

## *Supporting Information for*

# Global Transcriptomic Analysis of Model Human Cell Lines Exposed to Surface-Modified Gold Nanoparticles: The Effect of Surface Chemistry

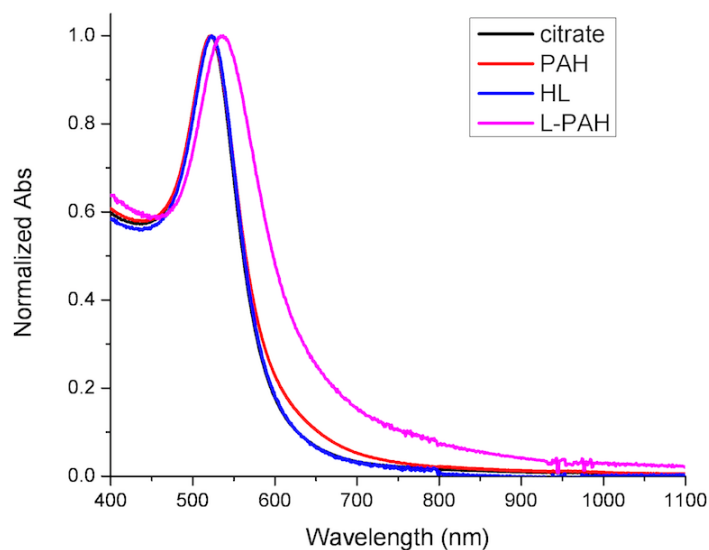
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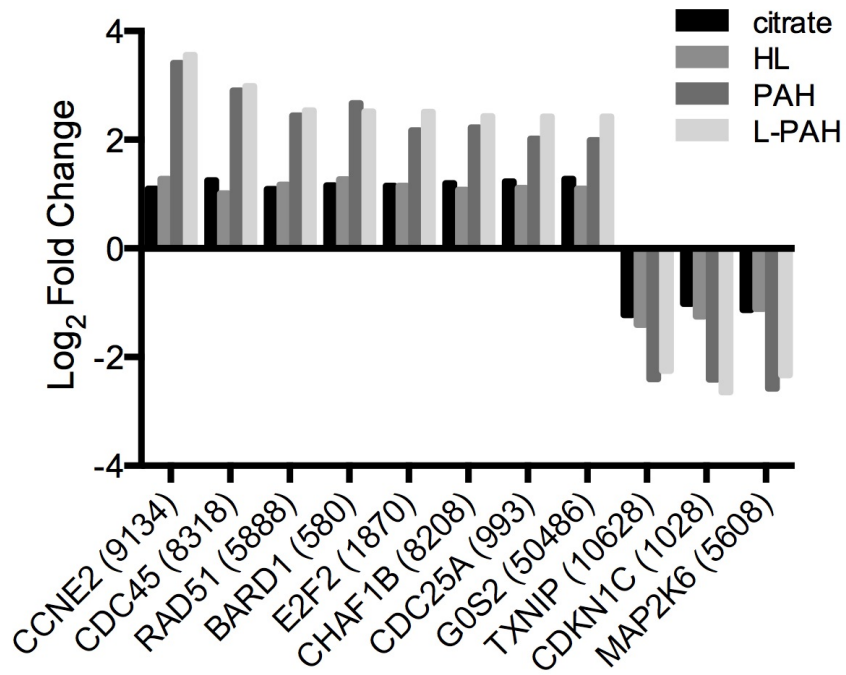
**Figure S1.** UV-Vis spectra of citrate, PAH, HL and L-PAH Au NPs in water.

**Table S1.** Analysis of selected gene categories after treatment of HDF cells with 0.1 nM Au NPs

GO accession number (class) <sup>a</sup>	Gene category annotation	Reg. <sup>b</sup>	Number of genes in category <sup>c</sup>	% genes in category <sup>d</sup>	p-value <sup>e</sup>
<u>HL Au NPs</u>					
GO:0044421 (CC)	extracellular region part	Down	5	23.8	0.0342
<u>PAH Au NPs</u>					
GO:0007049 (BP)	cell cycle	Up	119	22.9	6.8x10 <sup>-53</sup>
GO:0000279 (BP)	M phase	Up	72	13.9	2.1x10 <sup>-41</sup>
GO:0006259 (BP)	DNA metabolic process	Up	80	15.4	1.9x10 <sup>-35</sup>
GO:0031981 (CC)	nuclear lumen	Up	108	20.8	2.4x10 <sup>-21</sup>
GO:0015630 (CC)	microtubule cytoskeleton	Up	60	11.6	5.2x10 <sup>-19</sup>
GO:0000075 (BP)	cell cycle checkpoint	Up	24	4.62	1.4x10 <sup>-15</sup>
GO:0000082 (BP)	G1/S transition of mitotic cell cycle	Up	8	1.5	1.3x10 <sup>-3</sup>
GO:0031012 (CC)	extracellular matrix	Down	32	4.9	3.2x10 <sup>-7</sup>
GO:0006631 (BP)	fatty acid metabolic process	Down	19	2.9	1.2x10 <sup>-4</sup>
GO:0006350 (BP)	transcription	Down	98	15.0	4.9x10 <sup>-4</sup>

GO:0042981 (BP)	regulation of apoptosis	Down	45	6.9	$9.3 \times 10^{-4}$
GO:0004175 (MF)	endopeptidase activity	Down	25	3.8	$2.2 \times 10^{-3}$
GO:0030247 (MF)	polysaccharide binding	Down	14	2.2	$2.3 \times 10^{-3}$
GO:0016477 (BP)	cell migration	Down	19	2.9	$5.6 \times 10^{-3}$
GO:0046872 (MF)	metal ion binding	Down	161	24.7	$2.6 \times 10^{-2}$
<u>L-PAH Au NPs</u>					
GO:0007049 (BP)	cell cycle	Up	129	22.5	$2.2 \times 10^{-57}$
GO:0000279 (BP)	M phase	Up	83	14.5	$2.9 \times 10^{-50}$
GO:0006259 (BP)	DNA metabolic process	Up	85	14.8	$5.8 \times 10^{-37}$
GO:0031981 (CC)	nuclear lumen	Up	113	19.7	$5.9 \times 10^{-21}$
GO:0015630 (CC)	microtubule cytoskeleton	Up	63	11.0	$3.1 \times 10^{-19}$
GO:0000075 (BP)	cell cycle checkpoint	Up	24	4.2	$8.5 \times 10^{-15}$
GO:0000082 (BP)	G1/S transition of mitotic cell cycle	Up	7	1.2	$9.2 \times 10^{-3}$
GO:0031012 (CC)	extracellular matrix	Down	31	5.3	$8.1 \times 10^{-8}$
GO:0046872 (MF)	metal ion binding	Down	156	26.7	$2.3 \times 10^{-4}$
GO:0042981 (BP)	regulation of apoptosis	Down	43	7.4	$2.7 \times 10^{-4}$
GO:0030247 (MF)	polysaccharide binding	Down	12	2.1	$6.1 \times 10^{-3}$
GO:0004175 (MF)	endopeptidase activity	Down	21	3.6	$8.1 \times 10^{-3}$
GO:0016477 (BP)	cell migration	Down	17	2.9	$8.7 \times 10^{-3}$

<sup>a</sup>Gene ontology classifications are cellular component (CC), biological process (BP) or molecular function (MF). <sup>b</sup>Denotes up for up-regulation, down for down-regulation. <sup>c</sup>Genes that were sufficiently up-regulated (raw p-value < 0.05, FC > 1.5) and down-regulated (raw p-value < 0.05, FC < -1.5) were separately entered into DAVID using medium stringency threshold. The number of genes that fall into the GO category for either the up- or down-regulated genes is shown. <sup>d</sup>Percent of up- or down-regulated genes entered into DAVID that fall under selected GO category. <sup>e</sup>One-tail Fisher Exact p-value for gene-enrichment analysis. The smaller the value, the more enriched the gene category; p-value < 0.05 considered significant.



**Figure S2.** Most significantly changed genes of HDF cells after 0.1 nM Au NP incubation that fall under the “cell cycle” gene category (GO accession number GO:0007049)

**Table S2.** Analysis of selected gene categories after treatment of PC3 cells with 1 nM Au NPs

GO accession number (class) <sup>a</sup>	Gene category annotation	Reg. <sup>b</sup>	Number of genes in category <sup>c</sup>	% genes in category <sup>d</sup>	p-value <sup>e</sup>
<u>Citrate Au NPs</u>					
GO:0010498 (BP)	proteasomal protein catabolic process	Down	3	17.7	5.5x10 <sup>-3</sup>
GO:0031396 (BP)	regulation of protein ubiquitination	Down	3	17.7	5.3x10 <sup>-3</sup>
<u>HL Au NPs</u>					
GO:0046870 (MF)	cadmium ion binding	Up	6	7.6	2.1x10 <sup>-10</sup>
GO:0005507 (MF)	copper ion binding	Up	6	7.6	7.8x10 <sup>-6</sup>
GO:0001525 (BP)	angiogenesis	Up	6	7.6	3.9x10 <sup>-4</sup>
GO:0040012 (BP)	regulation of locomotion	Up	6	7.6	1.3x10 <sup>-3</sup>
GO:0001944 (BP)	vasculature development	Up	6	7.6	4.0x10 <sup>-3</sup>
GO:0016477 (BP)	cell migration	Up	6	7.6	6.0x10 <sup>-3</sup>
GO:0005125 (MF)	cytokine activity	Up	4	5.1	4.3x10 <sup>-2</sup>
GO:0016408 (MF)	C-acyltransferase activity	Down	3	3.2	2.4x10 <sup>-3</sup>
GO:0015293 (MF)	symporter activity	Down	5	5.3	3.7x10 <sup>-3</sup>
GO:0006839 (BP)	mitochondrial transport	Down	3	3.2	4.2x10 <sup>-2</sup>
GO:0006955 (BP)	immune response	Down	8	8.5	4.4x10 <sup>-2</sup>
<u>PAH Au NPs</u>					
GO:0005524 (MF)	ATP binding	Down	65	15.7	1.3x10 <sup>-7</sup>
GO:0000166 (MF)	nucleotide binding	Down	84	20.2	1.1x10 <sup>-6</sup>
GO:0042325 (BP)	regulation of phosphorylation	Down	24	5.8	3.2x10 <sup>-4</sup>
GO:0045859 (BP)	regulation of protein kinase activity	Down	16	4.6	7.6x10 <sup>-4</sup>
GO:0004386 (MF)	helicase activity	Down	11	2.7	1.2x10 <sup>-3</sup>
GO:0006325 (BP)	chromatin organization	Down	18	4.3	5.0x10 <sup>-3</sup>
GO:0051276 (BP)	chromosome organization	Down	21	5.1	6.3x10 <sup>-3</sup>
GO:0007049 (BP)	cell cycle	Down	26	6.3	4.1x10 <sup>-2</sup>
<u>L-PAH Au NPs</u>					
GO:0005125 (MF)	cytokine activity	Up	17	4.7	7.2x10 <sup>-8</sup>
GO:0006955 (BP)	immune response	Up	34	9.3	9.3x10 <sup>-8</sup>
GO:0006954 (BP)	inflammatory response	Up	20	5.5	3.5x10 <sup>-6</sup>
GO:0042981 (BP)	regulation of apoptosis	Up	32	8.8	2.1x10 <sup>-5</sup>
GO:0006916 (BP)	anti-apoptosis	Up	14	3.8	5.9x10 <sup>-5</sup>
GO:0043066 (BP)	negative regulation of apoptosis	Up	18	4.9	1.4x10 <sup>-4</sup>

GO:0016477 (BP)	cell migration	Up	14	3.8	1.0x10 <sup>-3</sup>
GO:0040012 (BP)	regulation of locomotion	Up	8	2.2	4.8x10 <sup>-2</sup>
GO:0005524 (MF)	ATP binding	Down	119	11.2	2.0x10 <sup>-5</sup>
GO:0046578 (BP)	regulation of Ras protein signal transduction	Down	26	2.5	2.1x10 <sup>-4</sup>
GO:0000166 (MF)	nucleotide binding	Down	160	15.1	3.8x10 <sup>-4</sup>
GO:0042981 (BP)	regulation of apoptosis	Down	67	6.3	5.7x10 <sup>-4</sup>
GO:0016192 (BP)	vesicle-mediated transport	Down	50	4.7	1.4x10 <sup>-3</sup>
GO:0043065 (BP)	positive regulation of apoptosis	Down	37	3.5	7.3x10 <sup>-3</sup>
GO:0035023 (BP)	regulation of Rho protein signal transduction	Down	13	1.2	7.7x10 <sup>-3</sup>
GO:0031012 (CC)	extracellular matrix	Down	31	2.9	7.9x10 <sup>-3</sup>
GO:0046834 (BP)	lipid phosphorylation	Down	5	0.5	9.5x10 <sup>-3</sup>
GO:0008289 (MF)	lipid binding	Down	37	3.5	1.7x10 <sup>-2</sup>
GO:0030036 (BP)	actin cytoskeleton organization	Down	20	1.9	4.1x10
GO:0032483 (BP)	regulation of Rab protein signal transduction	Down	7	0.7	4.2x10 <sup>-2</sup>

<sup>a</sup>Gene ontology classifications are cellular component (CC), biological process (BP) or molecular function (MF). <sup>b</sup>Denotes up for up-regulation, down for down-regulation. <sup>c</sup>Genes that were sufficiently up-regulated (raw p-value < 0.05, FC > 1.5) and down-regulated (raw p-value < 0.05, FC < -1.5) were separately entered into DAVID using medium stringency threshold. The number of genes that fall into the GO category for either the up- or down-regulated genes is shown. <sup>d</sup>Percent of up- or down-regulated genes entered into DAVID that fall under selected GO category. <sup>e</sup>One-tail Fisher Exact p-value for gene-enrichment analysis. The smaller the value, the more enriched the gene category; p-value < 0.05 considered significant.

**Table S3.** Primer/probe sets used for PCR validation of microarray results

Gene symbol	Entrez ID	Gene name	TaqMan® Assay ID	Cell Line
CXCL1	2919	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	Hs00236937_m1	HDF/PC3
CCNE2	9134	cyclin E2	Hs00180319_m1	HDF
DTL	51514	denticleless E3 ubiquitin protein ligase homolog	Hs00978565_m1	HDF
GAL	51083	galanin/GMAP prepropeptide	Hs00544355_m1	HDF
RRM2	6241	ribonucleotide reductase M2	Hs00357247_g1	HDF
WFDC1	58189	WAP four-disulfide core domain 1	Hs00221849_m1	HDF
SLC9A9	285195	solute carrier family 9, subfamily A (NHE9, cation proton antiporter 9), member 9	Hs00543518_m1	HDF

FAXDC 2	10826	fatty acid hydroylase domain containing 2	Hs00260753_m1	HDF
ADH1A	124	alcohol dehydrogenase 1A (class I), alpha polypeptide	Hs00605167_g1	HDF
AKR1C3	8644	aldo-keto reductase family 1, member C3	Hs00366267_m1	HDF
IL8	3576	interleukin 8	Hs00174103_m1	PC3
LTB	4050	lymphotoxin beta (TNF superfamily, member 3)	Hs00242739_m1	PC3
BCL2A1	597	BCL2-related protein A1	Hs00187845_m1	PC3
BAK1	578	BCL2-antagonist/killer 1	Hs00832876_g1	PC3
LAMB2	3913	laminin, beta 2 (laminin S)	Hs00158642_m1	PC3
DDR1	780	discoidin domain receptor tyrosine kinase 1	Hs01058430_m1	PC3
BAP1	8314	BRCA1 associated protein-1 (ubiquitin carboxyl-terminal hydrolase)	Hs01109276_g1	PC3
TNK2	10188	tyrosine kinase, non-receptor, 2	Hs00416477_m1	PC3
NES	10763	nestin	Hs04187831_g1	PC3
GAPDH	2597	glyceraldehyde-3-phosphate dehydrogenase	Hs99999905_m1	HDF/PC3
B2M	567	beta-2-microglobulin	Hs99999907_m1	HDF/PC3
HPRT1	3251	hypoxanthine phosphoribosyltransferase 1	Hs99999909_m1	HDF/PC3