Electronic Supplementary Information for

Anchored protease-activatable polymersome for molecular diagnostics of metastatic cancer cells

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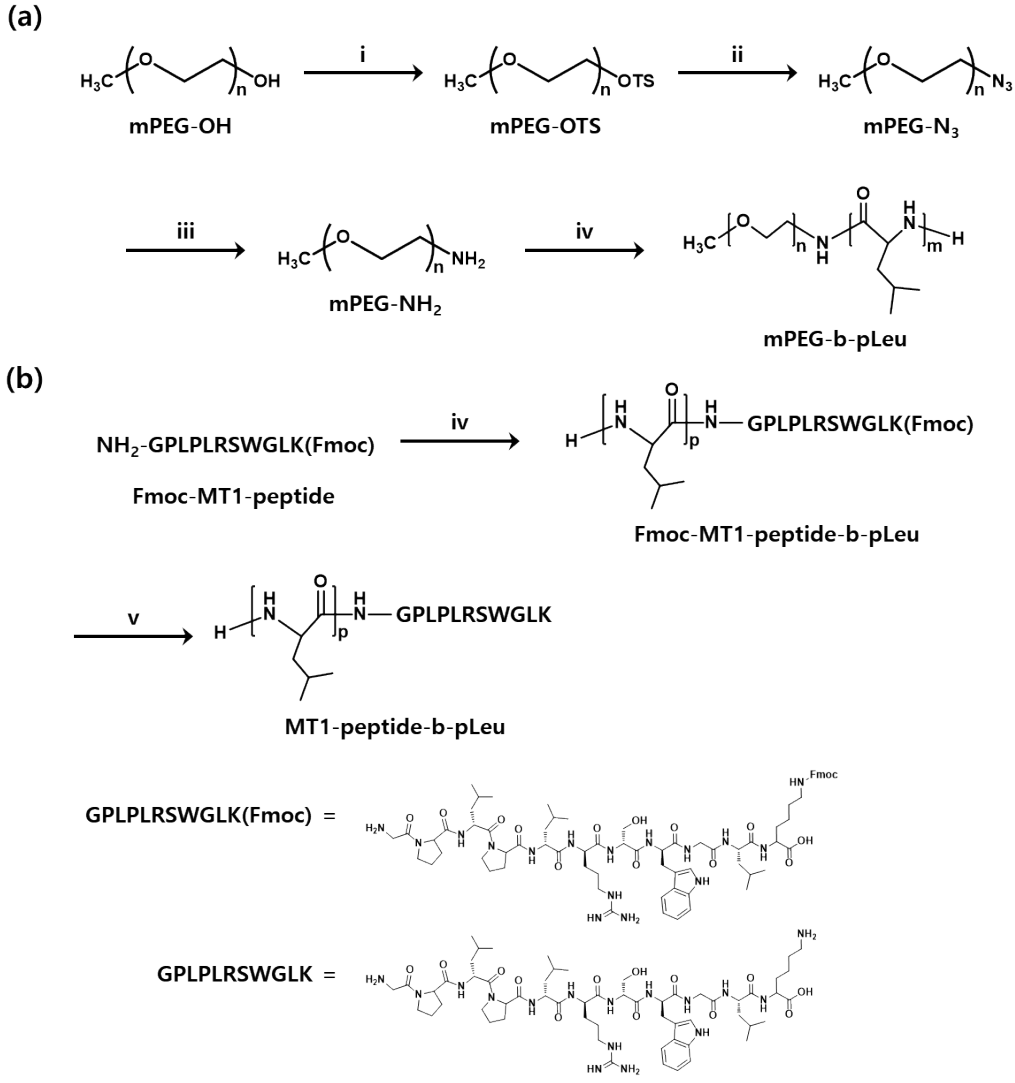

Fig S1. Synthesis and characterization of MT1-MMP-antagonist peptide formulated PSomes. Syntheses pathways to (a) mPEG-b-pLeu and (b) MT1-Peptide-b-pLeu: (i) 4-Toluenesulfonyl chloride, Toluene, R.T., (ii) NaN3, DMF, 90℃, (iii) PPh3, MeOH, 70℃, (iv) Leu-NCA, DMF, 40℃, and (v) 20% pepridine, DMSO, R.T.

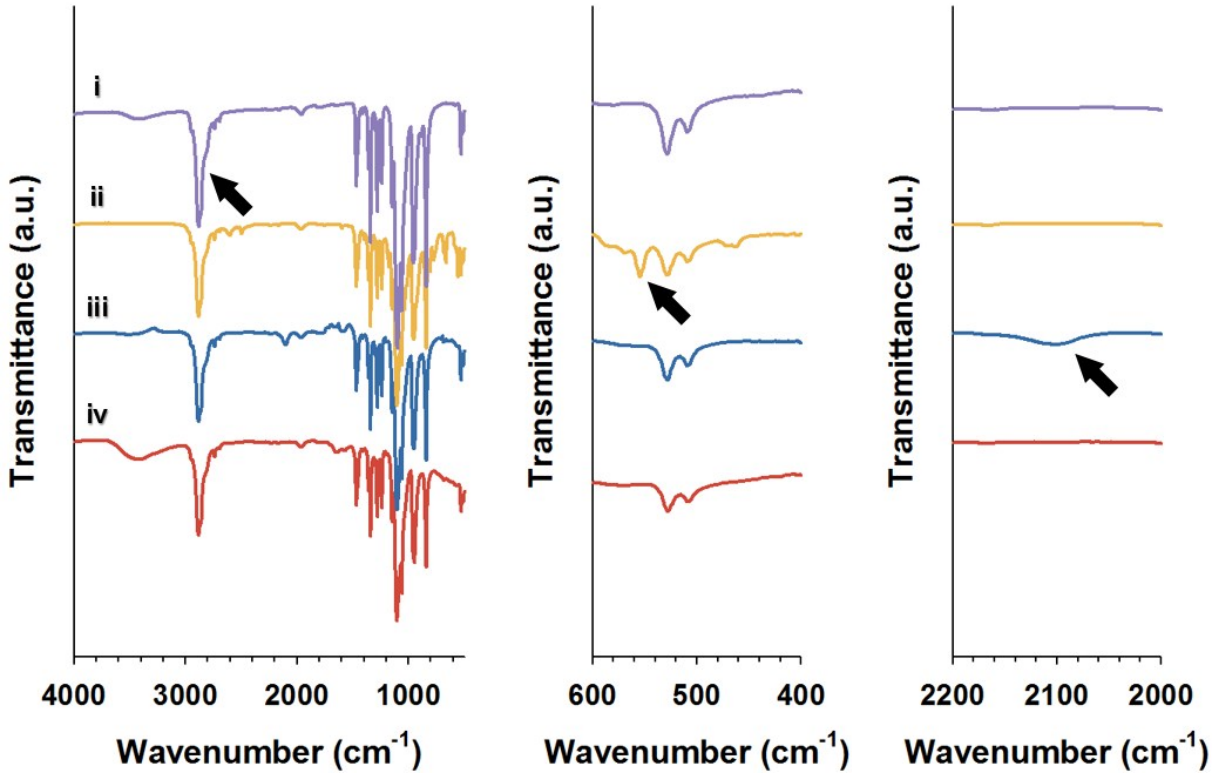

Fig S2. FT-IR spectra of: (i) mPEG, (ii) mPEG-TsCl, (iii) mPEG-N_3, and (iv) mPEG-NH_2. The typical **CH_3** of mPEG at 2850cm^{-1}, **S-O** of the mPEG-TsCl at 560 cm^{-1}, and **N_3** of the mPEG-N_3 at 2103 cm^{-1}.

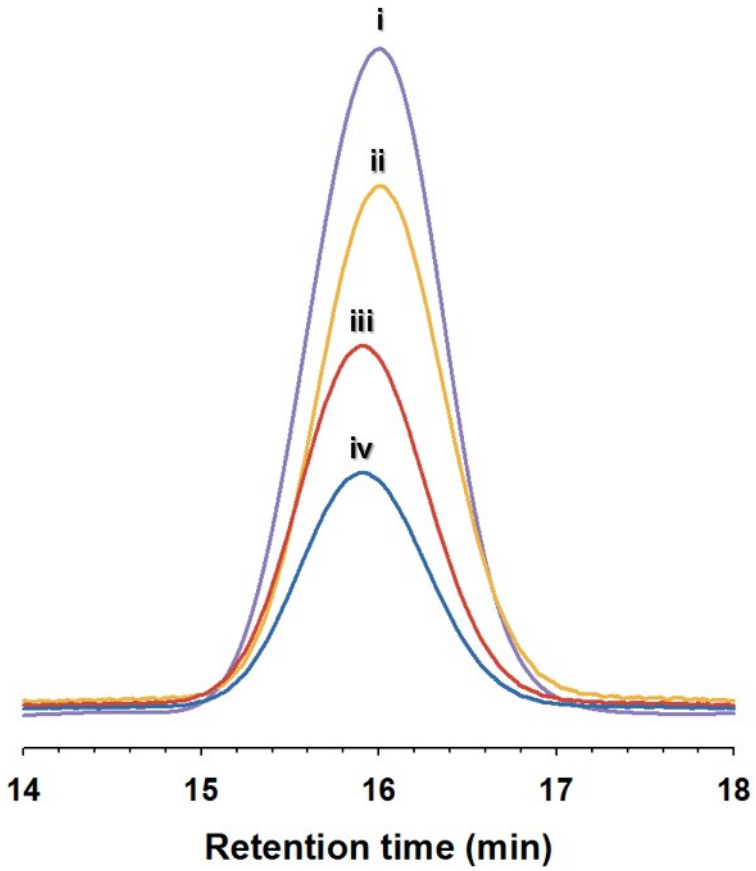

Fig S3. GPC profiles of: (i) mPEG, (ii) mPEG-TsCl, (iii) mPEG-N_3, and (iv) mPEG-NH_2.

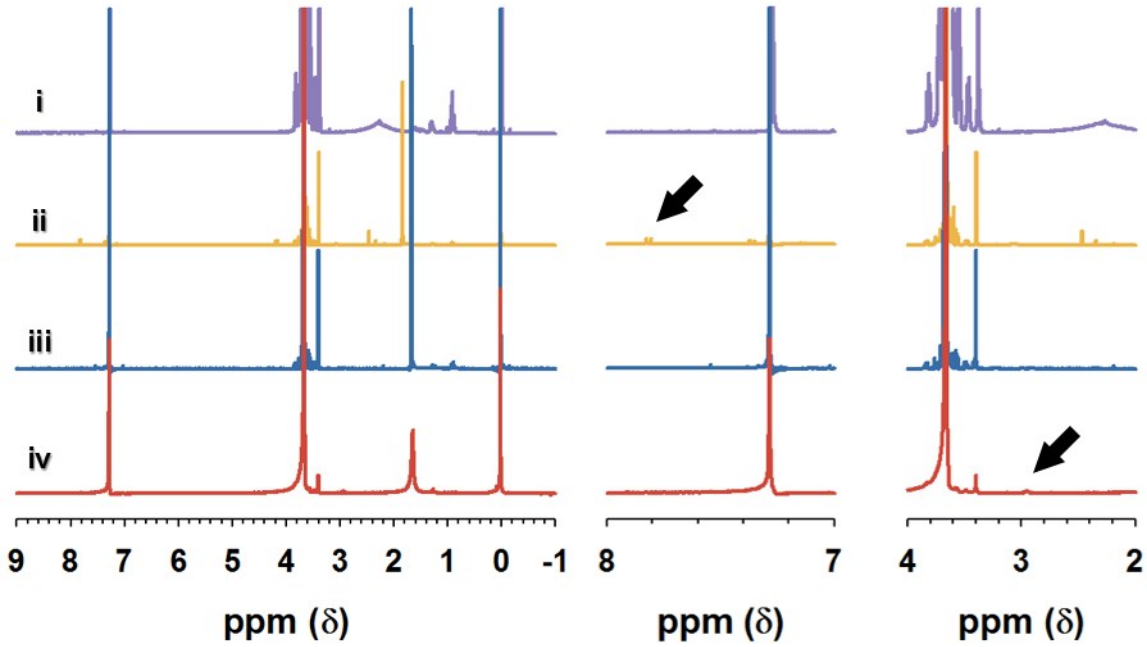

Fig S4. ^{1}H-NMR spectra of: (i) mPEG, (ii) mPEG-TsCl, (iii) mPEG-N_3, and (iv) mPEG-NH_2. The typical **2H** of TsCl at 7.79 and 7.49 ppm, and **CH_2-NH_2** of the mPEG-NH_2 at 2.90 ppm.

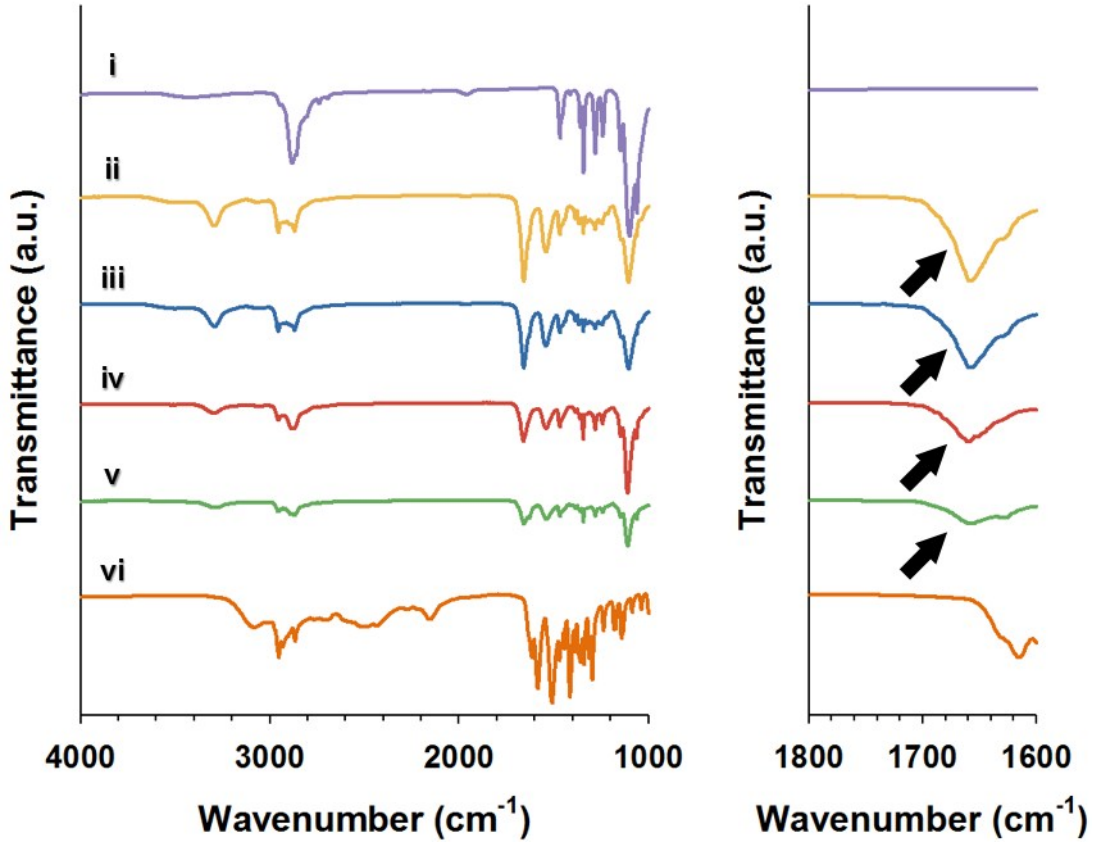

Fig S5. FT-IR spectra of: (i) mPEG, (ii-v) mPEG-b-pLeu (f_{mPEG} = 0.33, 0.39, 0.54, and 0.64), and (vi) DL-leucine. Typical **amide I** and **amide II bonds** of mPEG-b-pLeu at 1660 and 1754 cm^{-1}, respectively.

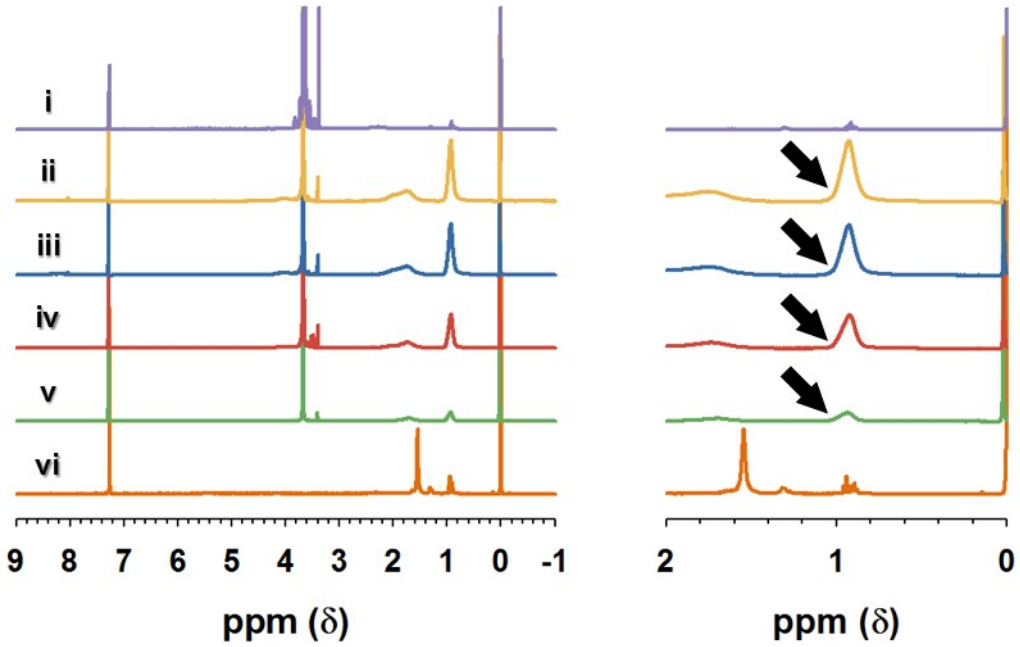

Fig S6. ^{1}H-NMR spectra of: (i) mPEG, (ii-v) mPEG-b-pLeu (f_{mPEG} = 0.33, 0.39, 0.54, and 0.64), and (vi) DL-leucine. Typical **methyl protons** of pLeu at 0.90 ppm.

MT1-MMP	DL-Leucine	DP_{Leu}
$2CH_2$ (7.55 ppm)	$2CH_3$ (0.87 ppm)	ea
1	4.33	2.89

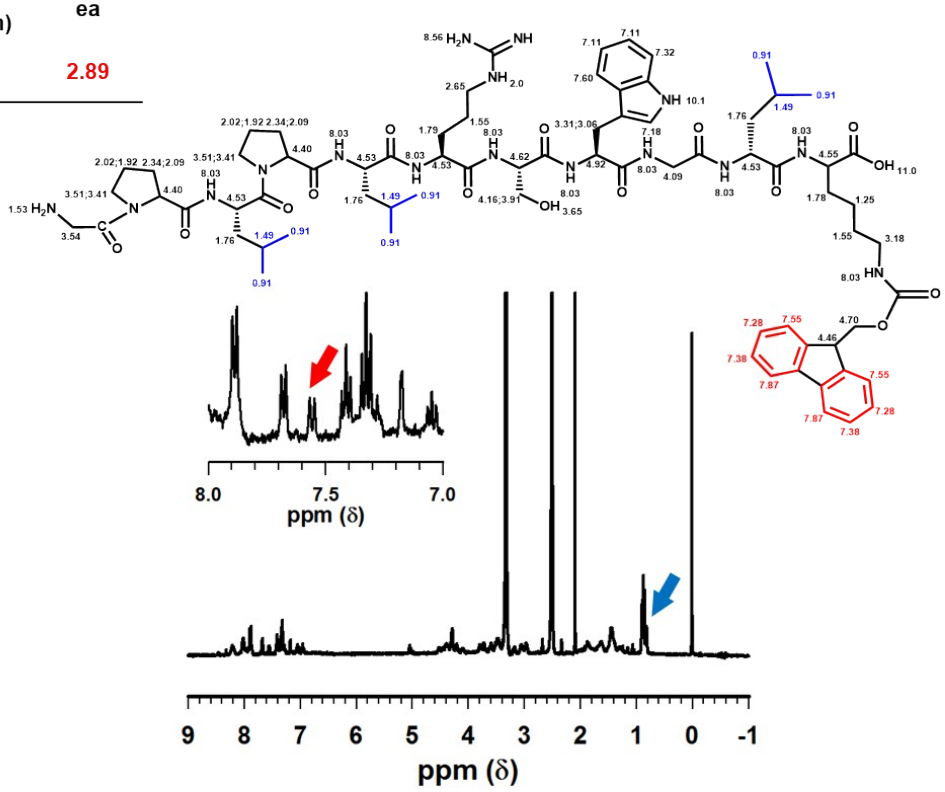

Fig S7. ^{1}H-NMR spectra of: Fmoc-MT1-MMP-antagonist peptide. The typical **2C$\underline{H}_2$** of MT1-MMP antagonist peptide at 7.55 ppm and the **2C$\underline{H}_3$** of leucine at 0.87 ppm.

MT1-MMP	DL-Leucine	DP_{Leu}	MW	f_{mPEG}
$2CH_2$ (7.55 ppm)	$2CH_3$ (0.87 ppm)	ea	g/mol	%
1	4.33	29.6	5882.9	0.34

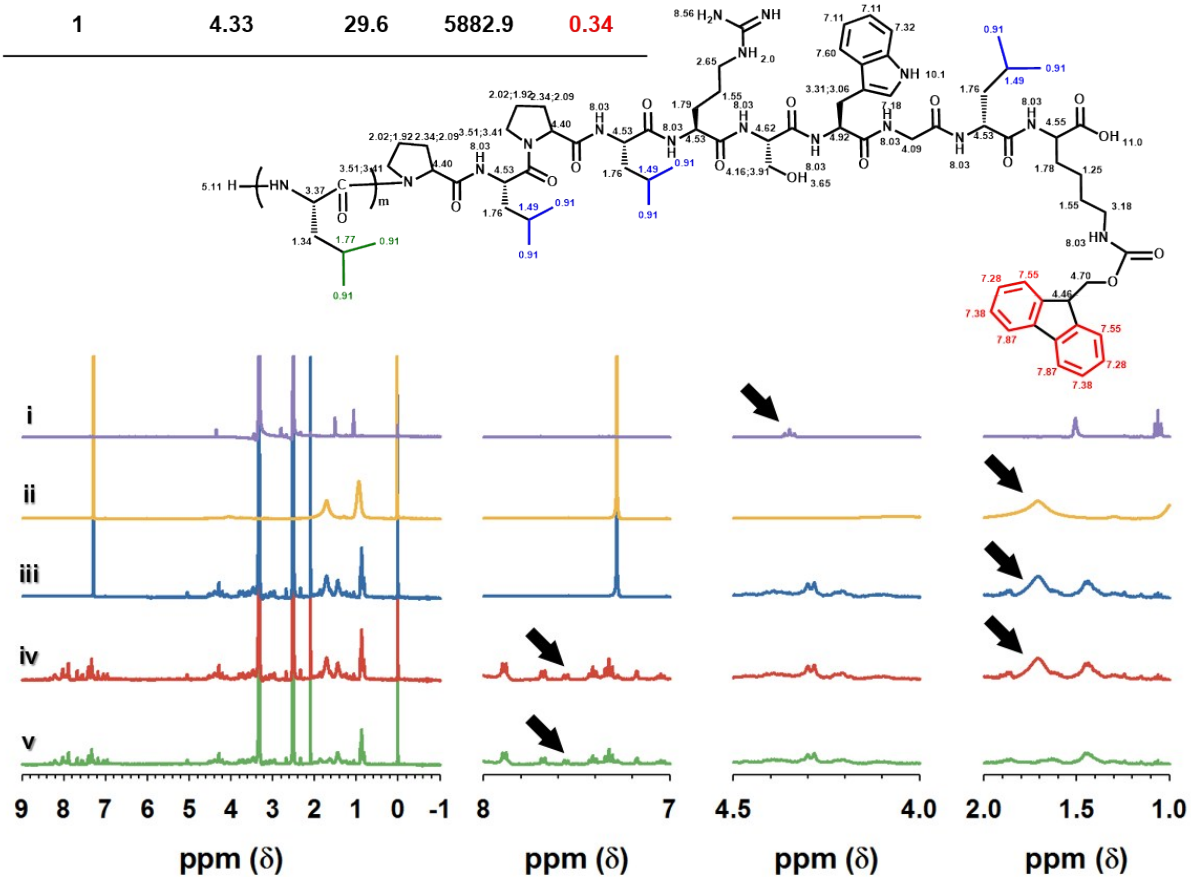

Fig S8. ^{1}H-NMR spectra of: (i) Leu-NCA, (ii) pLeu, (iii) MT1-MMP-antagonist peptide-b-pLeu (Dep.), (iv) Fmoc-MT1-MMP-antagonist peptide-b-pLeu, and Fmoc-MT1-MMP-antagonist peptide.

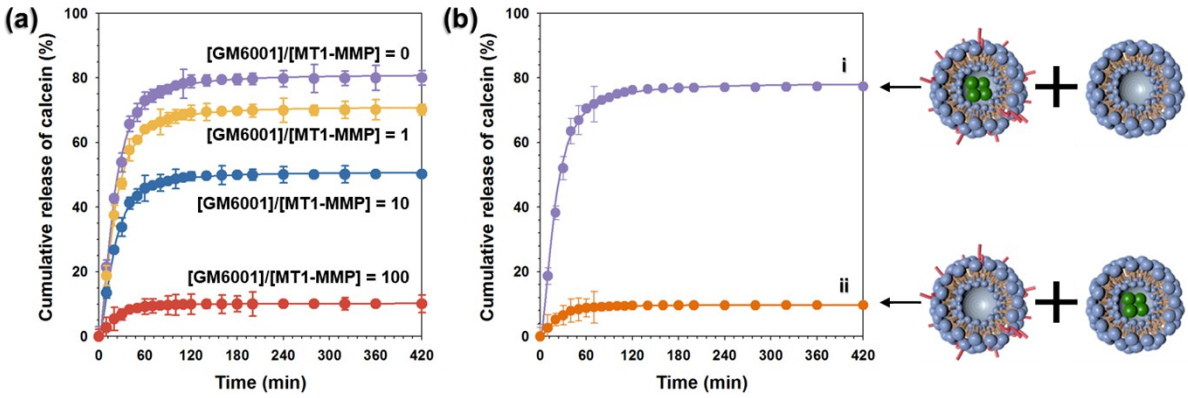

Fig S9. Kinetics of cargo release from calcein-loaded PeptiSomes and PSomes induced by MT1-MMP. (a) Release profiles of calcein-loaded PeptiSomes in the presence of the small-molecule inhibitor GM6001. (b) MT1-MMP sequence-specific release of calcein from a mixture of (i) calcein-loaded PeptiSomes and non-loaded PSomes, and (ii) a mixture of non-loaded PeptiSomes and calcein-loaded PSomes.

Table S1. Characterization of the synthesis of mPEG-NH_2.

Sample	Yield	Conversion Yield	Molar Mass (g/mol)	
	(%)	(%)	GPC	^{1}H-NMR
$mPEG_{2000}$	-	100	2000	-
mPEG-TsCl	88	93	1953	2168
mPEG-N_3	84	99	1988	2074
mPEG-NH_2	94	98	1988	2048

Table S2. Characterization of the synthesis of mPEG-b-pLeu.

Sample	f_{mPEG}[a]	Mw[b]	f_{mPEG}[c]	MW[d]
	(%)	(g/mol)	(%)	(g/mol)
$mPEG_{44}$-b-$pLeu_{35}$	0.30	6591.3	0.33	6066.6
$mPEG_{44}$-b-$pLeu_{23}$	0.40	5017.1	0.39	4885.9
$mPEG_{44}$-b-$pLeu_{15}$	0.50	3967.7	0.54	3705.3
$mPEG_{44}$-b-$pLeu_{10}$	0.60	3311.8	0.64	3115.0

[a, b] Calculated from the initial ratio of monomer to mPEG amine groups.
[c] Calculated weight fraction of mPEG in block copolymers based on (d).
[d] Determined from ^{1}H-NMR analysis by calculating the ratio of the methyl groups within pLeu.