Supporting Information

For the Article

Biodegradable PEG-poly(ω-pentadecalactone-*co*-*p*-dioxanone) Nanoparticles for Enhanced and Sustained Drug Delivery to Treat Brain Tumors

1. Thermal and crystalline properties of PEG-poly(PDL-*co*-DO) block copolymers

Table S1: Thermal Properties and Crystallinity of PEG-poly(PDL-*co*-DO) Copolymers

Sample	**TGA**	**DSC[a]**				**WAXS**
	T_{max} *(°C)*	$T_{m,1}$ *(°C)*	$\Delta H_{m,1}$ *(J/g)*	$T_{m,2}$ *(°C)*	$\Delta H_{m,2}$ *(J/g)*	X_c [b] *(%)*
MeO-PEG2K-OH	383	53	170	-	-	84
P56D44	396	47	54	75	53	51
P65D35	396	48	46	79	64	55
P71D29	401	47	43	82	74	54

a. Heating run (20 °C/min) following a cooling run at -10 °C/min

b. Crystallinity degree from WAXS (± 5%)

***Results and discussion*.** Thermal properties of PEG-poly(PDL-*co*-DO) diblock copolymers with approximately 40 wt% PEG content and different PDL/DO unit ratios were investigated by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC), and the results are summarized in **Table S1** (MeO-PEG2K-OH was tested as a reference polymer). All copolymers exhibit similar thermal degradation profiles with a temperature of maximum degradation rate (T_{max}) around 400 °C, which is slightly higher than the T_{max} of MeO-PEG2K-OH **(Fig. S1a)**. Moreover, the block copolymers show a wider degradation temperature range than MeO-PEG2K-OH, which is attributable to the repeat units (PDL, DO, and EG units) with remarkably different thermal stability. The DSC curves of heating runs after controlled cooling runs for all investigated samples are displayed in **Figure S1-b**. A single melting endotherm is observed for MeO-PEG2K-OH at T_m = 53 °C, whereas two melting phenomena occur for the copolymers. The low T_m around 47 °C remains almost constant for all copolymers, but the T_m corresponding to the higher temperature endotherm decreases with increasing DO content **(Fig. S1b and Table S1)**.

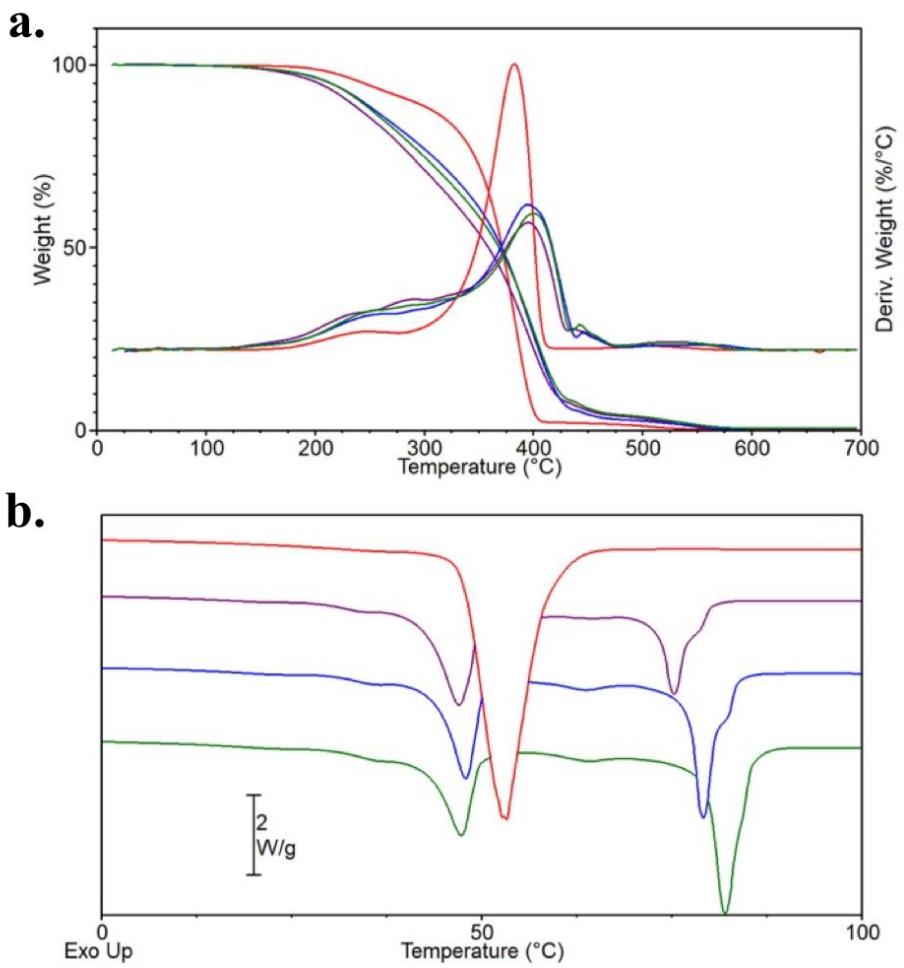

Figure S1. (a) TGA curves and (b) DSC curves of PEG and PEG-poly(PDL-*co*-DO) copolymers. Sample ID: 1-MeO-PEG2K-OH (red), 2-PEG-PPDL-co-DO (DO44) or P56D44 (blue), 3-PEG-PPDL-co-DO (DO35) or P65D35 (black), 4-PEG-PPDL-co-DO-4 (DO29) or P71D29 (green). DSC heating runs were conducted at 20 °C/min after controlled cooling runs at 10 °C/min.

In a previous study, a detailed investigation of poly(PDL-*co*-DO) random copolymers revealed that depending on copolymer composition, both poly(DO) and poly(PDL) crystal lattices were able to host units of the other comonomer and this behavior was interpreted as isodimorphism of poly(PDL-*co*-DO) [S1]. In particular, it was found that the copolymers containing up to 57 mol% DO units possess one melting endotherm attributed to the fusion of poly(PDL)-type crystal phases hosting DO units, and their T_m decreases with increasing DO content in the polymer chains. Thus, in the present work on DSC analysis of the PEG-poly(PDL-*co*-DO) samples, the low and higher

temperature melting endotherms can be attributed to the PEG segments and poly(PDL-*co*-DO) blocks respectively in the copolymers. The melting temperatures and enthalpy values associated with the poly(PDL-*co*-DO) chain blocks are in agreement with the previous data obtained on non-PEGylated poly(PDL-*co*-DO) copolyesters [S1]. Further, it is notable that the conjugation reduces the T_m and degree of crystallinity of PEG-poly(PDL-*co*-DO) copolymers as compared to the values of PEG and poly(PDL-*co*-DO).

The WAXS diffractograms of the PEG-poly(PDL-*co*-DO) copolymers are shown in **Figure S2**. The block copolymers exhibit the main reflections of MeO-PEG2K-OH (marked with broken arrows) and the typical X-ray diffraction pattern of poly(PDL-*co*-DO) with up to 50 mol% DO (marked with solid arrows) [S1]. The calculated total degree of crystallinity values are reported in **Table S1**, and the results are in line with the ΔH_m values obtained from the DSC measurements.

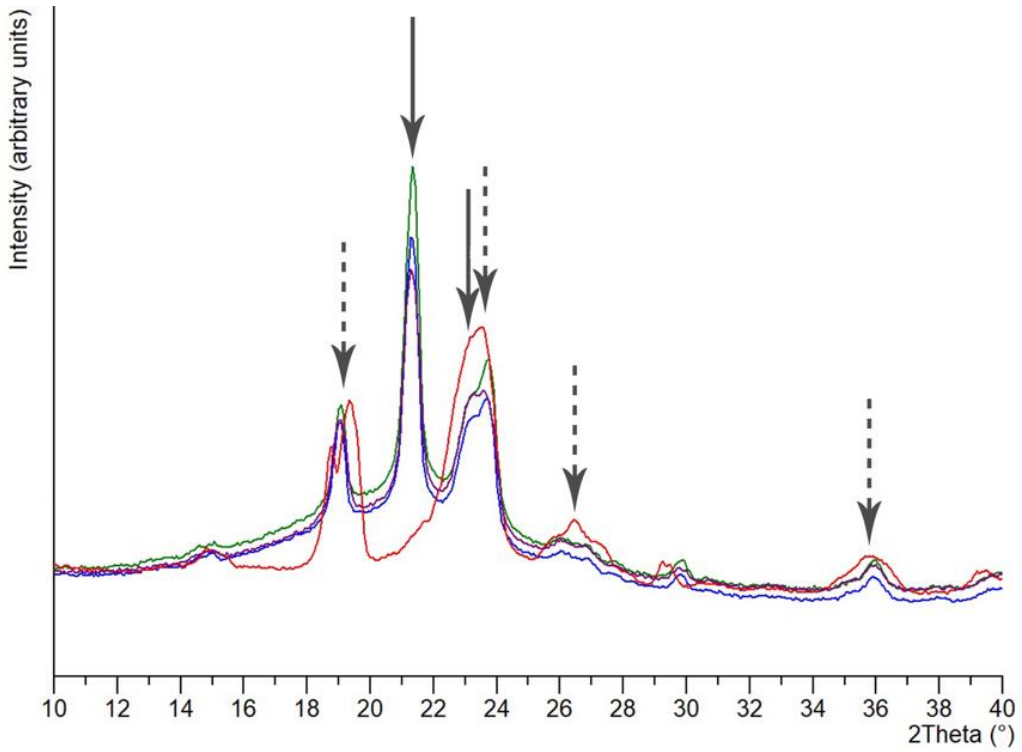

Figure S2. WAXS diffractograms of 1-MeO-PEG2K-OH (red), 2-PEG-PPDL-co-DO (DO44) or P56D44 (blue), 3-PEG-PPDL-co-DO (DO35) or P65D35 (black), 4-PEG-PPDL-co-DO-4 (DO29) or P71D29 (green). Broken and continuous arrows mark PEG reflections and poly(PDL-*co*-DO) reflections, respectively.

2. Normalized pChk1 Level and Western Blot of non-irradiated cells

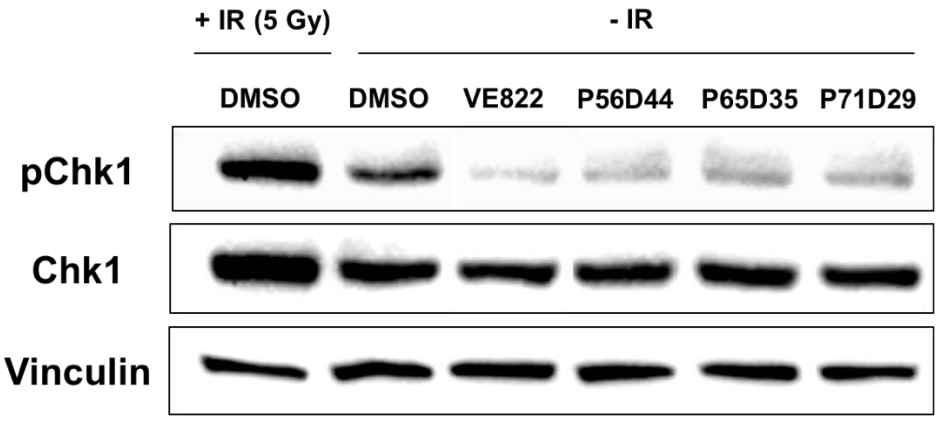

Figure S3. Western blot of Phospho-Chk1 levels in non-radiated (right five columns), and radiated (left column) RG2 cells. Cells were treated for 24 h with no treatment (DMSO), VE822-loaded P56D44 nanoparticles (P56D44), VE822-loaded P65D35 nanoparticles (P65D35), VE822-loaded P71D29 nanoparticles (P71D29) or free VE822 (VE822). Vinculin is shown as a loading control.

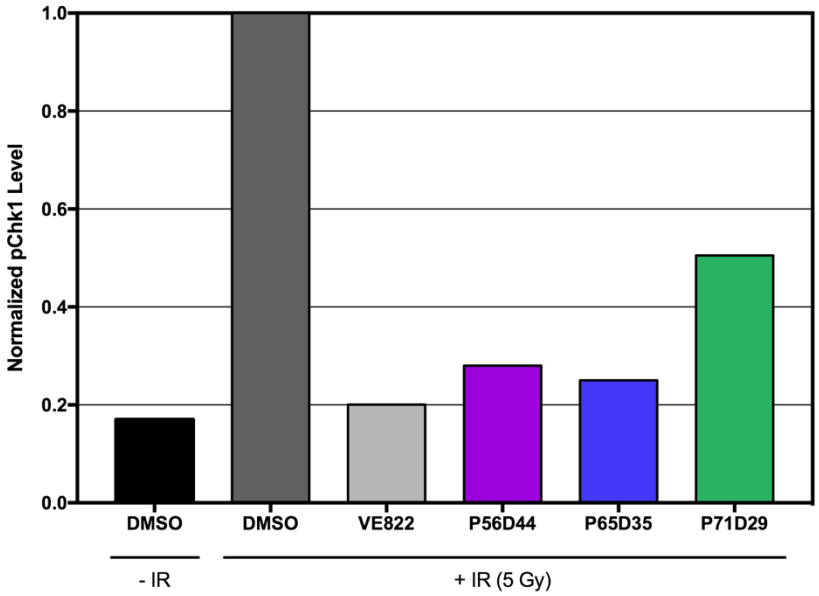

Figure S4. pChk1 protein levels normalized to both Vinculin and Chk1 levels as depicted in Figure 3. Cells were treated for 24 h with no treatment (DMSO), VE822-loaded P56D44 nanoparticles (P56D44), VE822-loaded P65D35 nanoparticles (P65D35), VE822-loaded P71D29 nanoparticles (P71D29) or free VE822 (VE822). Vinculin is shown as a loading control.

References

S1. Jiang Z, Azim H, Gross RA, Focarete ML, Scandola M. Lipase-catalyzed copolymerization of ω-pentadecalactone with *p*-dioxanone and characterization of copolymer thermal and crystalline properties. Biomacromolecules 2007; 8:2262-9.