

Modification of PLLA Nanotopography and Surface Chemistry with Selenium Nanoclusters for Reducing Cancer Cell Interactions

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Statement of Purpose: Cancer recurrence at the site of tumor resection is a common complication resulting from today's efforts to treat the disease. To combat this, we have previously investigated the effects of nanostructured surfaces on poly(lactic-co-glycolic acid) (PLGA)¹ as well as selenium-coated titanium.^{2,3} In both studies, cancerous cells were less able to proliferate on the nanostructured surfaces while non-cancerous cells were unaffected, if not more capable of growth. Additionally, nanostructured surfaces have been found to influence the activity of stromal cells that support tumor growth.⁴⁻⁶ Here, we now investigate the relationship between the coverage of selenium on 3-dimensional nanostructured substrates and respective cancer cell responses using cast or electrospun poly-l-lactic acid (PLLA) and coated selenium nanoclusters.

Methods: Poly(l-lactic acid) (PLLA) was used as a foundation substrate for selenium nanoclusters. To generate "nanosmooth" films, the PLLA was dissolved in chloroform and cast onto glass dishes. Nanostructured PLLA was also generated via electrospinning the polymer into fibers ranging from the micron to nanometer scale. Both forms of PLLA were cut into discs and coated with selenium nanoclusters as follows. PLLA discs were rinsed with EtOH and DIH₂O and placed into a solution containing equal parts DIH₂O, 0.1M glutathione and 0.025M Na₂SeO₃. To precipitate selenium, 1mL of 2N NaOH was added to bring the solution to the alkaline range. The solutions were gently mixed for various times to allow for varied selenium coverage. PLLA discs were rinsed in DIH₂O thoroughly to stop the reaction.

PLLA discs were prepared for *in vitro* viability assays by sterilizing them under UV for 2 hrs. One disc was placed in one well and each well was seeded with 5,000 MG-63 osteosarcoma cells (ATCC) in EMEM with 10% FBS and 1% PS. The plates were incubated for two days, and cell viability was determined via an MTS assay.

Results and Discussion: As expected, with an increase in development time, more selenium nanoclusters formed on PLLA. For example, there was a fourfold increase in coverage from 1 min to 5 min of development time with little change in selenium nanocluster size. Additionally, with increased selenium—and, thus, an increase in nanoroughness—osteosarcoma cells were less capable of adhering and proliferating on comparable PLLA discs (Fig 1). Although more experimentation is required, the present study indicates that PLLA can be easily transformed to keep bone cancer cells from returning after a bone tumor is resected. PLLA is already commonly used in bone tissue engineering applications and this study highlights for the first time that through a selenium coating, it can be easily used in bone cancer applications.

Conclusions: Nanostructures can be introduced onto polymer substrates in multiple ways, including casting

films onto other nanostructured surfaces, electrospinning the polymer into fibers and coating the surface with nanosized materials (as this study demonstrated for selenium). We demonstrated the anti-cancer properties of selenium when coated onto PLLA films, resulting in the decreased proliferation of osteosarcoma cells.

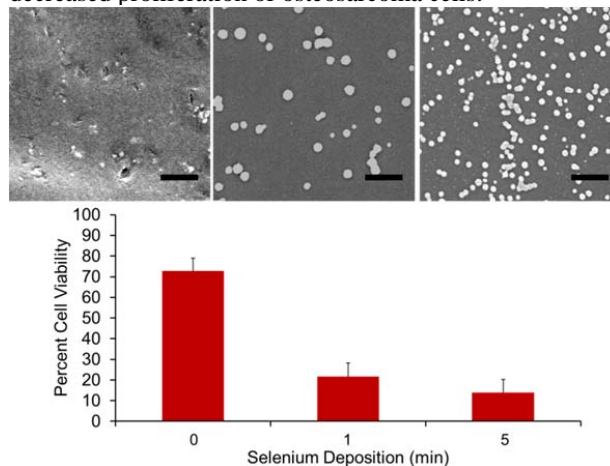


Figure 1. Cell viability of osteosarcoma cells on "nanosmooth" PLLA and PLLA coated with selenium for 1 and 5 min, with SEM showing increasing amounts of nano-selenium coverage with longer development times. SEM scale bars = 500 nm.

References:

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