## **Supporting Information**

## Platinum-loaded, selenium-doped hydroxyapatite nanoparticles selectively reduce proliferation of prostate and breast cancer cells co-cultured in the presence of stem cells.

Alessandra Barbanente, Robin A. Nadar, Lorenzo Degli Esposti, Barbara Palazzo, Michele Iafisco, Jeroen J. J. P. van den Beucken, Sander C. G. Leeuwenburgh, and Nicola Margiotta. **Equation 1** Description of the incorporation of Se anions into the apatitic lattice.

The substitution of a divalent Se anion for a trivalent orthophosphate anion creates a positively charged vacancy (+1). This charge defect is compensated by one calcium cation vacancy and one hydroxyl anion vacancy. As a consequence, we can observe a simultaneous decalcification and dehydroxylation in the apatite sample. In order to comply with the aforementioned formula, the amounts of reagents were calculated assuming that one orthophosphate ion and one calcium ion are replaced by one Se ion.

(10 - x)Ca2 + + (6 - x)PO43 - + xSeO32 - + (2 - x)OH - →Ca10 - x (PO4)6 - x (SeO3)x (OH)2 - x

(eqn (1))

## IR Characterization of HASe nanoparticles.

The characteristic hydroxyapatite bands were present in all spectra (Figure 1B). The dominant bands at around 1092 and 1037 cm<sup>-1</sup>, as well as the bands at 603 and 567 cm<sup>-1</sup>, correspond to the vibrations of the phosphate ( $PO_4^{3-}$ ) groups of hydroxyapatite. The intensity of the infrared  $PO_4^{3-}$  stretching bands (1037 cm<sup>-1</sup> with its shoulder at 1092 cm<sup>-1</sup>) intensity decreased with increasing Se substitution. Moreover, additional peaks were detected at 770 cm<sup>-1</sup> and in the range between 830 and 870 cm<sup>-1</sup>, which can be assigned to Se-O vibrations of the selenite ions in HA nanoparticles. Selenite absorptions were detected at 740, 790, 840 and 880 cm<sup>-1</sup>. Incorporation of selenite ions into HA nanoparticles resulted in shifting of the bands to lower/higher wavenumbers with increasing selenite substitution percentage. In the spectra of HASe1% only a band around 870 cm<sup>-1</sup> was detected. The spectra of HASe10% and a band at 846 cm<sup>-1</sup>. A general shifting of the band to lower wavenumbers was observed, which was attributed to a change in the counter ions surrounding incorporated selenite with respect to sodium selenite.

**Figure S1**. Schematic representation for synthesis of HASe nanoparticles and Ptloaded HASe nanoparticles.



## Adsorption of PtPP on Se-doped HA



**Figure S2.** Dose-response curves for prostate cancer, breast cancer and bone marrow stem cells treated with sodium selenite  $(Na_2SeO_3)$  measured using (A) CCK-8 assay and (B) DNA assay. Dose-response curves for prostate cancer, breast cancer and bone marrow stem cells treated with PtPP measured using (C) CCK-8 assay and (D) DNA assay. Cell viability is plotted against the logarithm of Pt concentrations.



**Figure S3.** In vitro effects of Pt or Se releasates from Pt-loaded or HASe. The cytotoxicity of Se releasates obtained at pH 7.4 on (A) viability and (B) proliferation of prostate cancer, breast cancer and bone marrow stem cells. The cytotoxicity of Se releasates obtained at pH 6.5 on (C) viability and (D) proliferation of prostate cancer, breast cancer and bone marrow stem cells. The cytotoxicity of Pt releasates obtained at pH 7.4 on (E) viability and (F) proliferation of prostate cancer, breast cancer and bone marrow stem cells. The cytotoxicity of Pt releasates obtained at pH 6.5 on (G) viability and (F) proliferation of prostate cancer, breast cancer and bone marrow stem cells. The cytotoxicity of Pt releasates obtained at pH 6.5 on (G) viability and (H) proliferation of prostate cancer, breast cancer and bone marrow stem cells. \*P <0.05; \*\*P < 0.01; \*\*\*P < 0.001; \*\*\*\*P <0.0001.



**Figure S4.** Viability and proliferation of prostate cancer, breast cancer and bone marrow stem cells treated with fixed concentration of 10  $\mu$ M Na<sub>2</sub>SeO<sub>3</sub> and increasing concentration of Pt drugs resulting in Pt/Se ratios between 0 and 8. (A, B) Viability and proliferation of prostate cancer, breast cancer and bone marrow stem cells treated with combination of PtPP and Na<sub>2</sub>SeO<sub>3</sub>. (C, D) Viability and proliferation of prostate cancer, breast cancer and bone marrow stem cells treated and Na<sub>2</sub>SeO<sub>3</sub>. (E, F) Viability and proliferation of prostate cancer and bone marrow stem cells treated with combination of Na<sub>2</sub>SeO<sub>3</sub>. (E, F) Viability and proliferation of prostate cancer and bone marrow stem cells treated with combination of Cisplatin and Na<sub>2</sub>SeO<sub>3</sub>. \*\*0.001 <P < 0.01; \*\*\*0.0001 <P < 0.001; \*\*\*\*P <0.0001. The labels for prostate cancer (PC3, blue), breast cancer (MDA-MB-231, red), and bone marrow stem (hBMSc, green) cells are the same in A—F and are reported in the upright corner of the figure.



**Figure S5.** Dose-response curves for prostate cancer, breast cancer and bone marrow stem cells treated with kiteplatin measured using (A) CCK-8 assay and (B) proliferation assay.

