Selectively Decreasing Malignant Melanoma Cell Viability with Polymersomes Loaded with Protoporphyrin IX (PPIX)

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Introduction: Traditional melanoma tumor treatments (such as surgery and radiotherapy) contain several limitations like incomplete ablation and multidrug resistance. It is well known that Protoporphyrin IX (PpIX) selectively kills cancer cells in two aspects: one is activated by a wavelength at 400 cm^{-1} and another is accumulation in cancer cells resulting in their death [1]. However, PpIX is difficult to deliver since it is a hydrophobic drug that aggregates in an aqueous phase [2]. Thus, it is clear that a new approach is needed to effectively deliver this drug to cells. To take advantage of this novel drug, polymersomes were used here as a carrier for PpIX to selectively kill melanoma cells.

Methods: PPIX was encapsulated inside the polymersomes by self-assembly. After being encapsulated, TEM and SEM were equipped to measure particle sizes and morphologies. Physical properties of those constructs were measured to analyze polymersome loading with PpIX as well as polymersome size, zeta potential, and chemistry compared to blank polymersomes. Fibroblast and melanoma (A375) cells were seeded at $2*10^4$ cells/ml density on a 96-well plate. After 24 hours, 3 days, and 5 days of incubation, cells were treated at different concentrations. Cell viability of the two cell lines was quantified by an MTT assay.

Results: The blank polymersomes were around 70 nm, while the diameter increased to 100 nm after loading with PpIX. Zeta potential also changed to a more negative surface charge after loading with PpIX, leading to a more stable polymersome than blank polymersomes. Photophysical properties were tested via UV spectrometry indicating that the PpIX-loaded polymersomes had better photophysical properties when compared to free PpIX in PBS. Most importantly, cell viability studies revealed that the polymersomes with PpIX were non-cytotoxic to fibroblasts but they showed a great potential to selectively kill melanoma cells. After a 24 hour cell culture study, melanoma cell viability decreased to 52% while 77% of fibroblasts were alive with 300 µg/ml of PpIX-loaded polymersomes. After 5 days of culture, the results showed a sustained selective anti-melanoma effect for the PpIX-loaded polymersomes.

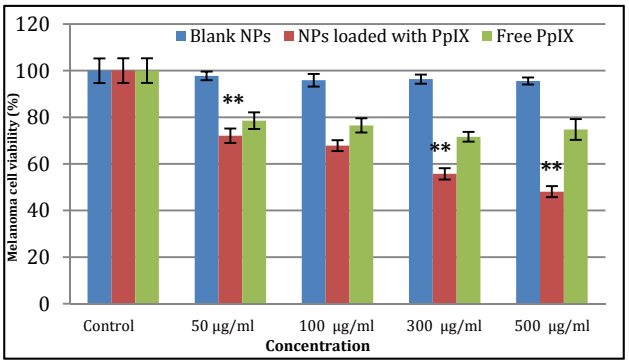

Figure 1. Cell viability for malignant melanoma A375 cells at different concentrations of blank nanoparticles, polymersomes loaded with PpIX, and free PpIX. Data are mean ±SEM; n = 3. **p < 0.01 compared to control. All values different (p<0.01) from controls.

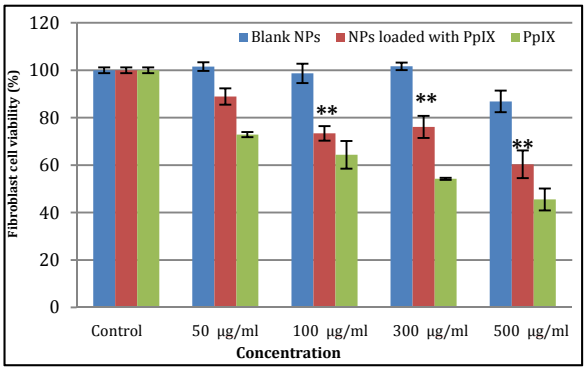

Figure 2. Cell viability for human dermal fibroblasts at different concentrations of blank nanoparticles, polymersomes loaded with PpIX, and free PpIX. Data are mean ±SEM; n = 3. **p < 0.01 compared to control. All values different (p<0.01) from controls.

Conclusions: In summary, these results indicate that PpIX-loaded polymersomes could be a promising treatment for skin cancer drug delivery with little to no adverse cytotoxic effects.

References: [1] L. M. Rossi, P. R. Silva, L. L. R. Vono, et al. Langmuir 2008, 24, 12534-12538

[2] R. Bonnett. Chem. Soc. Rev., 1995,24, 19-33