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Positive Charge of "Sticky" Peptides and Proteins Impedes Release from Negatively Charged PLGA Matrices

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SUPPLEMENTAL FIGURES & TABLES

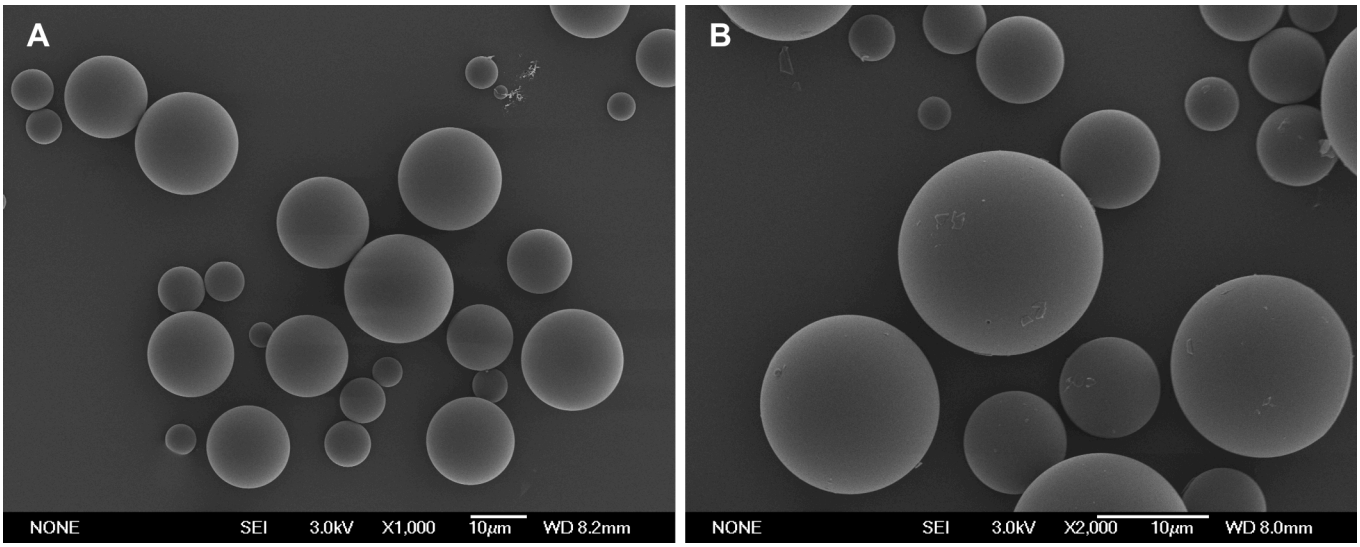

Fig S1: Scanning electron micrographs (SEM) of microparticles. Representative images show spherical particles with nonporous surface morphology, characteristic of all microparticle formulations used. (A) 43 kDa PLGA containing +1.5/kDa peptide at 1000x magnification. (B) 15 kDa PLGA containing +2.7/kDa peptide at 2000x magnification.

PLGA Polymer	*Positively Charged Peptides*					*Charge Changing Peptides*	
	0	*+0.5*	*+1.4*	*+2.7*	*+3.1*	*CK1sub*	*BA17*
7 kDa	20.3±9.3	21.7±12.0	19.5±12.2	21.3±11.9	20.9±9.1	23.5±9.9	---
15 kDa	20.3±8.1	19.6±8.6	17.3±6.8	17.4±7.8	22.9±13.6	23.2±9.3	11.3±3.5
43 kDa	23.2±9.3	17.4±7.9	16.8±6.5	21.7±8.9	25.8±14.2	18.9±8.9	---
15 kDa-E	20.7±10.9	19.1±8.9	17.4±7.3	14.8±5.1	19.8±9.6	15.7±8.2	14.9±5.6

Table S1: Volume averaged size distributions for microparticle formulations. Data represent Mean ± SD of particle diameters (μm) for 50,000 particle measurements by Multisizer 3 Coulter Counter.

PLGA Polymer	*Positively Charged Peptides*					*Charge Changing Peptides*	
	0	*+0.5*	*+1.4*	*+2.7*	*+3.1*	*CK1sub*	*BA17*
7 kDa	602±25	535±24	575±27	430±30	562±167	417±9	---
15 kDa	597±37	613±33	572±37	590±38	536±58	467±19	440±13
43 kDa	603±13	513±22	497±25	524±11	472±32	342±5	---
15 kDa-E	434±42	442±29	325±7	504±46	537±29	458±22	362±20

Table S2: Total peptide loading. Total mass of peptides encapsulated in 1 mg of MPs, as detected by fluorescence spectroscopy. Values correspond to 100% cumulative release. Data represent Mean ± SD (ng/mgMP) from 3 microparticle samples.

PLGA Polymer	*Positively Charged Peptides*					*Charge Changing Peptides*	
	0	*+0.5*	*+1.4*	*+2.7*	*+3.1*	*CK1sub*	*BA17*
7 kDa	96±4	86±4	92±4	69±5	90±27	67±1	---
15 kDa	95±6	98±5	91±6	94±6	86±9	75±3	70±2
43 kDa	97±2	82±4	80±4	84±2	76±10	55±1	---
15 kDa-E	69±7	71±5	52±1	81±7	86±5	73±4	58±3

Table S3: Encapsulation efficiency. Percent encapsulation based on total loading from Table S1 and theoretical loading of 625ng/mgMP. Data represent Mean ± SD from 3 microparticle samples.

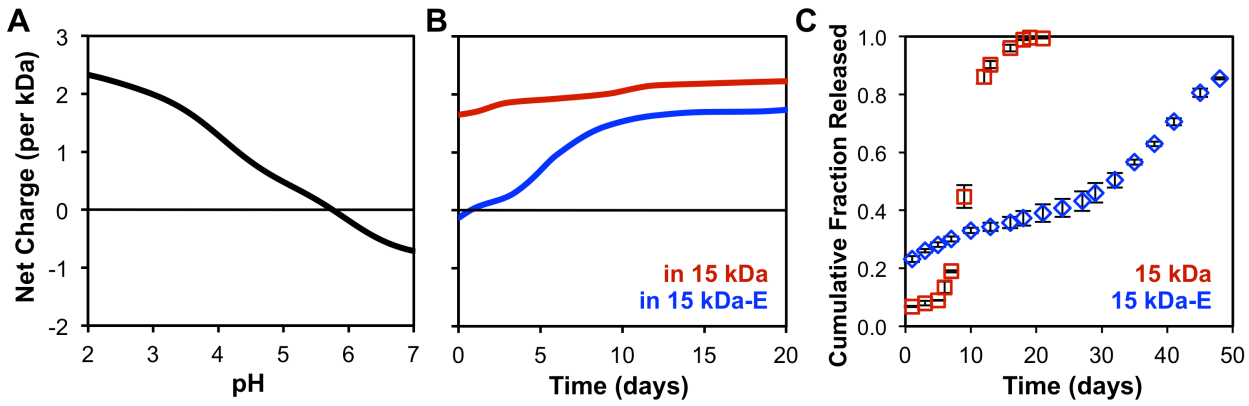

Fig S2: Initial burst of BA17 peptide is influenced by its initial charge, which depends on the initial pH of the microenvironment in hydrated MPs. (A) Net charge, normalized to peptide mass, as a function of pH for BA17 peptide, which has a low isoelectric point (pI < 6) and pH-dependent charge. **(B)** Temporally dynamic net charge estimates for BA17 peptide encapsulated in uncapped 15 kDa (red) or ester-capped 15 kDa (blue) PLGA MPs. Charge predictions are based on intraparticle pH measurements (Fig 4A) and pH-dependent peptide charge (Fig S2A). **(C)** Cumulative release profiles for BA17 peptide encapsulated in uncapped 15 kDa (red squares) or ester-capped 15 kDa (blue diamonds) PLGA MPs. Note the greater initial burst from ester-capped 15 kDa PLGA MPs.