Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B. This journal is © The Royal Society of Chemistry 2017

Supporting Information

Hyaluronic acid cloaked oleic acid nanoparticle inhibits MAPK signaling with sub-cellular DNA damage in colon

cancer

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Fig. S1: Characterization of OA-AZD-CDDP-NPs by (a) DLS, (b) seta potential, (c) FE-SEM and (d) AFM.



Fig. S2: Schematic representation of the plausible mechanism of self-assembly of OA-AZD-CDDP-NP.



Fig. S3: AFM analysis of HA-OA-NPs to show the diameter and height of the nanoparticles.



Fig. S4: (a-b) Concentration versus absorbance calibration graph of AZD6244 and cisplatin at characteristic $\lambda_{max} = 273$ nm and 706 nm respectively, determined by UV-Vis spectroscopy. (c) Loading of AZD6244 and cisplatin in HA-OA-NPs determined by the calibration graph.





Fig. S5: EDX spectra of HA-OA-NPs to confirm the presence of AZD6244 and cisplatin in the same particle.



Fig. S6: Stability of HA-OA-NPs in DMEM cell culture media with 10% FBS at 37 °C over 96h determined by (a) hydrodynamic diameter and (b) polydispersity index (PDI).



Fig. S7: Flow cytometry analysis of MCF7, DLD-1 and HCT-116 cells to determine the cell surface expression of CD44 receptors by FITC-labeled anti-human CD44 antibody.



Fig. S8: Flow cytometry analysis of HCT-116 cells pre-treated with chlorpromazine, amiloride and genistein followed by treatment with FITC-HA-OA-NPs.



Fig. S9: Flow cytometry analysis of HCT-116 cells after treatment with FITC-HA-OA-NPs at 4°C and 37°C.



Fig. S10: Quantification of expression of (a) p-ERK1, (b) p-ERK2 and (c) γH2AX from western blot analysis in HCT-116 cells after treatment with HA-OA-NPs for 24h.



Fig. S11: Concentration dependent cell viability of OA-AZD-CDDP-NPs in HCT-116 and DLD-1 colon cancer cells at 24h post-incubation determined by MTT assay.



Fig. S12: Concentration dependent cell viability of (a) HA-OA-AZD-CDDP-NPs and (b) OA-AZD-CDDP-NPs in MCF7 breast cancer cells at 24h post incubation determined by MTT assay.

OA- AZD (mg)	OA- CDDP (mg)	OA-ED- NH2 (mg)	Hyaluronic acid (HA) (mg)	Size (nm)	PDI	Zeta Potential (mV)	AZD : CDDP (Molar ratio)	Loading of drugs (uM) (AZD : CDDP)
1	1	2	0.2	178.25±8	0.321±0.08	-25.5±5	0.68:1	200.52+ 365.41 (0.54:1)
1	0.75	2	0.2	154.25±6	0.221±0.06	-43.8±3	0.97:1	194.24+ 241.56 (0.8:1)
1	0.5	1.5	0.2	198.25±5	0.521±0.96	-22.5±8	1:0.69	220.24+ 105.01 (1:0.47)
1	0.25	1.5	0.2	228.25±15	0.621±1.6	-32.5±3	1:0.34	173.04+ 30.45 (1:0.17)

Table S1: Optimization of size, zeta potential, PDI and dual drug loading in engineering HA-OA-NPs.