Supplementary Information
for
The accumulation and tissue distribution of gold nanoparticles exposure in pregnant rats

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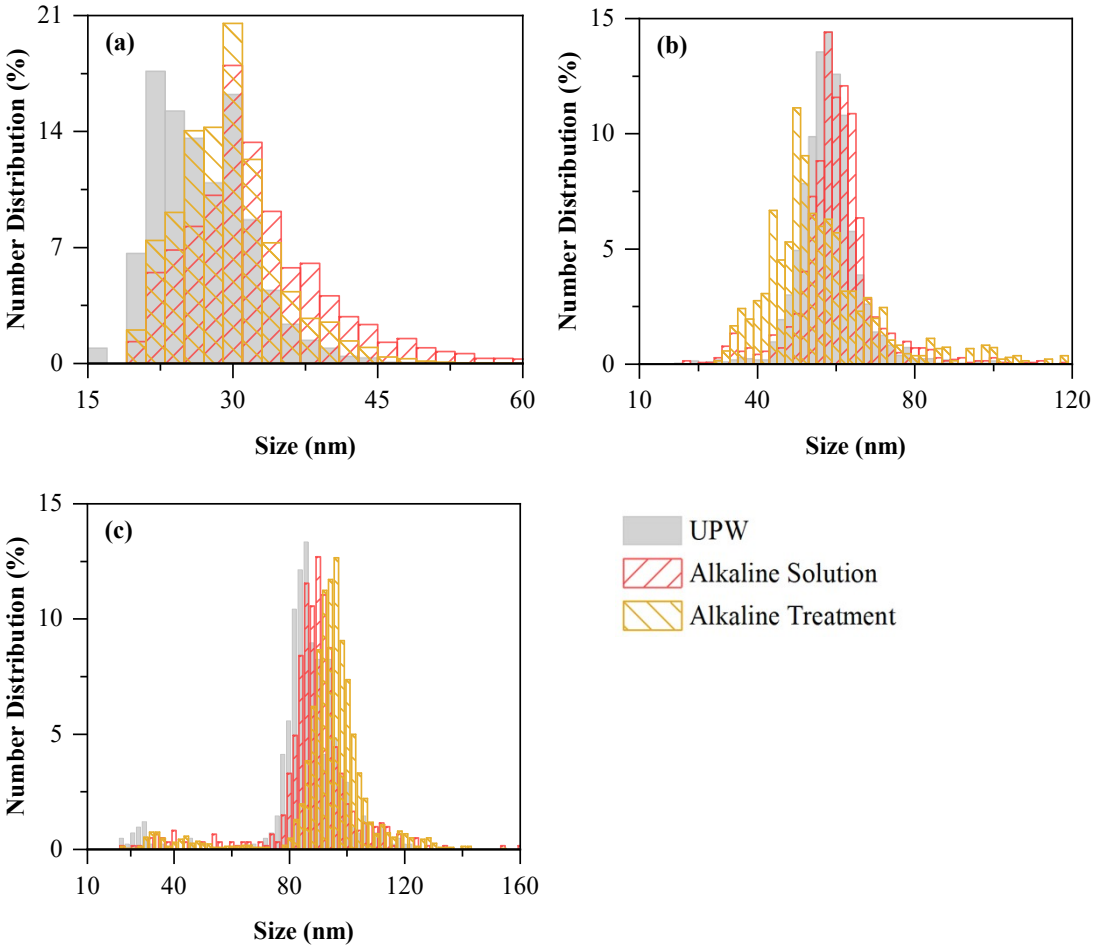


Figure S1. Method validation by spike recovery experiments in tissues of rat. Particle size distribution (bin size 2 nm) obtained by spICP-MS for (a) 20 nm; (b) 50 nm; and (c) 80 nm Au NPs suspended in ultrapure water (UPW), spiked to 1% w/w TMAH solution (alkaline solution), and extracted from tissues of rat after alkaline treatment (alkaline treatment). Tissue concentrations were 1 µg/g ww for Au NPs.

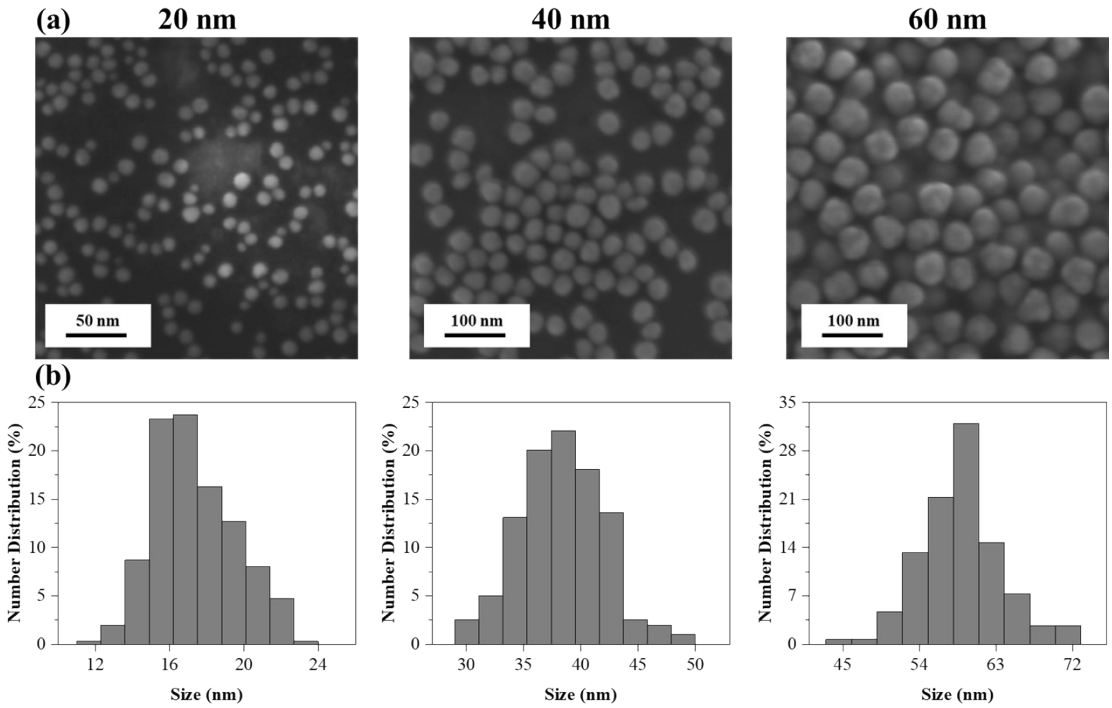


Figure S2. Characterization of gold nanoparticles (Au NPs): (a) SEM images of the colloidal Au NPs of different sizes and (b) size distributions of Au NPs.

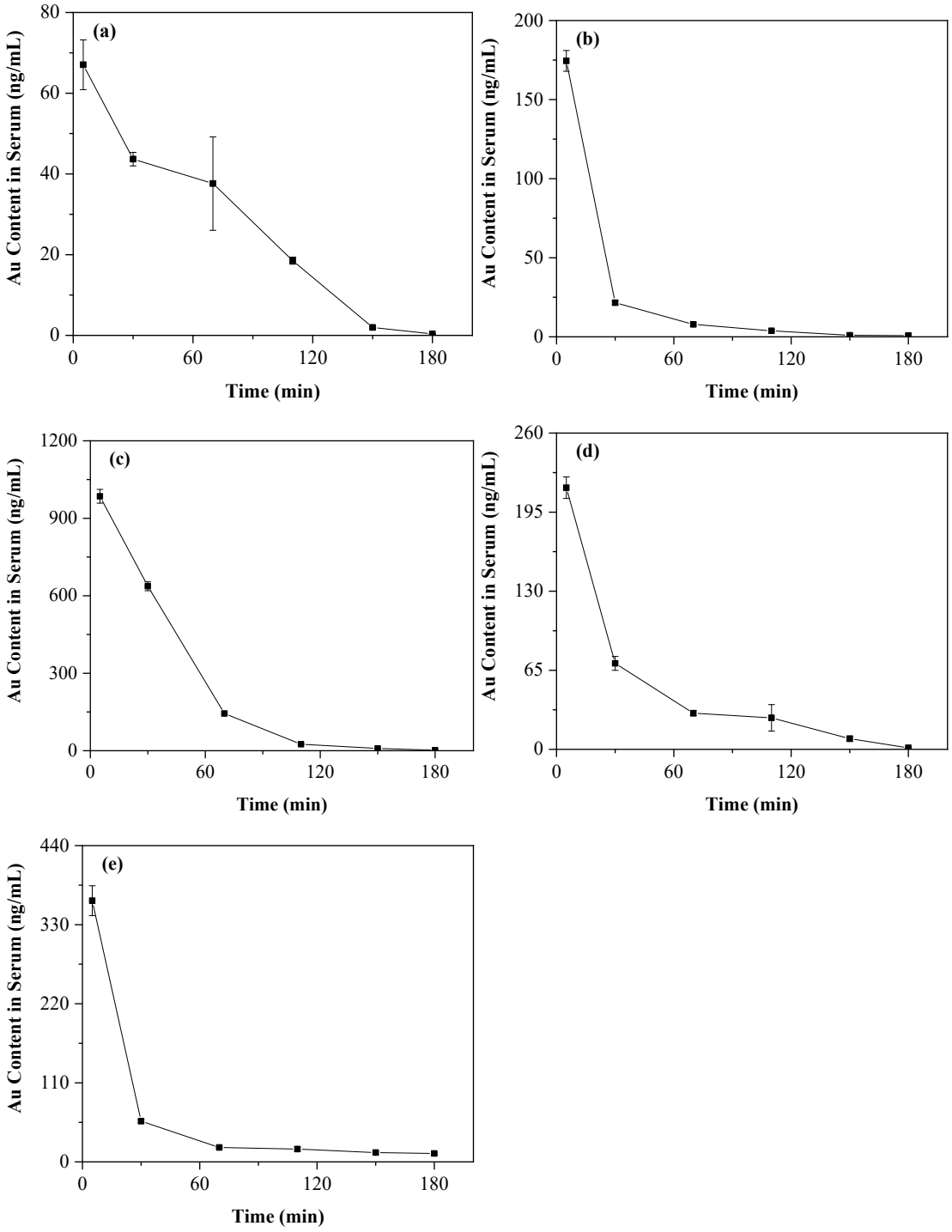


Figure S3. The total Au content in serum of different exposure groups at 5, 30, 70, 110, 150, and 180 minutes after tail vein injection: (a) 20 nm 0.25 μg/g bw; (b) 20 nm 1 μg/g bw; (c) 20 nm 5 μg/g bw; (d) 40 nm 1 μg/g bw; and (e) 60 nm 1 μg/g bw. The data presented represents the mean values ± standard error.

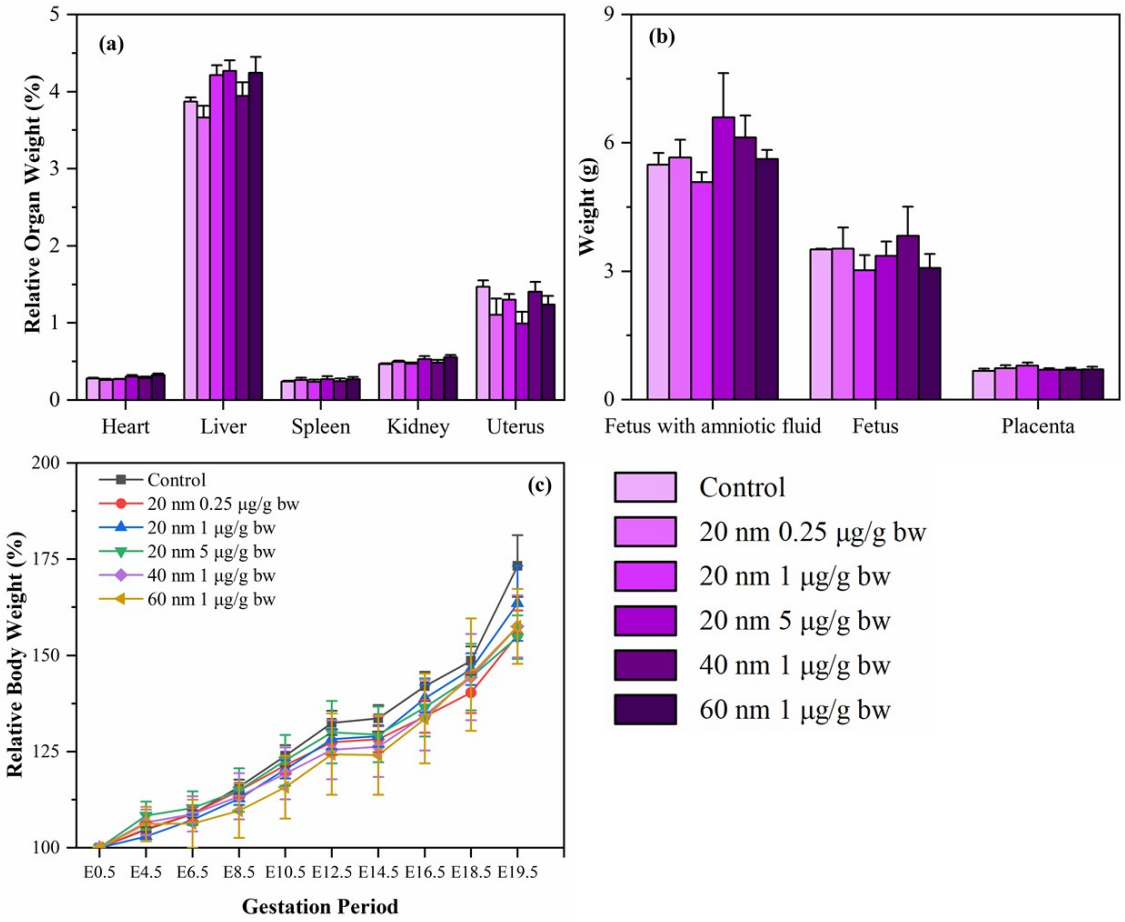


Figure S4. (a) The relative organ weight on E19.5; (b) weight of fetus with amniotic fluid, fetus, and placenta on E19.5; and (c) relative body weight during pregnancy. The data presented represents the mean values ± standard error.

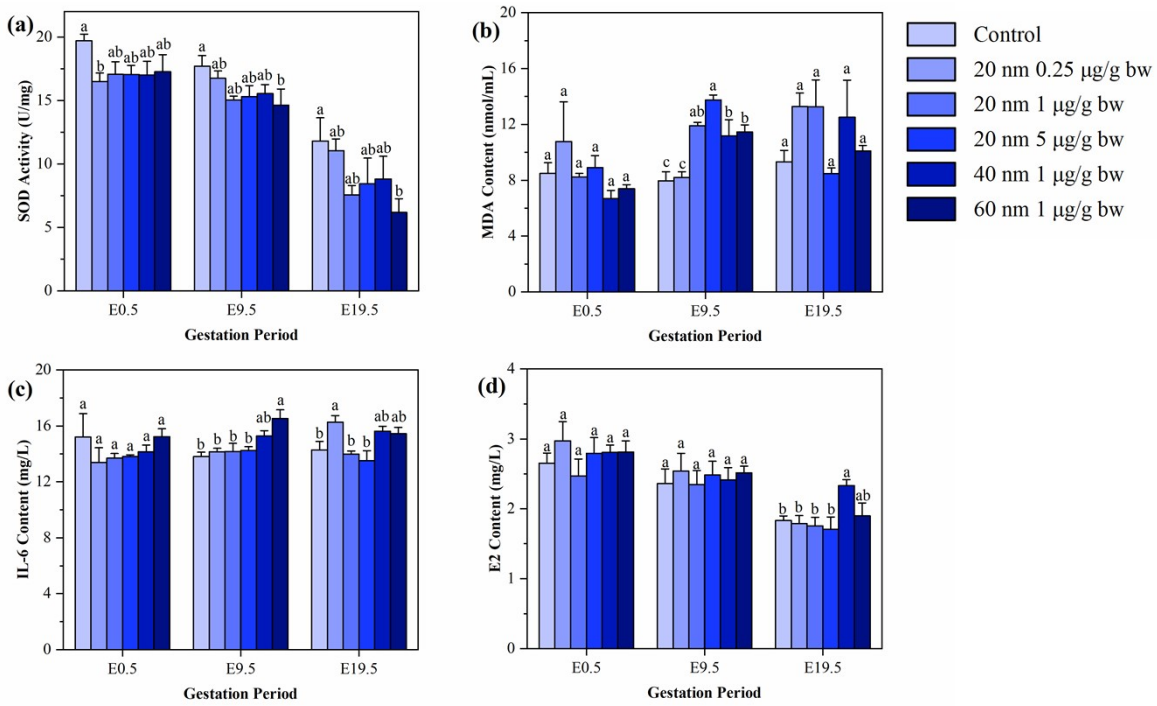
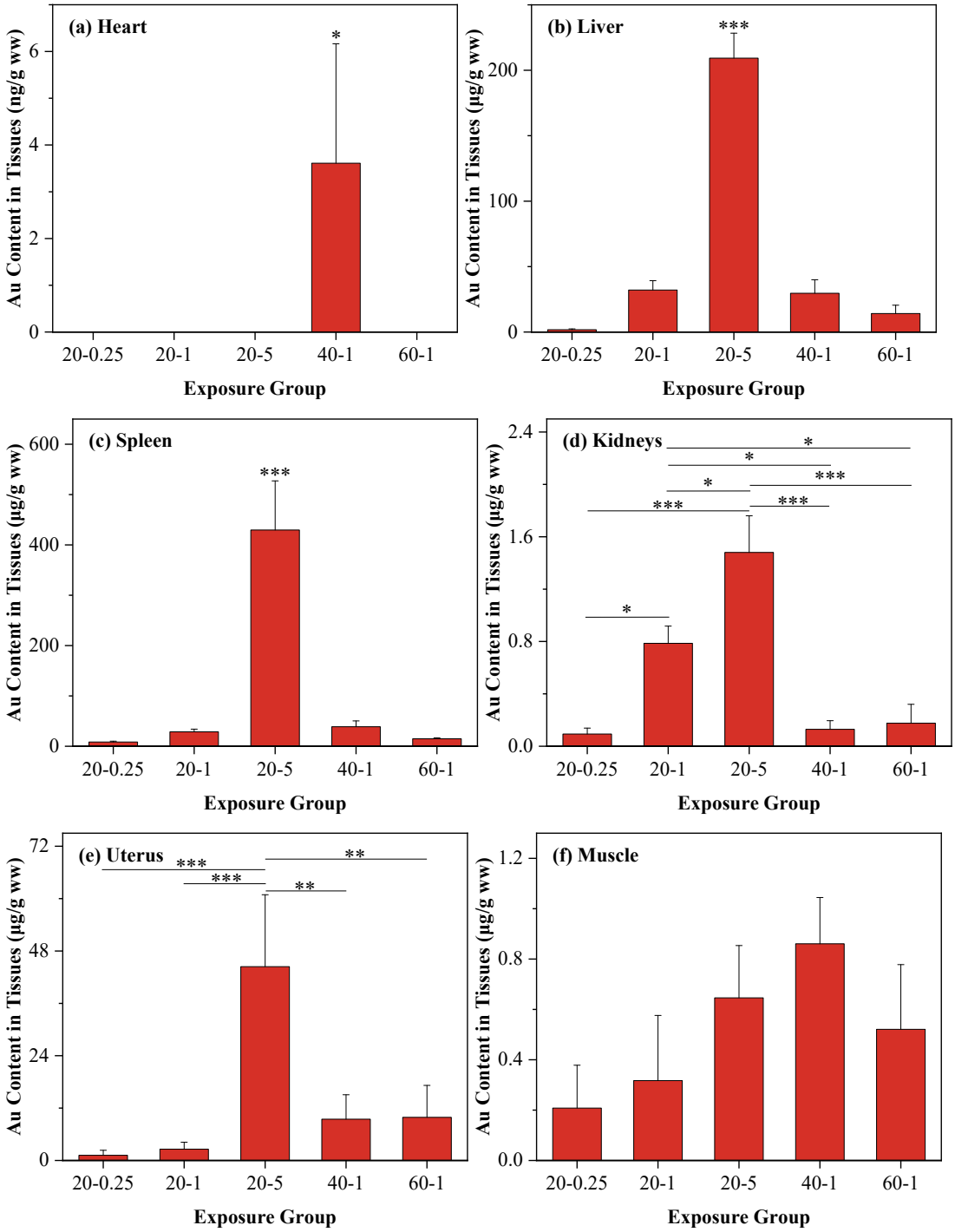


Figure S5. The biochemical indicators in maternal serum during different gestation periods: (a) the superoxide dismutase (SOD) activity; (b) malondialdehyde (MDA) content; (c) interleukin-6 (IL-6) content; and (d) estradiol (E2) content. The data presented represents the mean values ± standard error. Different letters indicate statistically significant differences ($p < 0.05$).


(a) Heart
Au Content in Tissues (ng/g ww)
0
2
4
6
*
20-0.25
20-1
20-5
40-1
60-1
Exposure Group
(b) Liver
Au Content in Tissues (μg/g ww)
0
100
200
***
20-0.25
20-1
20-5
40-1
60-1
Exposure Group
(c) Spleen
Au Content in Tissues (μg/g ww)
0
200
400
600
***
20-0.25
20-1
20-5
40-1
60-1
Exposure Group
(d) Kidneys
Au Content in Tissues (μg/g ww)
0.0
0.8
1.6
2.4
*
*
*
***
***
***
*
20-0.25
20-1
20-5
40-1
60-1
Exposure Group
(e) Uterus
Au Content in Tissues (μg/g ww)
0
24
48
72
***
***
**
**
20-0.25
20-1
20-5
40-1
60-1
Exposure Group
(f) Muscle
Au Content in Tissues (μg/g ww)
0.0
0.4
0.8
1.2
20-0.25
20-1
20-5
40-1
60-1
Exposure Group

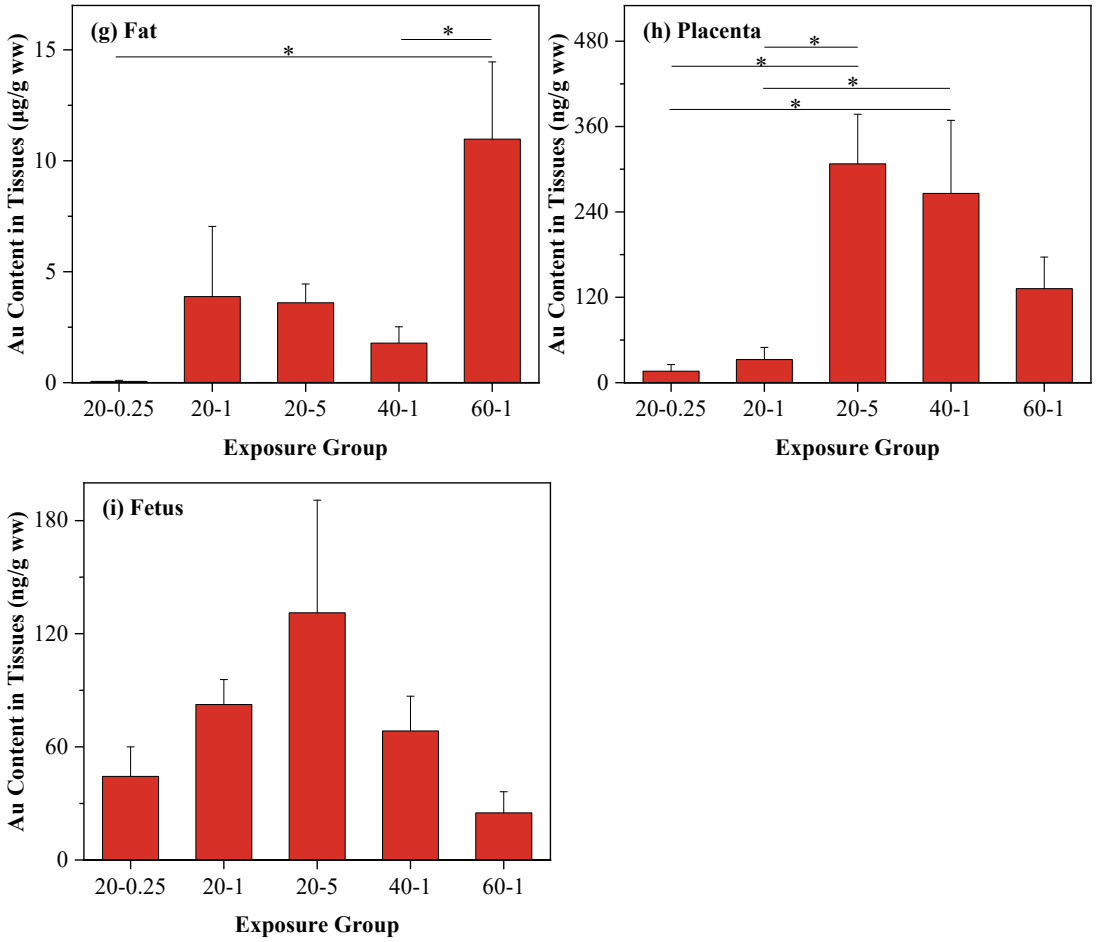
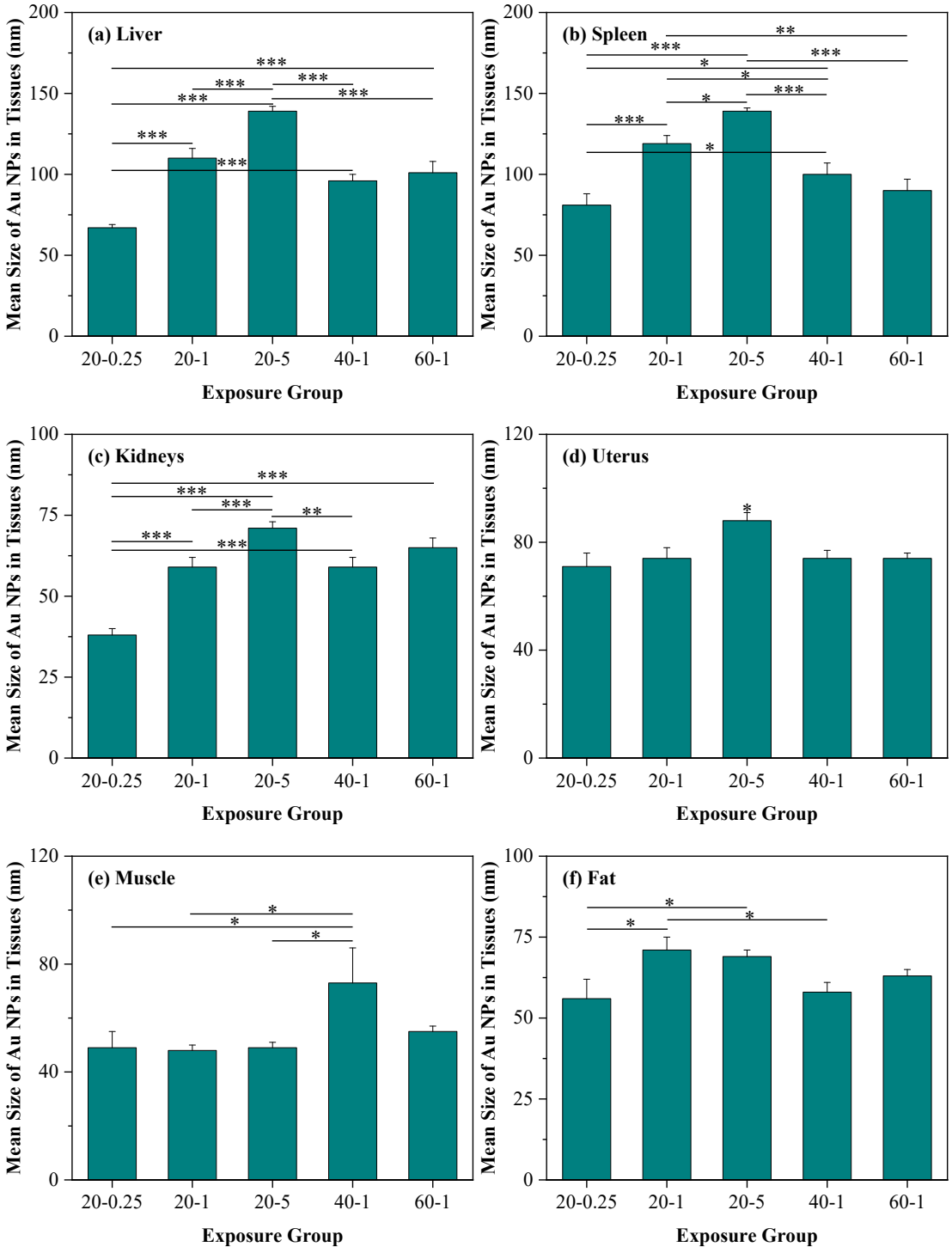


Figure S6. The bioaccumulation of Au in different exposure groups: (a) heart; (b) liver; (c) spleen; (d) kidneys; (e) uterus; (f) muscle; (g) fat; (h) placenta; and (i) fetus. The exposure groups are 20 nm 0.25 μg/g bw, 20 nm 1 μg/g bw, 20 nm 5 μg/g bw, 40 nm 1 μg/g bw, and 60 nm 1 μg/g bw, respectively. The data presented represents the mean values ± standard error. Significant codes: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.


(a) Liver
(b) Spleen
(c) Kidneys
(d) Uterus
(e) Muscle
(f) Fat
Mean Size of Au NPs in Tissues (nm)
Exposure Group
20-0.25
20-1
20-5
40-1
60-1

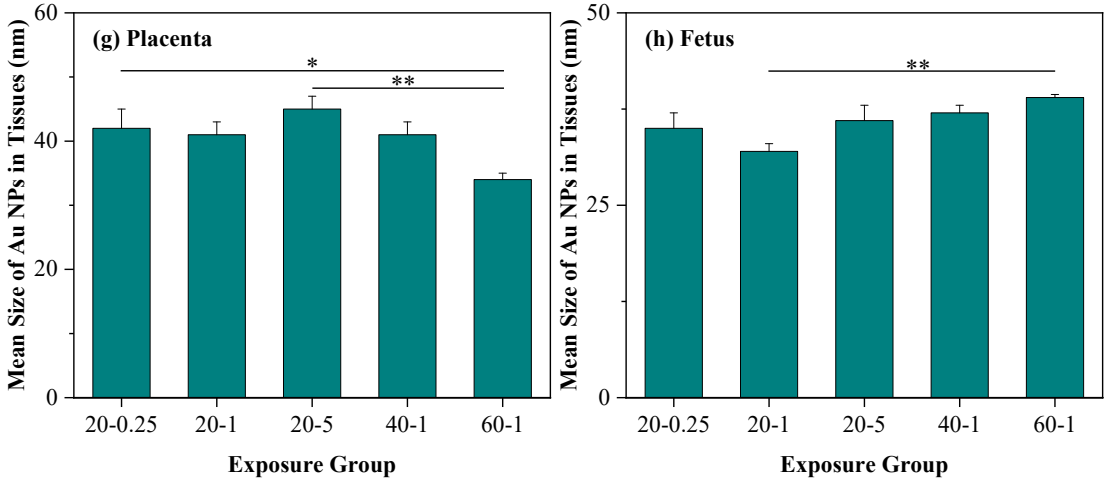


Figure S7. The mean size of Au NPs *in vivo* of different exposure groups: (a) liver; (b) spleen; (c) kidneys; (d) uterus; (e) muscle; (f) fat; (g) placenta; and (h) fetus. The exposure groups are 20 nm 0.25 μg/g bw, 20 nm 1 μg/g bw, 20 nm 5 μg/g bw, 40 nm 1 μg/g bw, and 60 nm 1 μg/g bw, respectively. The data presented represents the mean values ± standard error. Significant codes: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table S1. The mean size and particle concentration of Au NPs (mean ± standard error) in serum of rat during 180 minutes after tail vein injection.

Group	20 nm 0.25 μg/g bw		20 nm 1 μg/g bw		20 nm 5 μg/g bw		40 nm 1 μg/g bw		60 nm 1 μg/g bw	
Time (min)	Mean Size (nm)	Particle Concentration ($\times 10^6$ particles/mL)	Mean Size (nm)	Particle Concentration ($\times 10^6$ particles/mL)	Mean Size (nm)	Particle Concentration ($\times 10^6$ particles/mL)	Mean Size (nm)	Particle Concentration ($\times 10^6$ particles/mL)	Mean Size (nm)	Particle Concentration ($\times 10^6$ particles/mL)
5	26 ± 2	92 ± 0.5	34 ± 2	113 ± 16	77 ± 0.1	2.2 ± 0.5	32 ± 1	213 ± 40	36 ± 1	4.1 ± 0.3
30	21 ± 3	23 ± 4.7	24 ± 0.9	26 ± 3.5	76 ± 1	0.83 ± 0.06	21 ± 2	18 ± 0.9	22 ± 2	2.1 ± 0.3
70	16 ± 1	25 ± 4.5	19 ± 0.2	42 ± 1.5	67 ± 2	0.67 ± 0.02	19 ± 1	11 ± 0.6	31 ± 10	2.5 ± 0.6
110	26 ± 9	38 ± 4.3	19 ± 0.1	36 ± 8	47 ± 2	1.1 ± 0.1	15 ± 0.03	20 ± 1.1	19 ± 2	7.9 ± 2.6
150	15 ± 0	28 ± 0.1	23 ± 3	12 ± 4.4	32 ± 2	3.9 ± 1.4	15 ± 0.02	18 ± 0.5	24 ± 6	3.9 ± 1.1
180	16 ± 0.01	20 ± 5.3	15 ± 0.01	37 ± 2.5	30 ± 1	5.6 ± 0.9	15 ± 0.02	19 ± 0.9	21 ± 3	2.5 ± 0.7

Table S2. The number of embryo implantation and living fetuses in pregnant rats.

Exposure group	Embryo implantation	Living fetuses	Dead fetuses	Resorbed fetuses
Control	78	76 (97.4%)	2 (2.6%)	0 (0%)
20 nm 0.25 μg/g bw	68	62 (91.2%)	3 (4.4%)	3 (4.4%)
20 nm 1 μg/g bw	94	80 (85.1%)	2 (2.1%)	12 (12.8%)
20 nm 5 μg/g bw	64	59 (92.2%)	4 (6.2%)	1 (1.6%)
40 nm 1 μg/g bw	82	79 (96.3%)	2 (2.4%)	1 (1.3%)
60 nm 1 μg/g bw	58	56 (96.6%)	0 (0%)	2 (3.4%)

Table S3. The mean size and particle concentration of Au NPs (mean ± standard error) in organs and tissues of rat on E19.5.

Organ/Tissue		Liver	Spleen	Kidneys	Uterus	Placenta	Fetus	Heart	Muscle	Fat
20 nm 0.25 μg/g bw	Mean size (nm)	67 ± 2	81 ± 7	38 ± 2	71 ± 5	42 ± 3	35 ± 2	n.d.	49 ± 6	56 ± 6
	Particle concentration (× 10^6 particles/g ww)	54 ± 9	1.4 ± 0.3	4.6 ± 1.2	15 ± 1.2	0.7 ± 0.1	2.8 ± 0.6	n.d.	3.1 ± 0.5	12 ± 1.3
20 nm 1 μg/g bw	Mean size (nm)	110 ± 6	119 ± 5	59 ± 3	74 ± 4	41 ± 2	32 ± 1	n.d.	48 ± 2	71 ± 4
	Particle concentration (× 10^6 particles/g ww)	205 ± 23	1.6 ± 0.1	4.6 ± 0.5	18 ± 4	1.0 ± 0.2	2.1 ± 0.3	n.d.	7.2 ± 2.1	23 ± 8
20 nm 5 μg/g bw	Mean size (nm)	139 ± 3	139 ± 2	71 ± 2	88 ± 3	45 ± 2	36 ± 2	n.d.	49 ± 2	69 ± 2
	Particle concentration (× 10^6 particles/g ww)	113 ± 20	2.6 ± 0.3	15.4 ± 2.5	78 ± 11	4.2 ± 0.6	1.8 ± 0.5	n.d.	21 ± 3.7	54 ± 7
40 nm 1 μg/g bw	Mean size (nm)	96 ± 4	100 ± 7	59 ± 3	74 ± 3	41 ± 2	37 ± 1	n.d.	73 ± 13	58 ± 3
	Particle concentration (× 10^6 particles/g ww)	209 ± 19	3.1 ± 0.4	17.8 ± 2.3	66 ± 14	1.1 ± 0.4	1.2 ± 0.3	n.d.	47 ± 7	49 ± 9
60 nm 1 μg/g bw	Mean size (nm)	101 ± 7	90 ± 7	65 ± 3	74 ± 2	34 ± 1	39 ± 0.4	n.d.	55 ± 2	63 ± 2
	Particle concentration (× 10^6 particles/g ww)	250 ± 37	1.1 ± 0.4	19 ± 1.9	127 ± 17	4.6 ± 0.5	1.2 ± 0.1	n.d.	39 ± 6	58 ± 12

Note: n.d. means not detected.