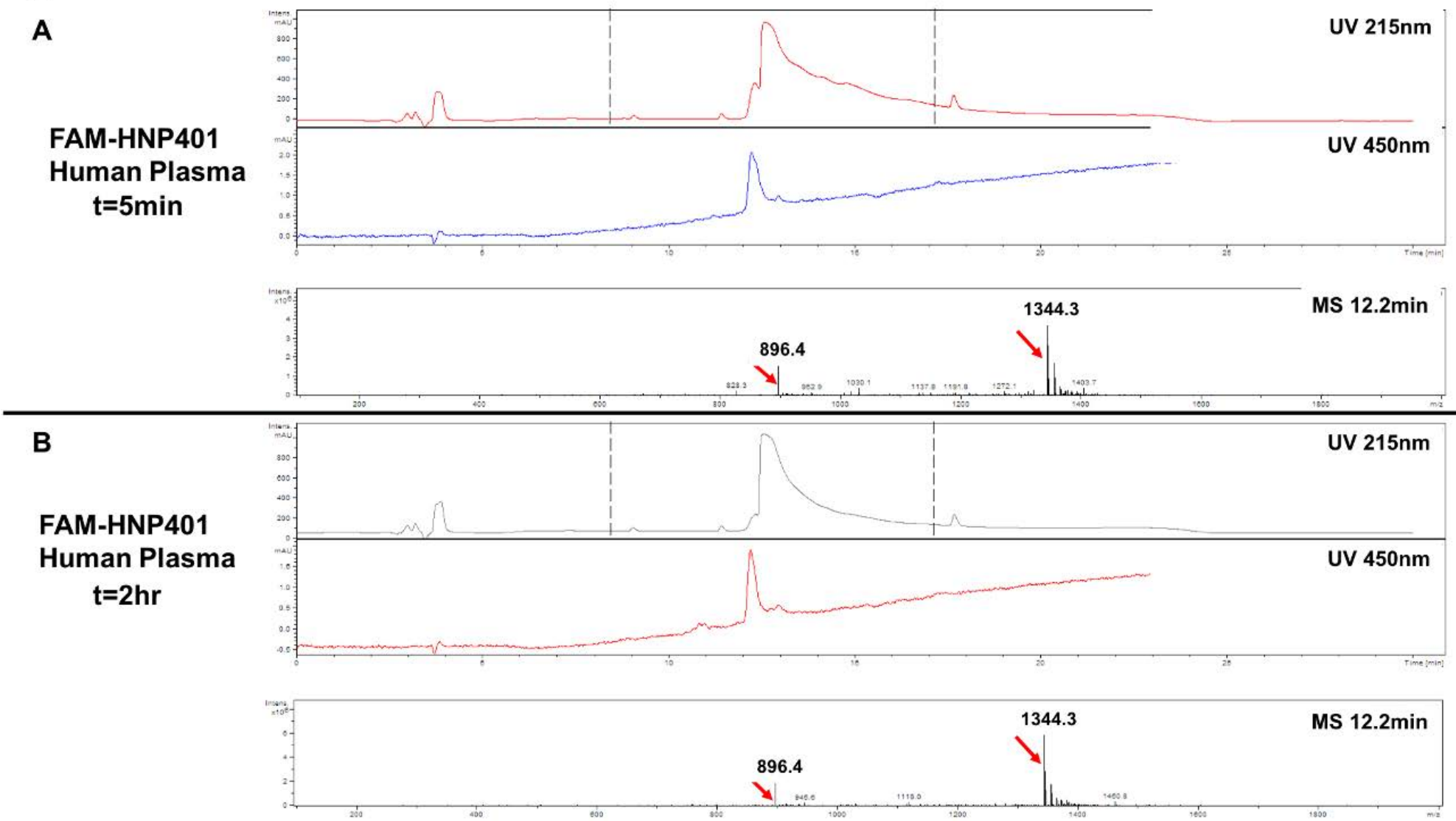

A
FAM-HNP401
348.20
428.00
462.00
201.00
530.20
Relative Abundance
molecular weight
462
428
348
B
FAM-NP41
504.153
505.156
-K-(FAM)
-G-K-(FAM)
Relative Abundance
molecular weight
C
FAM-dNP41
2204.9781
Ac-s-h-s-n-t-q-t-l-a-k-a-p-e-h-t-G-k-(FAM)
Relative Abundance
molecular weight

Fig. S8.


A
FAM-HNP401
Human Plasma
t=5min
UV 215nm
UV 450nm
MS 12.2min
1344.3
896.4
B
FAM-HNP401
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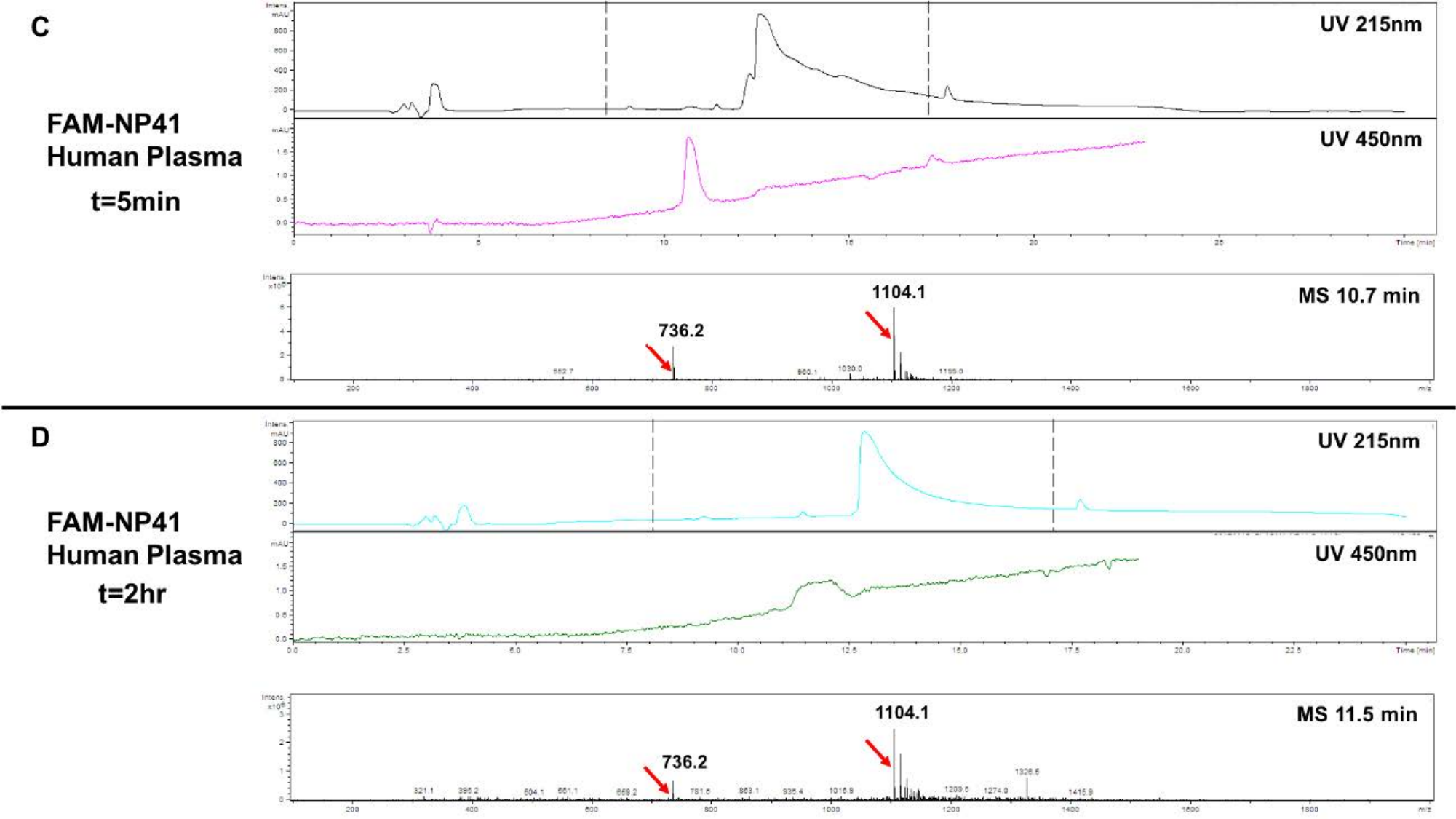
t=2hr
UV 215nm
UV 450nm
MS 12.2min
1344.3
896.4


C
FAM-NP41
Human Plasma
t=5min
UV 215nm
UV 450nm
MS 10.7 min
1104.1
736.2
D
FAM-NP41
Human Plasma
t=2hr
UV 215nm
UV 450nm
MS 11.5 min
1104.1
736.2

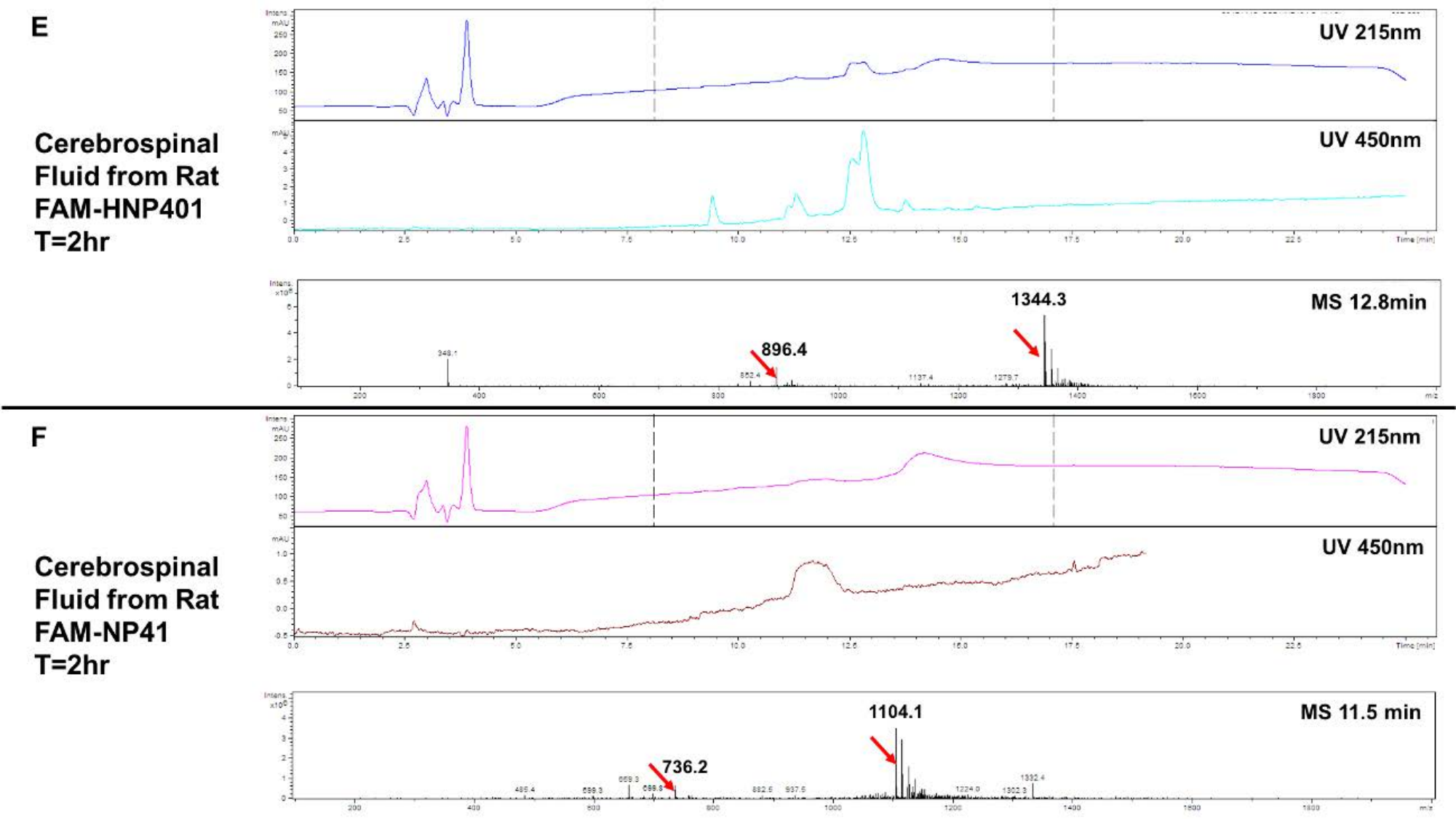

E
Cerebrospinal Fluid from Rat FAM-HNP401 T=2hr
UV 215nm
UV 450nm
MS 12.8min
1344.3
896.4
F
Cerebrospinal Fluid from Rat FAM-NP41 T=2hr
UV 215nm
UV 450nm
MS 11.5 min
1104.1
736.2

Fig. S9.

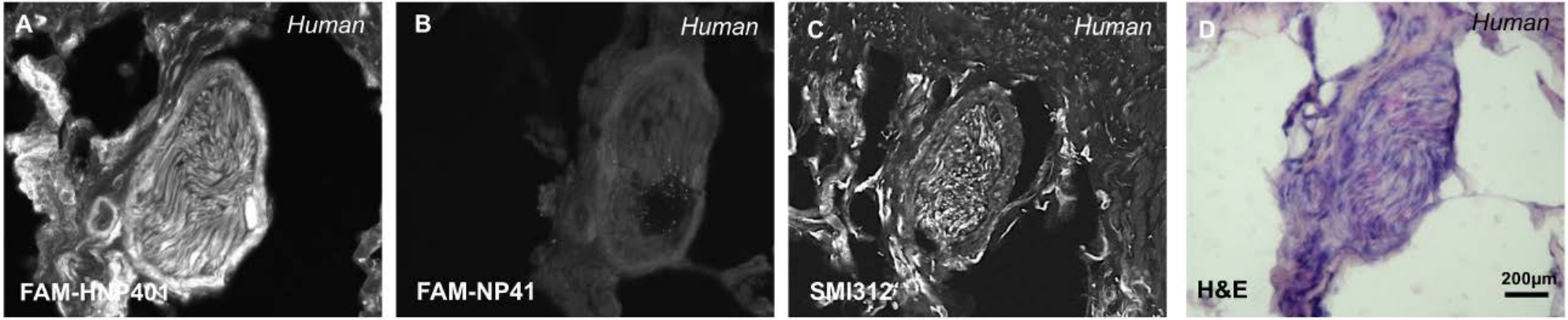
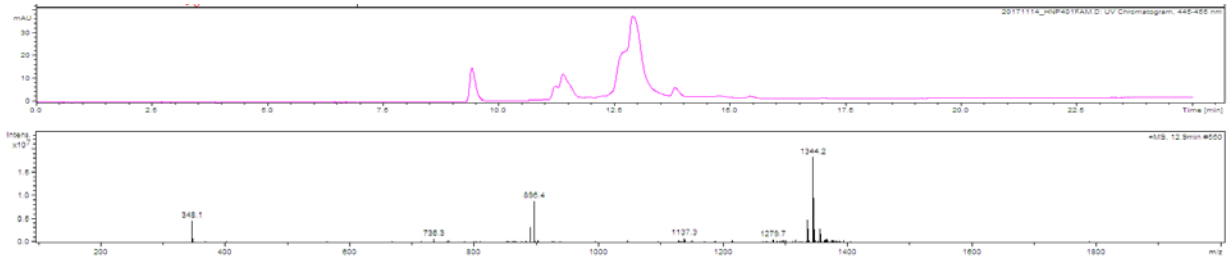

A
Human
FAM-HNP401
B
Human
FAM-NP41
C
Human
SMI312
D
Human
H&E
200μm

Table. S1.

Name	Peptide sequence
HNP401	Ac-SGQVPWEEPYYVVKKSSGGC
HNP402	Ac-WEYHYVDLNWTSQHPQGGC
HNP403	Ac-DLPDIIWDFNWETAGGC
NP41	Ac-SHSNTQTLAKAPEHTGC
N-2	Ac-QVPWEEPYYVVKKSSGGC
N-4	Ac-PWEEPYYVVKKSSGGC
N-6	Ac-EEPYYVVKKSSGGC
N-8	Ac-PYYVVKKSSGGC
C-2	Ac-SGQVPWEEPYYVVKKGGC
C-4	Ac-SGQVPWEEPYYVVGGC
C-6	Ac-SGQVPWEEPYYGGC
C-8	Ac-SGQVPWEEPGGC

LC-MS-data of all peptides synthesized according to Table 1.

FAM-HNP401



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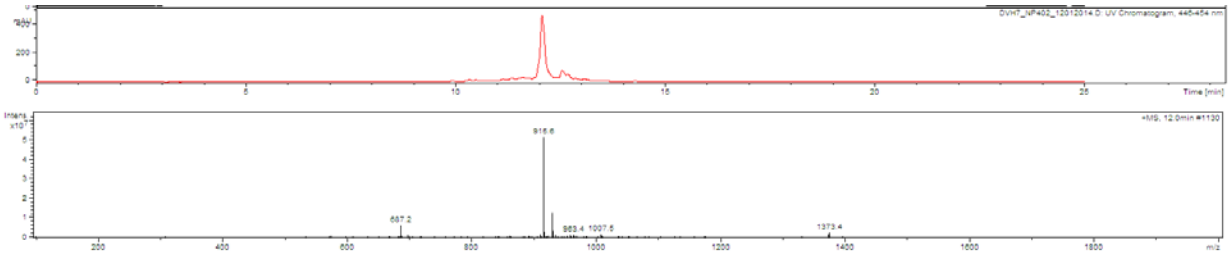

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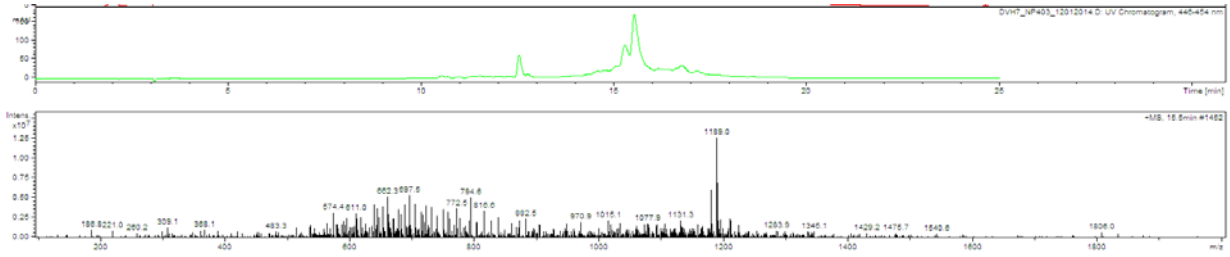
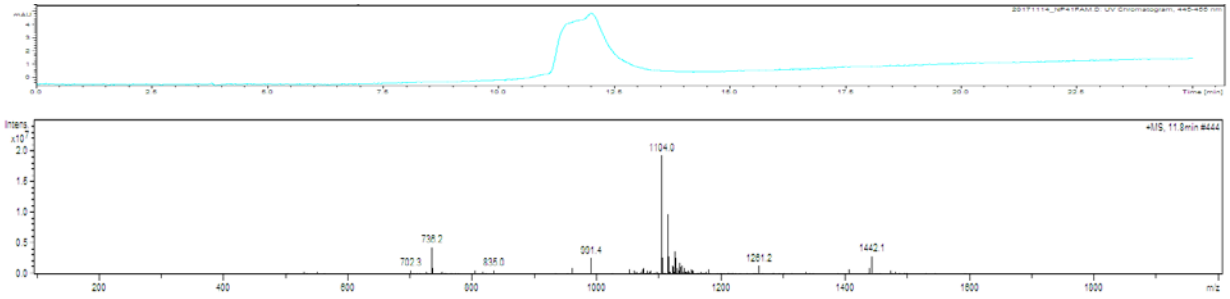
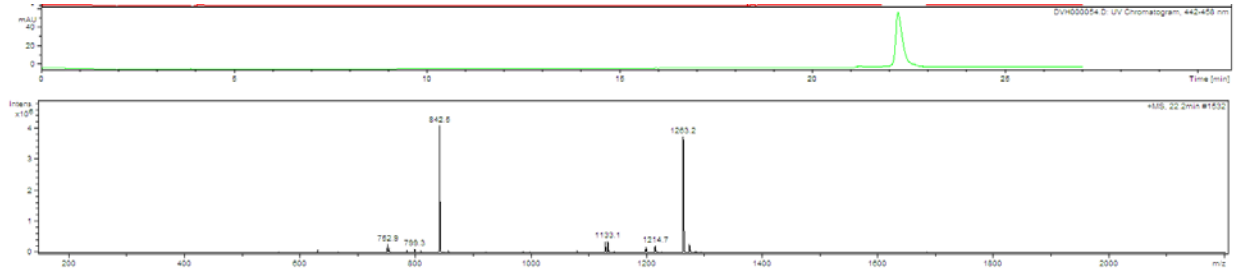


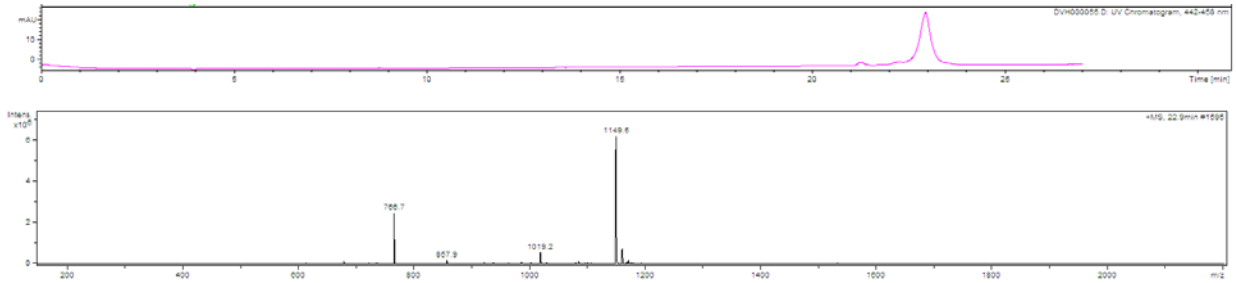
FAM-NP41



FAM-HNP401-N-2



FAM-HNP401-N-4



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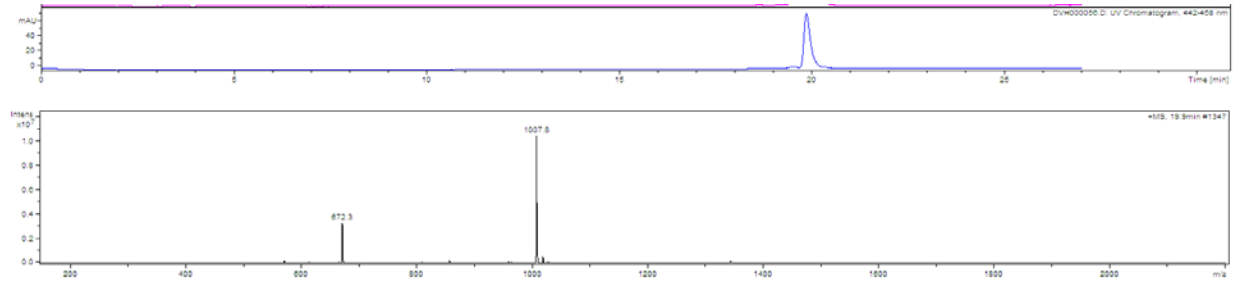
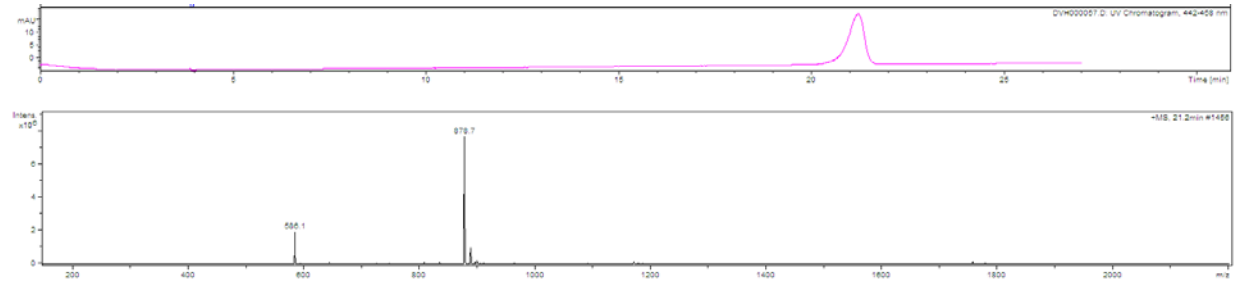


FAM-HNP401-N-8



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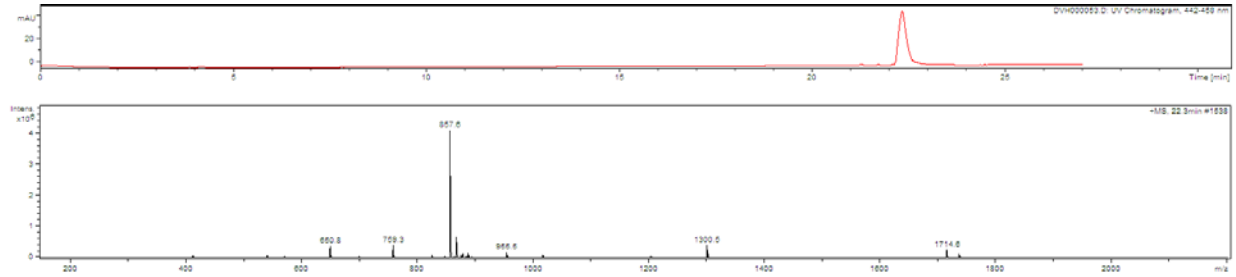

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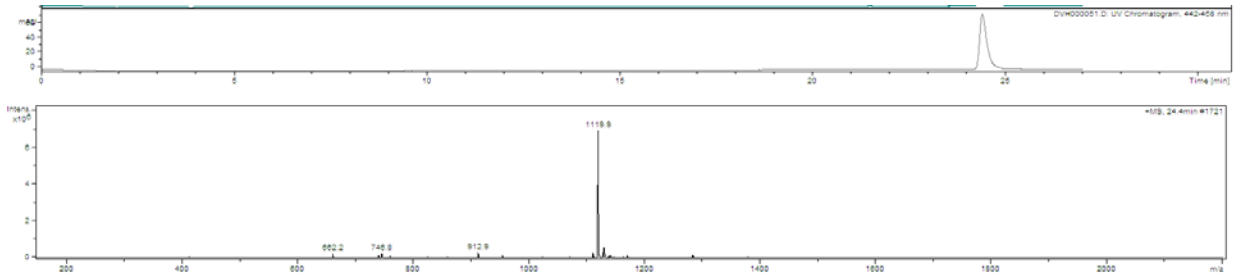

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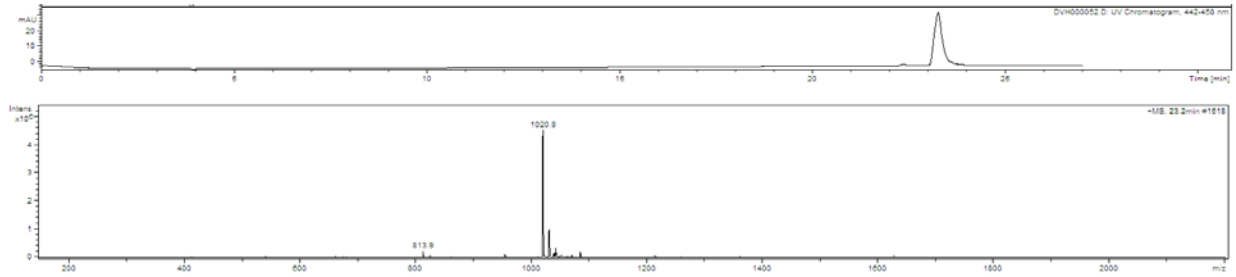

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