

Supplementary Information

Article

A Predictive Pharmacokinetic Model for Immune Cell-Mediated Uptake and Retention of Nanoparticles in Tumors

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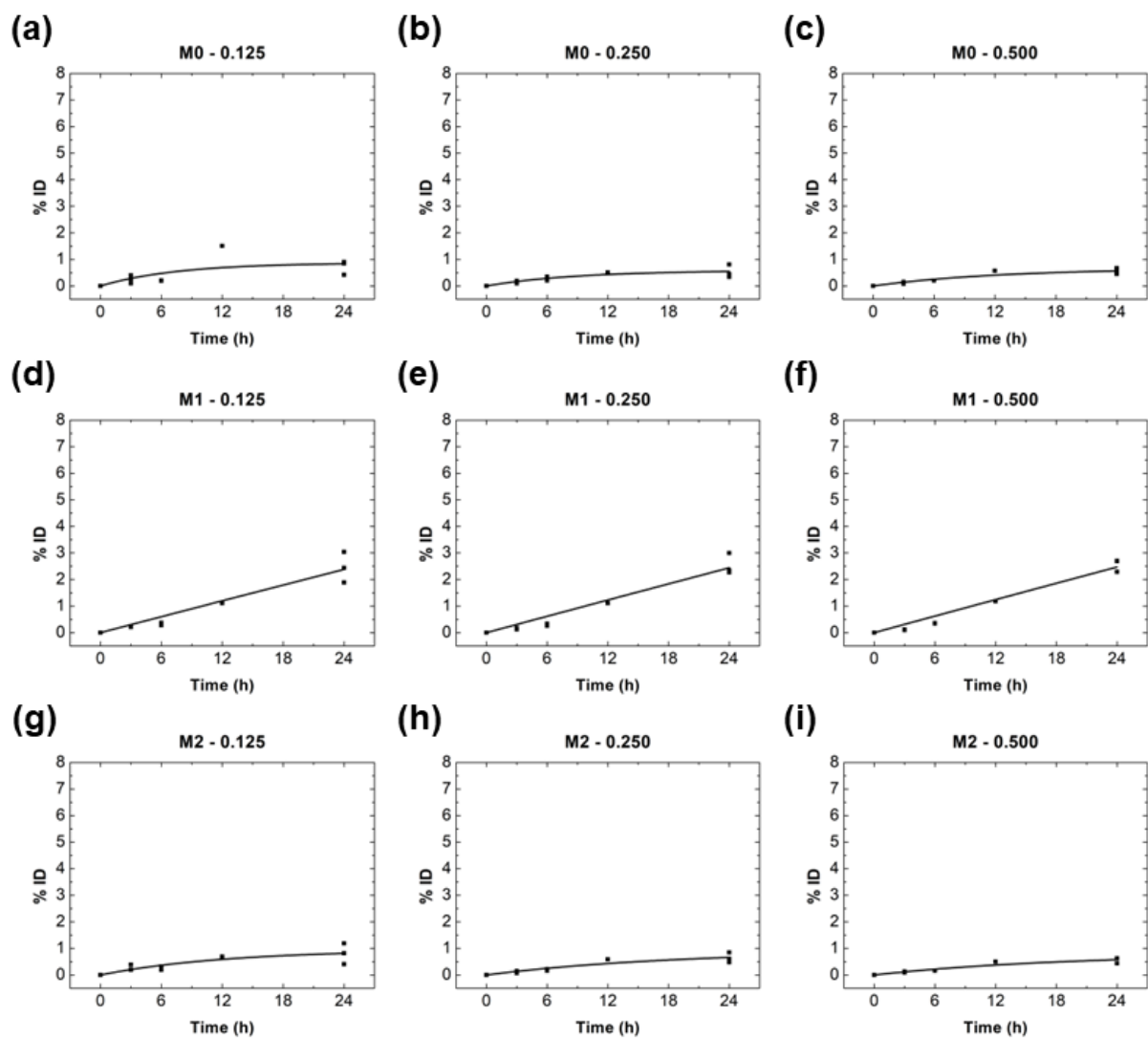


Figure S1. *In vitro* BNF-Plain uptake by macrophages. Fitting of the macrophage internalization kinetics $x_{in}(t)$ (Equation 17 in the manuscript) using all *in vitro* experimental values obtained for BNF-Plain (ferene-s assay at 3, 6, 12, and 24 h, replicates included), for three different initial doses (0.125, 0.250, or 0.500 mg of Fe) and three macrophage polarization states (M0, M1, and M2).

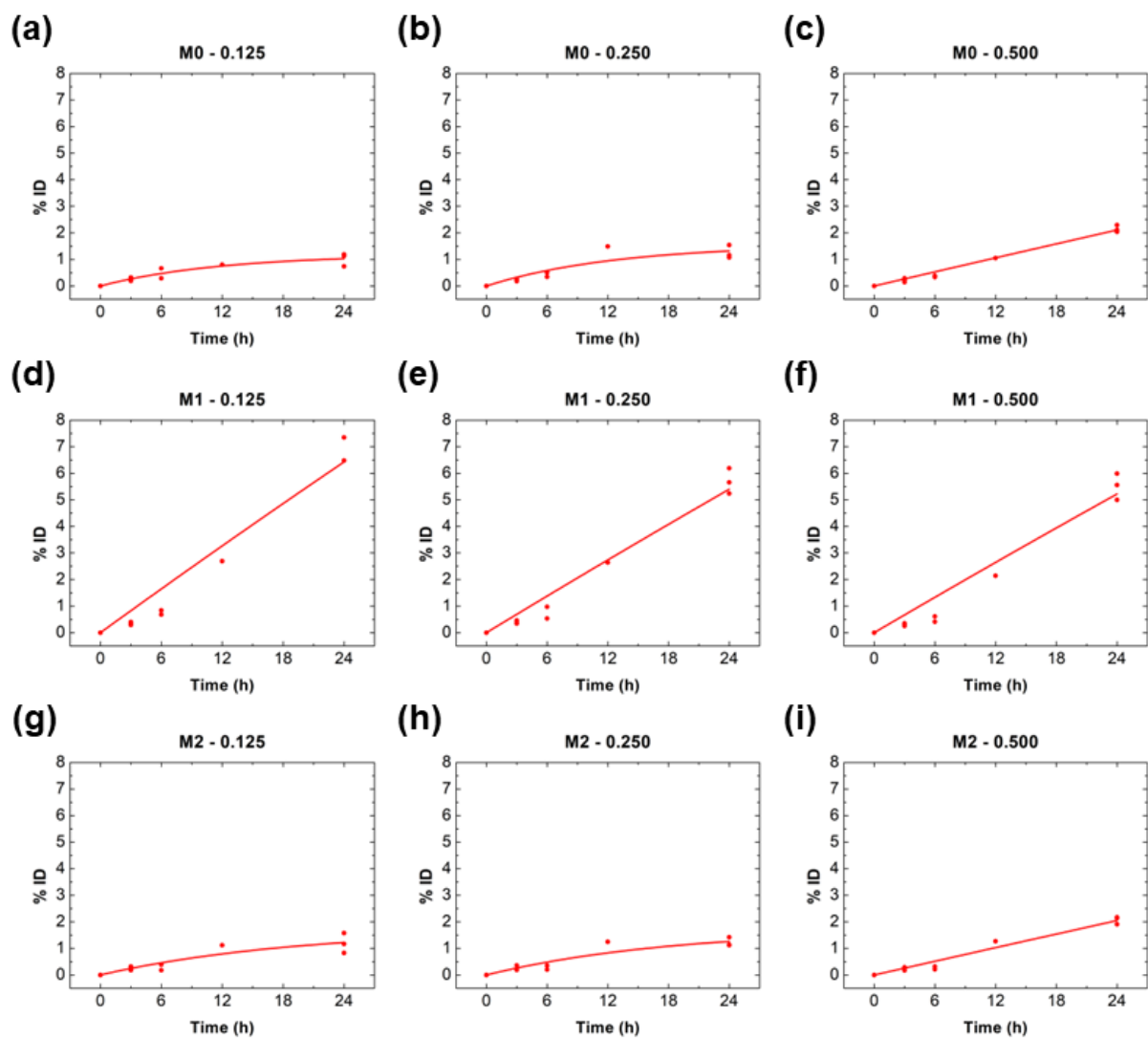


Figure S2. *In vitro* BNF-Her uptake by macrophages. Fitting of macrophage internalization kinetics $x_{in}(t)$ (Equation 17 in the manuscript) using all *in vitro* experimental values obtained for BNF-Her (ferene-s assay at 3, 6, 12, and 24 h, replicates included), for three different initial doses (0.125, 0.250, or 0.500 mg of Fe) and three macrophage polarization states (M0, M1, and M2).

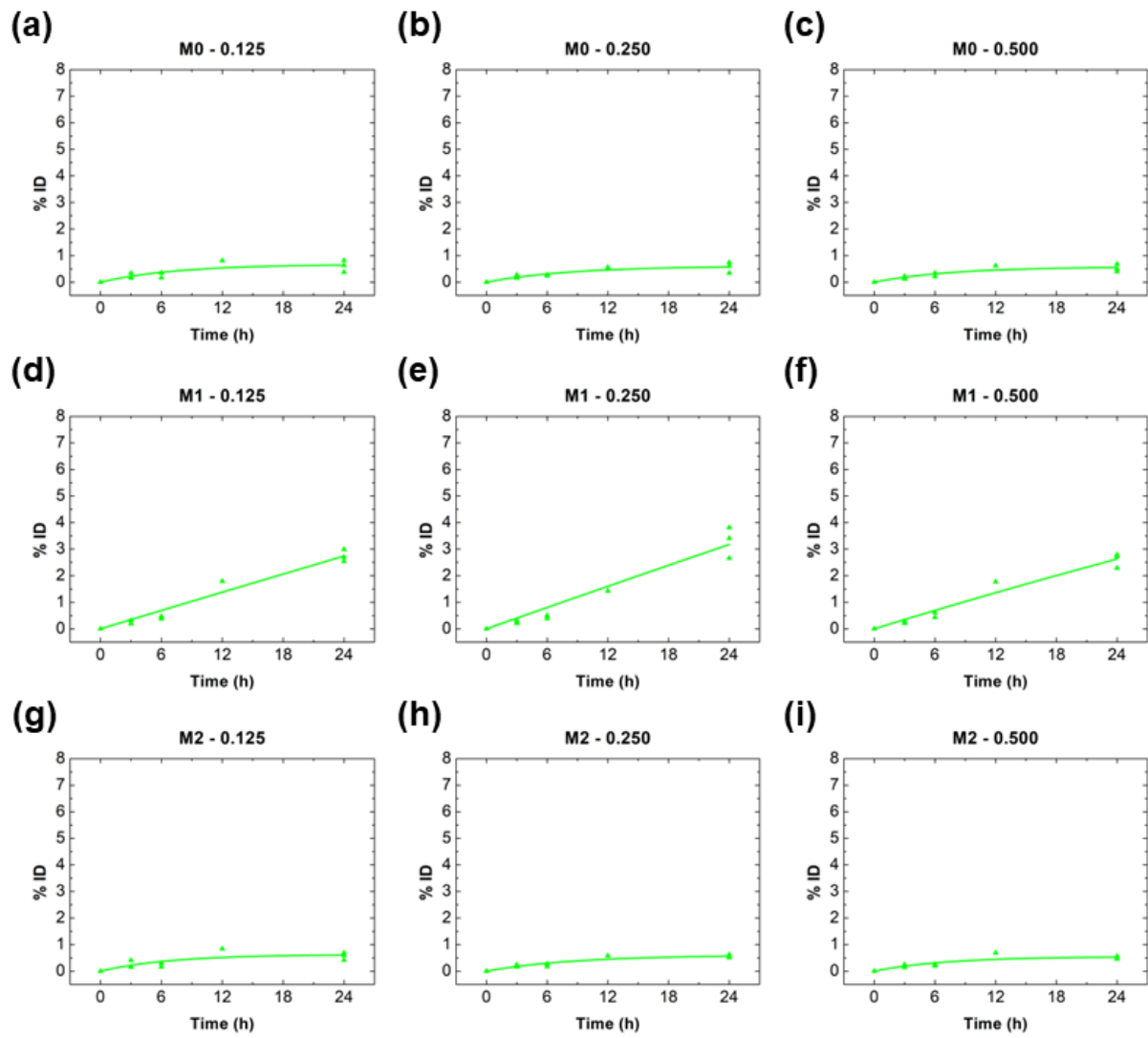


Figure S3. *In vitro* BNF-IgG uptake by macrophages. Fitting of macrophage internalization kinetics $x_{in}(t)$ (Equation 17 in the manuscript) for all *in vitro* experimental values obtained for BNF-IgG (ferene-s assay at 3, 6, 12, and 24 h, replicates included), for three different initial doses (0.125, 0.250, or 0.500 mg of Fe) and three macrophage polarization states (M0, M1, and M2).

Table S1. Values of K_{in} and K_{out} obtained from the fitting shown in Figures S1, S2, and S3 (fittings with all datapoints, including replicates, for each experimental setup)

BNF-Plain						
		0.125	0.250	0.500	Average*	
M0	K_{in}	0,00114 ± 0,00072	0,00065 ± 0,00024	0,00052 ± 0,00014	0,00077 ± 0,00026	
	K_{out}	0,12955 ± 0,11133	0,11112 ± 0,05940	0,07854 ± 0,03447	0,10640 ± 0,04360	
M1	K_{in}	0,00100 ± 0,00034	0,00103 ± 0,00029	0,00104 ± 0,00023	0,00102 ± 0,00017	
	K_{out}	0,00000 ± 0,02931	0,00000 ± 0,02459	0,00000 ± 0,01951	0,00000 ± 0,01432	
M2	K_{in}	0,00077 ± 0,00034	0,00049 ± 0,00016	0,00042 ± 0,00010	0,00056 ± 0,00013	
	K_{out}	0,07987 ± 0,05917	0,05260 ± 0,03734	0,05238 ± 0,02794	0,06162 ± 0,02511	

BNF-Her						
		0.125	0.250	0.500	Average*	
M0	K_{in}	0,00100 ± 0,00025	0,00121 ± 0,00039	0,00089 ± 0,00012	0,00103 ± 0,00016	
	K_{out}	0,08307 ± 0,03440	0,07694 ± 0,04265	0,00000 ± 0,01229	0,05334 ± 0,01872	
M1	K_{in}	0,00277 ± 0,00068	0,00231 ± 0,00050	0,00223 ± 0,00061	0,00244 ± 0,00035	
	K_{out}	0,00000 ± 0,02137	0,00000 ± 0,01884	0,00000 ± 0,02373	0,00000 ± 0,01236	
M2	K_{in}	0,00089 ± 0,00033	0,00095 ± 0,00028	0,00086 ± 0,00018	0,00090 ± 0,00016	
	K_{out}	0,05085 ± 0,04213	0,05385 ± 0,03495	0,00000 ± 0,01832	0,03490 ± 0,01924	

BNF-IgG						
		0.125	0.250	0.500	Average*	
M0	K_{in}	0,00089 ± 0,00034	0,00072 ± 0,00022	0,00075 ± 0,00021	0,00078 ± 0,00015	
	K_{out}	0,13067 ± 0,06873	0,11783 ± 0,05018	0,12914 ± 0,04866	0,12588 ± 0,03268	
M1	K_{in}	0,00116 ± 0,00025	0,00134 ± 0,00038	0,00117 ± 0,00025	0,00122 ± 0,00017	
	K_{out}	0,00000 ± 0,01879	0,00000 ± 0,02460	0,00450 ± 0,01867	0,00150 ± 0,01205	
M2	K_{in}	0,00091 ± 0,00036	0,00068 ± 0,00014	0,00076 ± 0,00022	0,00078 ± 0,00015	
	K_{out}	0,14298 ± 0,07659	0,11205 ± 0,03244	0,13642 ± 0,05334	0,13048 ± 0,03294	

*Average of the values found for each initial dose (0.125, 0.250, and 0.500 mg of Fe).

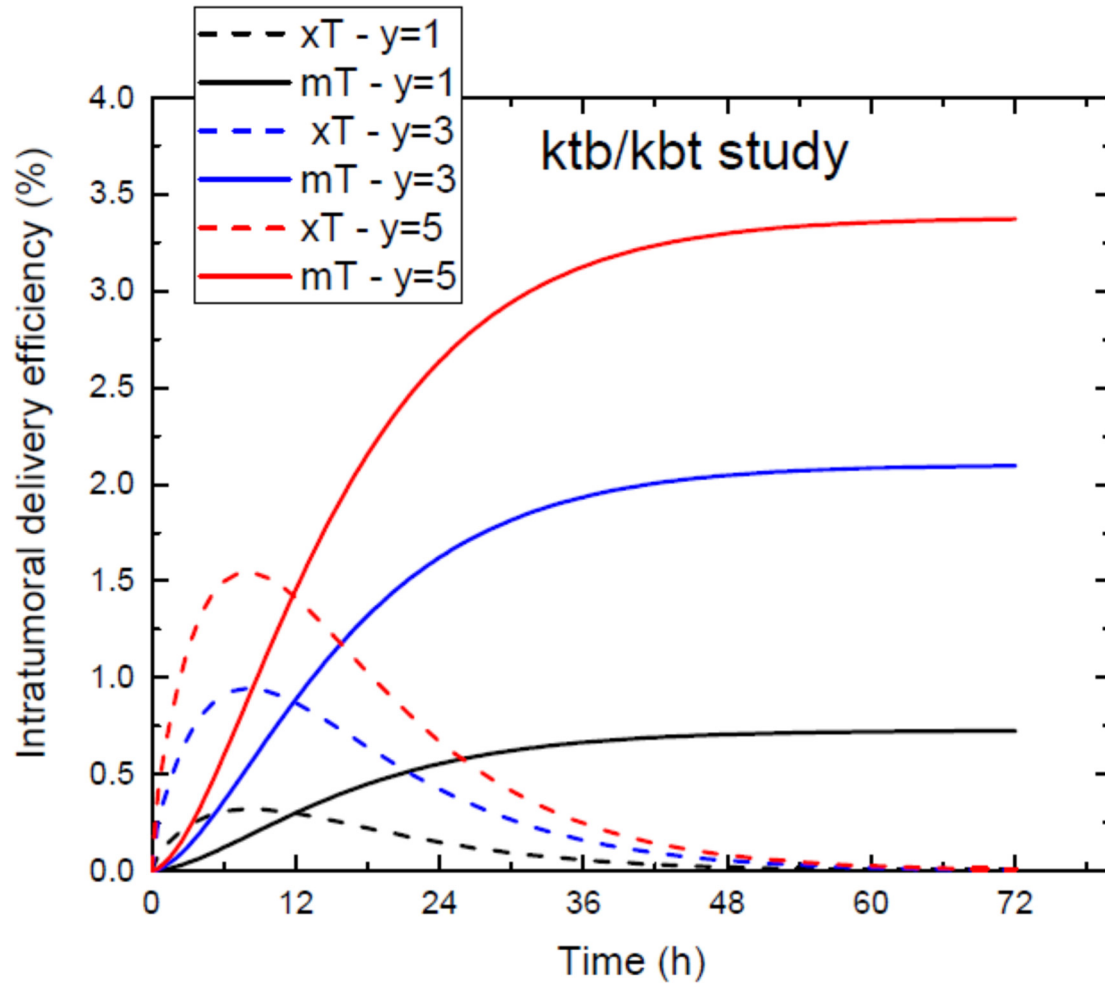


Figure S4. Simulated intratumor retention of BNF-Her nanoparticles. Simulated tumor retention of 100-nm BNF-Her nanoparticles varying the parameter K_{bt} and K_{tb} by increasing a factor y . Dashed lines represent passive retention (x_i), and solid-colored lines represent active retention by macrophages (m_i).