Table S1. Impact of AuNP size, morphology and functionalization on cellular uptake, subcellular localization and cell survival. Mammalian cells were incubated with AuNPs and different parameters related to AuNP – cell interactions were measured. It should be emphasized that AuNPs, even if not functionalized, acquire a serum protein coat when exposed to the growth medium. Results listed in the table are not comprehensive; we focus on data that are relevant to the subcellular distribution of AuNPs. Peptide sequences are shown in the one-letter code. Of note, some publications report AuNP size based on transmission electron microscopy, whereas others provide data for dynamic light scattering.

Cells analyzed	AuNP morphology	AuNP size	AuNP surface modification	Incubation time	Cellular Uptake	Subcellular localization	Elimination	Cytotoxicity	Ref.
HeLa (human cervix carcinoma)	Spheres, rods	Spheres: 14, 30, 50, 74, 100nm diameter; Rods: 40x14nm, 74x14nm	Citrate, transferrin	6h	Receptor mediated endocytosis. Size-dependent uptake of AuNPs; Uptake of spheres 14nm: 622/h; 50nm: 1294/h; 74nm: 417/h; uptake of nanorods less efficient than spheres; less uptake of transferrin-coated AuNPs	Cytoplasmic vesicles	N.D.	Viability 98%	[49]
HeLa (human cervix carcinoma); SNB19 (human glioblastoma); STO (mouse embryonic fibroblasts)	Spheres, rods	Spheres: 14, 30, 50, 74, 100nm; Rods: 20x30, 14x50, 7x42nm	Transferrin	Not specified	Receptor mediated endocytosis; time [h] to reach 50% of equilibrium concentration; 14nm AuNPs: HeLa – 1.19, SNB19 – 2.02, STO - 2.45 50nm AuNPs: HeLa – 1.71, SNB19 - 1.88, STO - 2.10 74nm AuNPs: HeLa - 2.12 SNB19 - 2.52 STO - 2.88; Lower uptake of transferrin-coated rods as compared to transferrin-coated spheres; less uptake of transferring-coated AuNPs as compared to uncoated AuNPs	Intracellular	Removal; time [min] to reach 50% of equilibrium concentration; 14nm AuNPs: HeLa – 0.33, SNB19 – 0.41, STO – 0.33 50nm AuNPs: HeLa – 0.50, SNB19 - 0.58, STO - 0.41 74 nm AuNPs: HeLa – 0.75 SNB19 – 0.66 STO - 0.58 14nm spheres more efficiently removed than 50nm spheres; rods more efficiently removed than spheres	N.D., but not toxic in earlier studies.	[50]
TE85 (human osteosarcoma)	Spherical	~5nm diameter	Unmodified AuNPs; cell penetrating peptide: AAVALLPAVLLA LLAP; NLS:PKKKRKV; combination peptide: PKKKRKVAAVA LLPAVLLALLAP	3h	Low entry of unmodified AuNPs; uptake when modified with cell penetrating peptide or NLS; highest uptake with combination peptide	Membrane-bound compartments; likely endosomes	N.D.	N.D.	[51]
A549 (human lung carcinoma); 16HBE (human bronchial epithelium); MSCs (bone marrow	Nanorods	Length 55.6 ± 7.8nm, width 13.3 ± 1.8nm	Cetyltrimethylammonium bromide (CTAB) bilayer	0.5 , 1.5 , 3 , 6 , 12 , 24, 48, 72h	Endocytosis; mostly clathrin-dependent; AuNPs/cell after 72h incubation; A549 : 12783±1787;	A549: mitochondria 16HBE: endosomes, lysosomes, MSCs: endosomes, lysosomes	A549 and 16HBE: not eliminated after 72h; MSCs: elimination begins within 24h	For 72h incubation; A549: mitochondrial damage; 27% viability with 50 µM AuNPs; 10% with 100µM AuNPs	[47]

mesenchymal stem cells)					16HBE: 2080±345 MSCs: faster uptake at early time points; reach steady-state concentration faster			16HBE: minor toxicity MSCs: almost no toxicity	
HeLa (human cervix carcinoma)	Not specified	13, 30, 60nm	CALNN and/or CALNNR8 (R8 = 8 arginine residues)	0-24h	CALNN alone - poor internalization CALNNR8: CALNN (ratio 1:9); number of AuNPs internalized depends on their size; 13nm>30nm>60nm	CALNN + CALNNR8: Nucleus CALNNR8: ER	N.D.	95% cell death with 0.32nM AuNP for 24h (CALNNR8:CALNN ratio 1:9)	[52]
CHO (Chinese hamster ovary)	Not specified	13nm	Fluorescein isothiocyanate (FITC), cell penetrating peptides Penetratin: CRQILIWFQNRRMKWKK; TAT: CYGRKKRRQRRR, combined with lysosomal sorting peptides: L1: YQRLC, L2: CNPGY	12h	Uptake after 12h: 0.2-1μM/μg total cell protein; AuNPs conjugated with Penetratin and lysosomal sorting peptides show highest uptake	Lysosome	N.D.	Viability ≥70% for different peptide combinations tested	[53]
SKBR3 (human breast carcinoma, HER2-overexpression); MCF7 (human breast carcinoma)	Not specified	14nm	Raman reporter, mixed polymer brushes of hydrophilic PEG and hydrophobic copolymer of methyl methacrylate and 4-vinylpyridine; anti-Her2 antibody	30 – 90min	SKBR3: receptor mediated uptake ; MCF7: low level uptake	Endosome / lysosome	N.D.	Viability for SKBR3 cells reduced by pH-dependent release of doxorubicin	[54]
HeLa (human cervix carcinoma); A549 (human lung carcinoma); NIH3T3-L1 (mouse fibroblasts)	Spheres	25nm	Functionalized with one of four cell penetrating peptides Peptide RF: GLKKLA**R**-L**F**HKLLKLGC Peptide RA: GLKKLA**R**-L**A**HKLLKLGC Peptide EF: GLKKLA**E**L**F**HKLLKLGC Peptide EA : GLKKLA**E**-L**A**HKLLKLGC Peptide TAT: GRK-KRRQRRRGC; PEG-linked doxorubicin	24h	Endocytosis	Close to cell nucleus	N.D.	Cell death increased when peptide-functionalized AuNPs are further loaded with doxorubicin; cell type dependent differences	[24]
HeLa (human cervix carcinoma); MCF10A (non-malignant breast cell line); OVCAR-3 (human ovarian carcinoma)	Nanostars	25nm, (32nm hydrodynamic diameter after functionalization)	Single-stranded DNA aptamer AS1411, binds nucleolin	5, 7, 24, 72h	Uptake correlates with nucleolin presence on cell surface	7h: cytoplasm, nuclear vicinity; nucleus	N.D.	70% reduction in HeLa cell viability after light-triggered aptamer release; 25% reduction in viability without aptamer release	[55]
HSC-3 (human oral squamous cell carcinoma), overexpress alpha V beta6 integrins; HaCaT (immortalized	Not specified	30nm	PEGylated; functionalized with RGD or RGD plus SV40-NLS (KKKRK)	24h	Uptake higher for HSC-3 cells as compared to HaCaT cells	HSC-3: RGD - cytoplasm RGD + NLS - nucleus	N.D.	24h with 0.4nM AuNPs containing RGD/NLS. HSC-3: ~30% decrease in cell number HaCaT: no significant cell	[56]

human keratinocytes)						HaCaT: AuNP uptake lower than for HSC-3		loss	
LNCaP-Pro 5 (human prostate carcinoma)	Spheres	30nm	PEGylated	2, 12, 24h	AuNPs/cell 2h: 19.9 ± 0.97; 12h: 28.0 ± 0.44; 24h: 284 ± 5.5	2h: cell membrane; 12h: intracellular; 24h: close to nucleus; vesicles with AuNPs concentrate at nuclear periphery	N.D.	N.D.	[57]
HeLa (human cervix carcinoma)	Not specified	3.7 ± 0.5nm	3-mercaptopropionic acid; PEG; citrate; functionalized with-FITC	1, 3, 6, 9, 12, 24, 36, 48, 72h	Time-dependent uptake; number of PEGylated AuNPs rising during first 6h; plateau at 24h.	PEGylated AuNPs in cytoplasm, vesicles, nucleus	N.D.	Viability for 10μM PEGylated AuNPs. 24h: >85%; 36h: >80 % 72h: 70%	[58]
HeLa (human cervix carcinoma)	Not specified	5, 10, 15, 20nm	Rhodamine-labeled SV40-NLS; (rhodamine-CGGGPKKKRKVGG), conjugated to BSA; number of NLSs/AuNP varied	1-6h	AuNP uptake stimulated by NLS	At 6h, NLS increased nuclear localization of 5nm AuNPs; no NLS/AuNP: 37.5% in nucleus; 150 NLSs/AuNP: 96.3% in nucleus	N.D.	Viability at 6h dependent on number of NLSs/5nm AuNP; for 150 NLSs/5nm AuNPs 65.9% cells viable	[59]
HepG2 (human hepatocellular carcinoma)	Not specified	20nm 24.5 nm (non-functionalized AuNPs); 28 nm (AuNP + BSA); 29.5 nm (AuNP +BSA +peptide)	BSA conjugated to different peptides (i) SV40-NLS; CGGGPKKKRKVGG (ii) adenoviral NLS; CGGFSTSLRARKA (iii) adenoviral signal, promotes receptor mediated endocytosis (RME); CKKKKKKSEDEYPYVPN (iv) adenoviral fiber protein; CKKKKKKKSEDEYPYVPNFSTSLRARKA (v) combination of (ii) and (iii)	2h, 12h	Possibly receptor-mediated endocytosis for SV40-NLS	(i) Cytoplasm, trapped in the endosome (ii) No uptake (iii) Cellular entry, but trapped in the endosome (iv) Nuclear targeting (v) Enhanced nuclear targeting for combination of peptides	N.D.	Loss of cell viability <5% after 12h incubation with AuNPs modified with adenoviral NLS or adenoviral RME	[39]
HeLa (human cervix carcinoma); NIH3T3 (murine fibroblasts); HepG2(human hepatocarcinoma)	Not specified	20nm diameter Hydrodynamic diameter of AuNP only 22nm Hydrodynamic diameter of BSA-AuNP 26nm	(i) SV40-NLS; CGGGPKKKRKVGG (ii) adenovirus NLS; CGGFSTSLRARKA (iii) HIV-1 Tat-NLS; CGGRKKRRQRRRAP (iv) oligolysine plus integrin binding domain; CKKKKKKGGRGDMFG	0.5 - 6h	Uptake likely predominantly by endocytosis; cell-type and peptide dependent uptake	Cell-type and peptide dependent intracellular distribution	N.D.	adenovirus-NLS-BSA-AuNP: 20% death of HeLa cells, 5% death of NIH3T3 cells	[48]
MCF7 (human breast carcinoma)	Spherical	2, 6,10, 16nm	Tiopronin plus triplex forming oligonucleo-	24h	24h, 100nM 2nm AuNPs; up to 40% in nucleus	Nucleus: 2nm, 6nm; cytoplasm,	N.D.	Viability 70% at 1μM	[60]

			tide that can bind to c-MYC promoter P2			vesicles: 10nm, 16nm			
hTERT-BJ1 (telomerase-immortalized human fibroblasts)	Not specified	2.8nm (average)	Tiopronin or tiopronin plus TAT-peptide	1h, 24h	N.D.	Tiopronin: vacuoles, or in vicinity of mitochondria Tiopronin plus TAT-peptide: nucleus	N.D.	24h, 10μM AuNPs with tiopronin or tiopronin+TAT-peptide: viability ≥80%	[61]
hTERT-BJ1 (telomerase immortalized primary human fibroblasts)	Not specified	5, 35nm	Tiopronin and further functionalization; 5nm: -/+ TAT peptide; 30nm: PEG, -/+ TAT peptide	1h	Uptake does not require clathrin-mediated endocytosis	5nm +TAT: nucleus; 30nm + PEG: cell periphery, cytoplasm; 30nm +PEG +TAT: cytoplasm	N.D.	N.D.	[62]
CP70 (human ovarian carcinoma); A2780 (human ovarian carcinoma); BECs (human bronchial epithelium); ASM (human airway smooth muscle)	Not specified	~2nm core; hydrodynamic diameter of AuNPs: positive charge, 9.31nm; negative charge, 9.49nm; neutral, 11.43nm, zwitterionic, 11.15 nm	AuNP carrying different charges; positive, negative, neutral, zwitterionic	5, 30min; 2, 6h	In all cells uptake of positively charged AuNPs significantly higher than other AuNPs tested. CP70 cells take up only positively charged AuNPs only	Intracellular	N.D.	30min treatment with positively charged AuNPs decreased viability of BECs and ASM	[63]
1BR3G (transformed human skin fibroblasts)	Spherical	4, 9, 13nm	11-amino-1-undecanethiol (positive charge); CIPGNVG-PEG-NH_2 (positive charge); CIPGNVG-PEG-COOH (negative charge)	30min, 1, 3h	Uptake likely through endocytosis; higher for CIPGNVG-PEG-NH_3^+ than CIPGNVG-PEG-COO^-	AuNPs functionalized with CIPGNVG-PEG-NH_3^+ locate to intracellular vesicles, nucleus	N.D.	No significant toxicity of peptide-coated particles after 3 or 24h	[64]
MCF7 (human breast carcinoma); MDA-MB-468 (human breast carcinoma)	Not specified	14, 50, 74nm; hydrodynamic diameter upon BSA- coating: 14nm → 28.5 ± 2.5; 50nm→ 78 ± 3 .1; 74nm→ 95 ± 4.2	coated with BSA- Alexa-647 (fluorescent), transferrin and EGF	30min, 8h	Receptor mediated endocytosis; uptake depends on size and surface modification; highest uptake for 50nm AuNPs; highest uptake for uncoated AuNPs	Endosomes or lysosomes	N.D.	N.D.	[65]
MCF7 (human breast carcinoma); HuMEC, (human myoepithelial breast cells)	Spheres, flowers	Small spheres 15.6 ± 1.6nm; large spheres, 60 ± 2nm; flowers, 40-120nm	PEGylated	24h, overnight	N.D.	MCF7; small spheres: nucleus, cytoplasm, nanoflowers: nucleus, cytoplasm, large spheres: nuclear surface HuMEC; nanoflowers and large spheres associated with nuclei	N.D.	Small spheres more toxic than nanoflowers; large spheres not toxic	[46]
HeLa (human cervix carcinoma)	Not specified	16nm	PEGylated and further functionalized with CALNN and peptides containing the CALNN sequence; CALNN-TAT peptide: CALNN-AGRKKRRQRRR; CALNN-Pntn peptide: CALNN-GRQIKIWFQNRRM-	2h	Likely multiple uptake routes, including clathrin-independent and clathrin-dependent pathways	Endosomes (CALNN-TAT, CALNN-Pntn); Cytosol and endosome (CALNN-TAT + CALNN-Pntn); Endosomes and nucleus, but not cytosol	Most particles eliminated after 48h	N.D.	[66]

			KWKK; CALNN-NLS peptide: CALNN-GGFSTSLRARKA Combination of the peptides			(CALNN-NLS) cytosol, endosomes, nucleus (CALNN-NLS + CALNN-TAT + CALNN-Pntn)			
HSC-3 (human oral squamous cell carcinoma); HaCaT (immortalized human keratinocytes)	Nanorods	Not specified, aspect ratio 2.4	SV40-NLS	2h	N.D., possibly receptor-mediated endocytosis; NLS stimulates cellular uptake	Cytoplasm and nucleus; higher abundance of nanorods in nuclei of cancer HSC-3 cells	N.D.	N.D.	[67]
HeLa (human cervix carcinoma)	Spheres	15nm; hydrodynamic diameter citrate-capped 18.2 ± 0.1nm, with peptides 20.5 ± 0.2nm	Citrate-capped or peptide-modified; stabilizing peptide: CALNN, cellular uptake: RGD, nuclear targeting: CGGRK-KRRQRRRAP, cellular uptake + nuclear targeting: CKKKKKKGGRGDMFG, or RGD plus CGGRK-KRRQRRRAP	6, 8h	Endocytosis, higher uptake when RGD sequence present	Citrate-capped: endosomes, lysosomes; NLS-carrying AuNPs: cytoplasm and nucleus	Smaller percentage exocytosed if AuNPs capped with peptides	No toxicity short-term or in clonogenic assays	[68]
K562 (human chronic myelogenous leukemia)	Spheres	4, 12, 18nm diameter	4nm AuNPs: cysteine and citrate-capped; 12nm AuNPs: glucose-reduced; 18nm AuNPs: citrate, biotin, cetyltrimethylammonium bromide (CTAB)	15min-24h (uptake evaluation); up to 5 days for cytotoxicity	Rapid uptake of 18nm citrate-capped AuNPs; AuNP concentration in medium plateaus after 1h	Possibly endocytic vesicles	N.D.	No toxicity observed	[69]
KB (human carcinoma, overexpress folate receptors); WI-38 (human fetal lung fibroblasts)	Spherical	10nm diameter	Citrate-capped; mPEG-thioctamide or folate-PEG-thioctamide functionalized	1, 2h	KB: ~0.25-1.0 × 10^{15} folate-PEG-thioctic acid modified AuNPs/ml WI-38: sporadic uptake of folate-PEG-thioctic acid modified AuNPs	KB: lysosomes close to nucleus, endosomes	N.D.	N.D.	[70]
KB (human carcinoma)	Nanorods	Not specified	Coated with cetyltrimethylammonium bromide (CTAB, cationic), bis(p-sulfonatophenyl) phenylphosphine (BSP, anionic), mPEG-dithiocarbamate (mPEG-DTC, hydrophilic)	24h	CTAB coat promotes nonspecific uptake; nonspecific uptake reduced to 6% when CTAB replaced with mPEG-DTC	Most AuNPs internalized; shift to perinuclear region within 24h	No excretion over 5-day period; aggregate formation	No apparent toxicity	[71]
KB (human carcinoma)	Nanorods	Not specified	CTAB, folate functionalization	5h	Endocytic vesicles	CTAB: readily internalized, perinuclear, Folate: initially several hours located at cell surface; followed by endocytosis	N.D.	Photothermal damage after 30sec NIR irradiation (membrane blebbing, increased membrane permeability)	[72]
SKOV-3, OVCAR-5, OV-202, OV-167 (ovarian carci-	Spherical	5nm	Folic acid combined with different PEG backbones	5min, 1h	Endocytosis; folate receptor abundance correlates with uptake; for ovarian carcinoma cells OV-167	Late and early endosomes	N.D.	N.D.	[73]

noma); OPM-1, RPMI, U266 (multiple myeloma)					with highest, OVCAR-5 with lowest uptake				
SKOV-3 (ovarian carcinoma); CCRF-CEM (human acute lymphoblastic leukemia); CCD-18Co (human colon myofibroblasts)	Spherical, triangular, ball- or sponge-like; shape depending on peptide	Linear peptide: individual AuNPs, spherical 4-35nm; multiple AuNPs in ball-shaped structures, 900-1000nm; Circular peptide: individual AuNPs, spherical, triangular, 6-60nm; multiple AuNPs in sponge-like agglomerates, 250-450nm	Linear peptide, $l(KW)_5$; cyclic peptide, $c[KW]_5$	1h, 24-72h for toxicity; 2, 12, 24, 48h for doxorubicin release	Likely several uptake routes; not limited to clathrin-mediated endocytosis, caveolae-mediated endocytosis or macropinocytosis; higher uptake with cyclic peptide	Cytoplasm for linear peptide; mostly nuclear for cyclic peptide	N.D.	No toxicity in SKOV-3 cells for AuNPs coated with cyclic peptide; antiproliferative effect of camptothecin increased by AuNPs coated with cyclic peptide	[74]
RAW264.7 (mouse macrophage)	Spherical on average	3-8nm	Uncapped, capped with lysine or poly-L-lysine, functionalized with FITC	24, 48, 72h	Endocytosis, possibly pinocytosis	Lysosomes, located in perinuclear region	N.D.	Viability (100nM un capped AuNPs): 48h - 90%, 72h - 85%	[75]
Hep3B hepatocellular carcinoma), cultured cells and xenograft in Balb/c nude mice; 293T cells (human embryonic kidney cells containing SV40 T-antigen)	Spherical	Without dexamethasone: 87.3 ± 6.16nm, 55.3 ± 5.37nm, 40.8 ± 2.47nm; with dexamethasone: 99.2 ± 7.33nm, 56.2 ± 6.91nm, 38.2 ± 1.56nm	DNA, polyethyleneimine, without or with deaxamethasone	4h; for toxicity 24h	Endocytosis	Nucleus and cytoplasm; significant increase of nuclear targeting with dexamethasone	N.D.	Viability of cultured cells ≥ 80% for EGFP-encoding plasmid; AuNP-mediated synthesis of TRAIL inhibits tumor growth in mice	[76]
Mouse embryonic fibroblasts	Clusters	2nm	DNA; photolabile AuNPs; UV-induced release of DNA	6h	N.D.	Intracellular; DNA released by UV irradiation; DNA in nucleus	N.D.	N.D.	[77]
HOC-313 clone 8 (human head and neck squamous cell carcinoma); HSC-3 (human oral squamous cell carcinoma); HaCaT (immortalized human keratinocytes)	Not specified	35nm	Unconjugated, conjugated to anti-EGFR antibodies	48h for colloidal gold; 40min for anti-EGFR conjugated AuNPs	Endocytosis	Unconjugated AuNPs: in cytoplasm of all cells tested; anti-EGFR-AuNPs: HOC-313 and HSC-3 cells – cell surface; HaCaT – weak labeling	N.D.	N.D.	[78]
HOC-313 clone 8 (human head and neck squamous cell carcinoma); HSC-3 (human oral squamous cell carcinoma); HaCaT (immortalized human keratinocytes)	Nanorods	<5nm, aspect ratio 3.9	CTAB-capped; further modified and conjugated to anti-EGFR antibodies	30min; room temperature	Higher AuNP uptake by malignant cells, because of higher EGFR abundance in plasma membrane	N.D.	N.D.	NIR laser-induced killing more efficient for cancer cells	[79]
HeLa (human cervix carcinoma)	Nanorods	18x40nm	Original coating CTAB; further modified with	6h	Surface coat and charge determine uptake; highest uptake for	Intracellular vesicles	N.D.	CTAB: 79.2% viability in serum-	[80]

			polyelectrolytes to produce nanorods with different surface charges; Examples: positive charge - poly(diallyldimethyl ammonium chloride); negative charge - poly(4-styrene sulfonic acid)		poly(diallyldimethyl ammonium chloride); lowest uptake for poly(4-styrenesulfonic acid)			free medium; not toxic in medium with serum; poly(diallyldimethyl ammonium chloride): 88.3% viability in medium with serum	
MCF7 (human breast carcinoma); MCF10A (non-malignant breast cell line)	Not specified	10.8nm	Cysteamine-capped (AuNPs positively charged), thioglucose-capped	2h	MCF7 cells; cysteamine-capped: 1.187×10^5 AuNPs/cell; thioglucose-capped: 2.96×10^4/cell	In MCF7 cysteamine-capped AuNPS bound to cell membrane; thioglucose-capped AuNPs in cytoplasm	N.D.	No significant changes in MCF7 cell viability at 24, 48, 72h; AuNPs enhance toxicity of low-energy X-rays in MCF7 cells	[27]
COS-1 (African green monkey kidney cells)	Not specified	2.4, 5.5, 8.2, 16, 38, 89nm	PEG-functionalized dithiolane ligands that end with methoxy or carboxyl group; carboxyl group covalently attached to cell penetrating peptides	2-3h	Uptake likely by endocytosis, facilitated by cell penetrating peptides	Cell penetrating peptide-AuNPs: 2.4nm – nucleus; 5.5nm – mostly perinuclear; 8.2nm – mostly cell membrane; 16, 38, 89nm – no uptake; 16, 38nm – cell periphery; 89nm – aggregates	N.D.	Viability with cell penetrating peptide-AuNPs (200nM, 2h): 2.4nm - 97%; 8.2nm - 94%	[81]
HepG2 (human hepatocellular carcinoma; non-phagocytic); RAW264.7 (virus transformed macrophage; phagocytic)	Not specified	16-58nm	Citrate-capped; further modification produced surfaces with positive quaternary ammonium groups or negative carboxyl groups	12, 24h	Cell type, particle size and surface charge determine uptake; Cell type: higher uptake of AuNPs with positive charges in HepG2 cells; similar uptake of AuNPs with positive or negative charges by RAW264.7 cells; Size: positive charge, highest uptake for 58nm; negative charge, highest uptake for 40nm	40nm AuNPs with negative or positive charges; HepG2: secondary lysosomes RAW264.7: AuNP aggregates in phagosomes, myelin whorls	N.D.	Based on MTT assay; HepG2: positive surface charges more cytotoxic than negative RAW 264.7: negative surface charges more cytotoxic than positive	[82]
SKBR3 (human breast carcinoma, HER2-overexpression)	Spheres	17.7 ± 1.6nm	Citrate (negative charges); poly(vinyl alcohol) (PVA, neutral); poly(allyamine hydrochloride) (PAA, positive charges)	0-24h	Higher uptake with positive charges	Internalized, location not specified	N.D.	Viability >90% (24h, 0.027 nM AuNPs)	[45]
Balb/3T3 (mouse fibroblasts)	Not specified	5, 15nm	Citrate stabilized	2, 24, 72h	At each time point more 5nm AuNPs internalized than 15nm particles	Intracellular vesicles, endosomes/lysosomes	N.D.	72h, ≥50μM; 5nm, but not 15nm, AuNPs cause significant loss of colony formation. Both AuNPs - no cytotoxicity in Trypan blue assays	[83]
HeLa (human cervix carcinoma); SK-Mel-28 (human melanoma); L929 (mouse fibroblasts); J774A1 (mouse monocyte/macrophage)	Not specified	0.8-15nm	Triphenylphosphine monosulfonate, tris-sulfonated triphenylphosphine	up to 48h	N.D.	1.4nm cluster binds major groove of B-DNA; 20-25% AuNPs associated with DNA-containing fractions of the nucleus	N.D.	AuNPs of 1-2nm particularly toxic; highest toxicity for 1.4nm cluster; death by apoptosis and/or necrosis; toxicity during logarithmic growth higher than in stationary phase	[84]

MCF7 (human breast carcinoma) monolayer, MCF7 spheroids, xenograft mouse model (MCF7-S cells)	Spherical	2, 6, 15nm	Tiopronin	3, 24h	Size-dependent uptake; (i) Monolayer, AuNPs/cell, 2nm >> 6nm ≈ 15nm (ii) AuNPs/ spheroid 2nm >6nm > 15nm (iii) Mouse model; Tumor: 2nm>6nm>15nm	Monolayer; 2, 6nm: nucleus, cytoplasm; 15nm: cytoplasm Spheroids; 2, 6nm: inner and outer cell layers; nucleus, cytoplasm; 15nm: mostly on spheroid surface; cytoplasm; Tumor; 2, 6nm: nucleus, cytoplasm; 15nm: cytoplasm	All AuNPs eliminated from blood; fastest elimination for 15nm AuNPs	Not toxic for MCF7 monolayers during 24h incubation	[85]
HeLa (human cervix carcinoma)	N.D.	Non- functionalized 13.4nm; with pro-apoptotic peptide 14.6nm	Without and with pro-apoptotic peptide AD-DA-ADDA-GG-$_D$(KLAKLAK)$_2$	4, 12, 24, 48, 72h;	Endocytosis	Endosomal vesicles	N.D.	72h, AuNPs with pro-apoptotic peptide: 59% apoptotic or necrotic cells; mitochondrial damage	[33]
Adult male Sprague-Dawley rat hearts; ventricular myocytes, permeabilized cells or isolated mitochondria	Not specified	3, 6nm	Polyvinylpyrrolidone	10, 20min	N.D.	Permeabilized myocytes: 3nm: accumulated in mitochondria; 6nm: predominantly in cytoplasm, no entry into mitochondria Isolated cardiac mitochondria: 3nm: mitochondrial intermembrane space 6nm: no entry into mitochondria; located close to outer mitochondrial membrane	N.D.	N.D.	[86]
HeLa (human cervix carcinoma)	Not specified	8-12nm	Not specified; embedded in high density octa-arginine –modified liposomes	1h	Macropinocytosis (clathrin-independent uptake)	Entry into mitochondria	N.D.	N.D.	[87]
A549 (human lung carcinoma)	Nanorods	aspect ratio 4.2; length 55.6±7.8nm; width 13.3±1.8nm	CTAB (positive surface charge); CTAB+ poly (diallyldimethyl ammonium chloride), (PDDAC, positive surface charge); CTAB + polystyrene sulfonate (PSS, negative surface charge), PEGylated (PEG, negative surface charge)	12, 24h	N.D.	CTAB: cell membrane PDDAC, PSS: endosomes, lysosomes PEG: very few internalized	N.D.	Highest toxicity for CTAB–AuNPs in serum-free medium; 50μM CTAB-AuNPs, 12h - 60% viability; 24h - 40% viability; CTAB-AuNPs with altered mitochondrial morphology and function	[88]
HeLa (human cervix carcinoma);	Nanoclusters	8.07±1.77 nm	Chitosan-coated; chitosan-coated plus cova-	0.5, 1, 2, 4, 24h	N.D.	Mitochondria	N.D	24h, 60μg/ml chitosan-TPP modified nanoclusters: sig-	[89]

HepG2 (human hepato-cellular carcinoma)			lently attached triphenylphosphonium (TPP) cations					nificant toxicity	
1.4E7 cells (hybrid cell line, fusion of human pancreatic islets cells with human pancreatic cancer cells, PANC-1); HeB5 non-cancerous mouse liver epithelial cell line	Not specified	Not specified	Near infrared (NIR) laser activation of AuNPs	1, 5, 30min, 1, 5, 24h	N.D.	Mitochondria	N.D.	NIR activation increased apoptosis of 1.4E7 cells	[90]
PC3 (human prostate carcinoma); DU145 (human prostate carcinoma); MCF7 (human breast carcinoma); RAW264.7 (mouse mac-rophage); human mesenchymal stem cells; Sprague Dawley rats	Spheres	Targeting AuNPs : T-AuNP, 3.1 ± 0.8nm; T-3-BP- AuNP, 4.3 ± 0.7nm Non-targeting AuNPs: NT-AuNP, 2.9 ± 1.2nm; NT-3-BP- AuNP, 3.1 ± 0.9nm	PEGylated, tri-phenylphosphonium (TPP), 3-bromopyruvate (3-BP)	4, 6, 12h; 72h for toxicity tests	N.D.	T-AuNP: mitochon-dria>> cytoplasm T-3-BP- AuNP : mito-chondria>>> cyto-plasm NT-AuNPs : mitochondria> cyto-plasm	$t_{1/2}$ for plasma clearance: T-AuNPs 4.3 ± 0.3h NT-AuNPs 8.8 ± 0.2h	Increased damage when 3-bromopyruvate coupled to AuNPs; T-AuNPs more toxic than NT-AuNPs; laser irradiation further reduces viability of AuNP-treated PC3 cells; T-AuNPs or NT-AuNPs do not trigger pro-inflammatory cytokine synthesis in macrophages	[91]