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**Supporting Information** 

PAMAM-guanylthiourea conjugates mask furin's substrate binding site: Mechanistic insights from molecular docking and molecular dynamics studies assist the design of potential furin inhibitors

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'n `N´

N

N' H ĥ

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NH

NH II

'n

NН

NH

29

N

33

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37

21

S

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s II

1 (G0 PheGTU)

`N´



14

NH ||

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'n

ΝН

2 (G0 3,5-bis(CF3)PheGTU)

Ň

6

















Figure S1: Designed PAMAM GTU library





**Figure S2.** 3D depiction of interaction of **(A)** G0 PAMAM with Asp154, Glu236, Pro256, Glu257, Asp258, Asp306 **(B)** 2 with Asp154, Asn192, Glu236, Gly255, Asp258, Asp264, Glu299, Asp301, Asp306, Tyr308 **(C)** 3 with Asp154, Asp191, Arg193, His194, Val231, Glu236, Gly255, Pro256, Asp258, Ser293, Asp306, Glu331 **(D)** 4 with Asp154, Asp191, Glu236, Pro256, Asp258, Asp264, Glu299, Asp306 **(E)** 5 with Glu236, Asp264, Asp258, Gly255, Glu257, Ala292, Asn295, Glu299, Asp306 residues of furin



Figure S3. 2D summary of interaction analysis results of (A) G0 PAMAM (B) 2 (C) 3 (D) 4 (E) 5 with furin



Figure S4: Protein-ligand RMSD plot of furin (A) G0 PAMAM (B) 1 (C) 2 (D) 3 (E) 4 (F) 5 in complex with furin.



🔳 H-bonds 🔲 Hydrophobic 📕 Ionic 🔳 Water bridges

Figure S5. Interaction fraction summary of (A) G0 PAMAM (B) 2 (C) 3 (D) 4 (E) 5 in contact with furin



Figure S6: <sup>1</sup>H NMR (400 MHz, Deuterium Oxide) of 1



Figure S7: <sup>13</sup>C NMR (100 MHz, Deuterium Oxide) of 1



Figure S8: <sup>1</sup>H NMR (400 MHz, Deuterium Oxide) of 2



Figure S9: <sup>13</sup>C NMR (100 MHz, Deuterium Oxide) of 2



Figure S10: DEPT-135 NMR of 2 (in D<sub>2</sub>O)



Figure S11: ESI-MS Spectrum of 1 calcd mass (M+H)<sup>+</sup>, 728.3904; found, 728.3927



Figure S12: ESI-MS Spectrum of 2 calcd mass (M+H)<sup>+</sup>, 694.4293; found, 694.4283



Figure S13: ESI-MS Spectrum of 3 calcd mass  $(M+H)^+$ , 724.4399; found, 746.4419



Figure S14: ESI-MS Spectrum of 6 calcd mass (M+H)<sup>+</sup>, 708.4450; found, 708.4419



Figure S15: ESI-MS Spectrum of 7 calcd mass  $(M+H)^+$ , 739.4144; found, 739.4165