Statement of significance

Several human pro-apoptotic peptides (namely BAK, BAX and PUMA) have been engineered as self-assembling protein nanoparticles targeted to the tumoral marker CXCR4. The systemic administration of the same final amounts of those materials as single drugs, or as combinations of two or three of them, shows disparate intensities of antitumoral effects in a mouse model of human colorectal cancer, which are boosted in the triple combination on a non-additive basis. The superiority of the combined administration of pro-apoptotic agents, acting at different levels of the apoptotic cascade, opens a plethora of possibilities for the development of effective and selective cancer therapies based on the precise cocktailing of pro-apoptotic nanoparticulate agents.