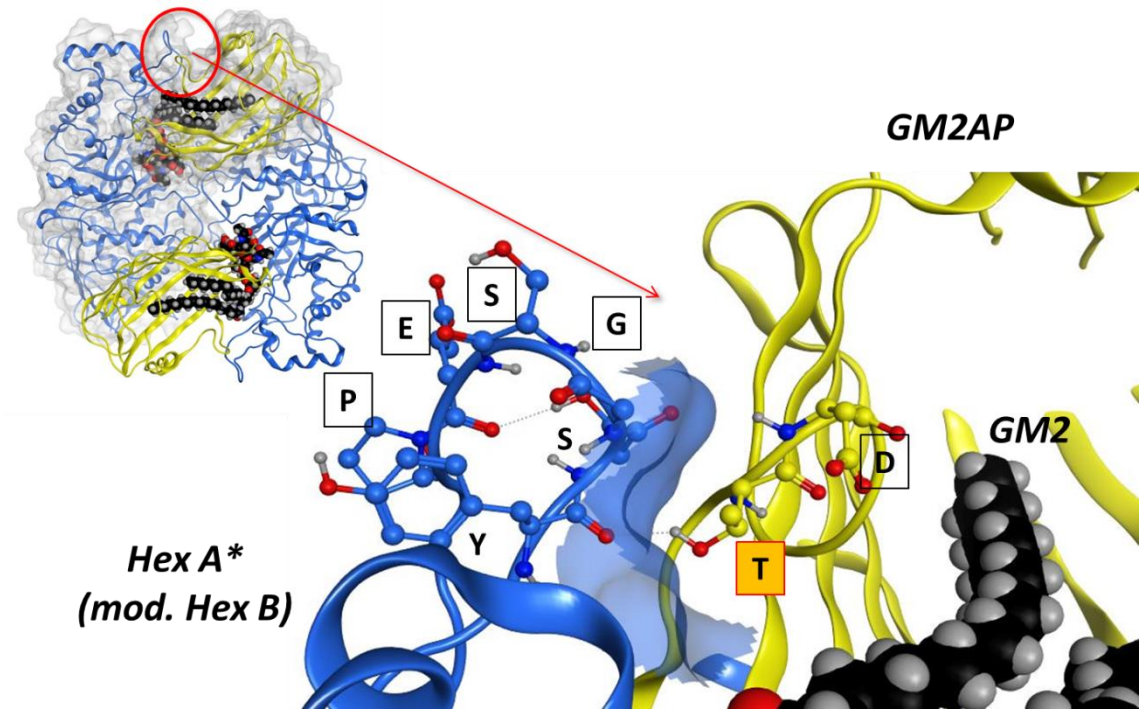
A)



B)

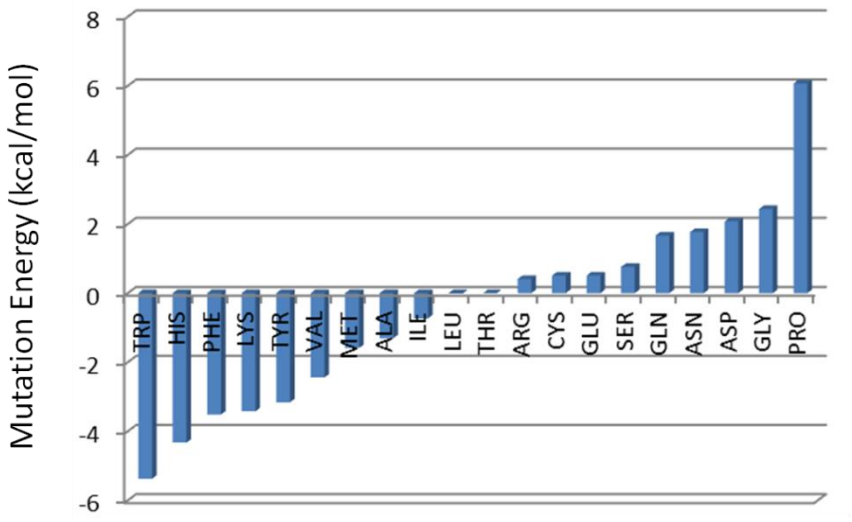


Fig. S1. A) Computational analysis of Hex A-GM2AP complex. The computational analysis indicated that a loop region located positions Cys68 to Ser74, especially position Thr69 in GM2AP might be highly responsible for formation of the stable complex. B) The computational analysis predicted that the substitution of several amino acid residues such as Trp, His, Phe and Lys for Thr69 might be highly involved in formation of the stable complex. *Loop region of amino acid sequence of modified Hex B (mod. Hex B) is identical to that of Hex A.

HPLC Monitoring of *S*-Tritylation Reactions of Unprotected Peptide Thioester **3**.

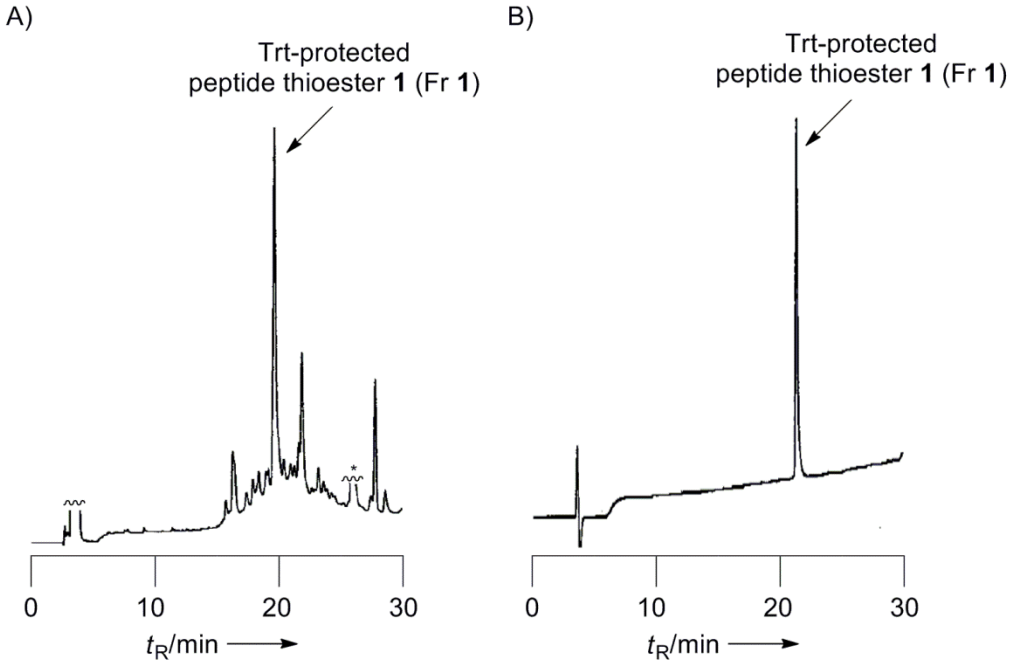


Fig. S2. *S*-Tritylation reactions of unprotected peptide thioester **3**. A) Analytical HPLC chart of the crude mixture of *S*-tritylation reactions. B) Analytical HPLC chart of the purified Trt-protected peptide thioester **1** (Fr **1**).

HPLC Monitoring of Reactions for the Synthesis of the Reduced GM2AP Analogues **9**.

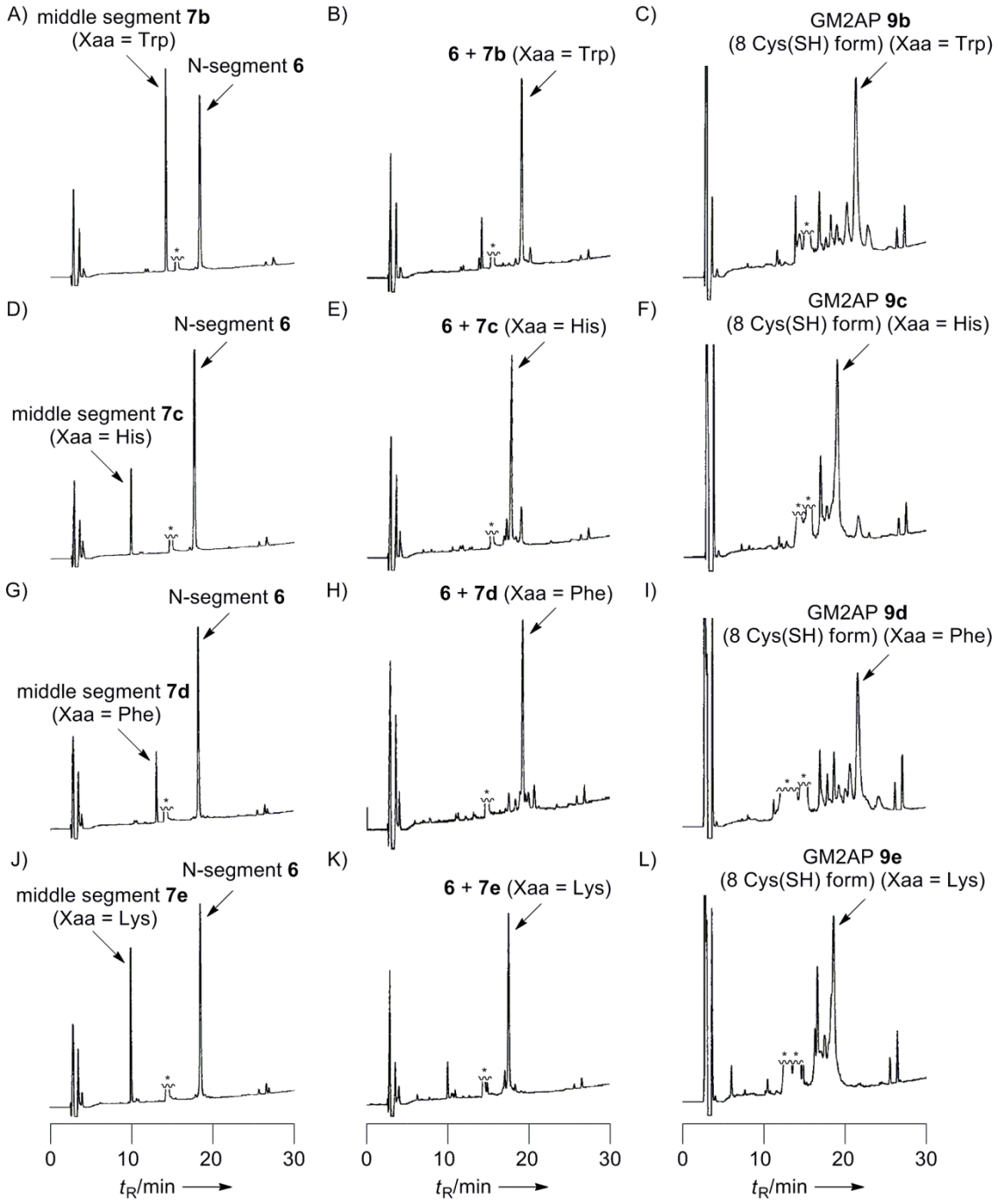


Fig. S3. A-C) Xaa = Trp; A) First NCL (t < 3 min). B) First NCL (t = 19 h). C) Second NCL (t = 3 days). D-F) Xaa = His; D) First NCL (t < 3 min). E) First NCL (t = 22 h). F) Second NCL (t = 3 days). G-I) Xaa = Phe; G) First NCL (t < 3 min). H) First NCL (t = 2 days). I) Second NCL (t = 3 days). J-L) Xaa = Lys; J) First NCL (t < 3 min). K) First NCL (t = 24 h). L) Second NCL (t = 3 days)

6 + 7a (Xaa = Thr): retention time = 18.2 min (analytical HPLC conditions: Cosmosil 5C_{18}-AR-II analytical column with a linear gradient of solvent B in solvent A, 20% to 70% over 30 min); MS (ESI-TOF) calcd for $C_{378}H_{603}N_{89}O_{118}S_5$ (average isotopes) 8442.7, found 8442.9.

6 + 7b (Xaa = Trp): retention time = 19.1 min (analytical HPLC conditions: Cosmosil 5C_{18}-AR-II analytical column with a linear gradient of solvent B in solvent A, 20% to 70% over 30 min); MS (ESI-TOF) calcd for $C_{385}H_{606}N_{90}O_{117}S_5$ (average isotopes) 8527.8, found 8527.4.

6 + 7c (Xaa = His): retention time = 17.7 min (analytical HPLC conditions: Cosmosil 5C_{18}-AR-II analytical column with a linear gradient of solvent B in solvent A, 20% to 70% over 30 min); MS (ESI-TOF) calcd for $C_{380}H_{603}N_{91}O_{117}S_5$ (average isotopes) 8478.7, found 8478.3.

6 + 7d (Xaa = Phe): retention time = 19.2 min (analytical HPLC conditions: Cosmosil 5C_{18}-AR-II analytical column with a linear gradient of solvent B in solvent A, 20% to 70% over 30 min); MS (ESI-TOF) calcd for $C_{383}H_{605}N_{89}O_{117}S_5$ (average isotopes) 8488.8, found 8489.1.

6 + 7e (Xaa = Lys): retention time = 17.5 min (analytical HPLC conditions: Cosmosil 5C_{18}-AR-II analytical column with a linear gradient of solvent B in solvent A, 20% to 70% over 30 min); MS (ESI-TOF) calcd for $C_{380}H_{608}N_{90}O_{117}S_5$ (average isotopes) 8469.8, found 8469.6.