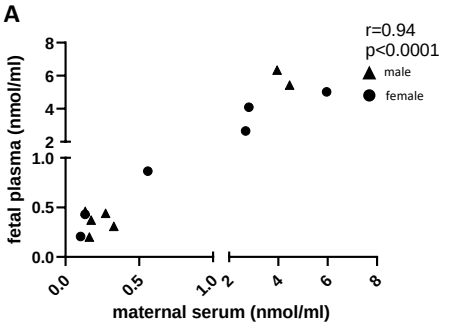
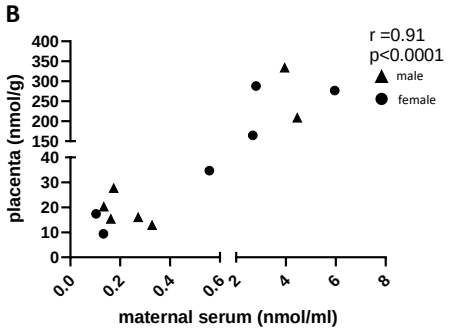
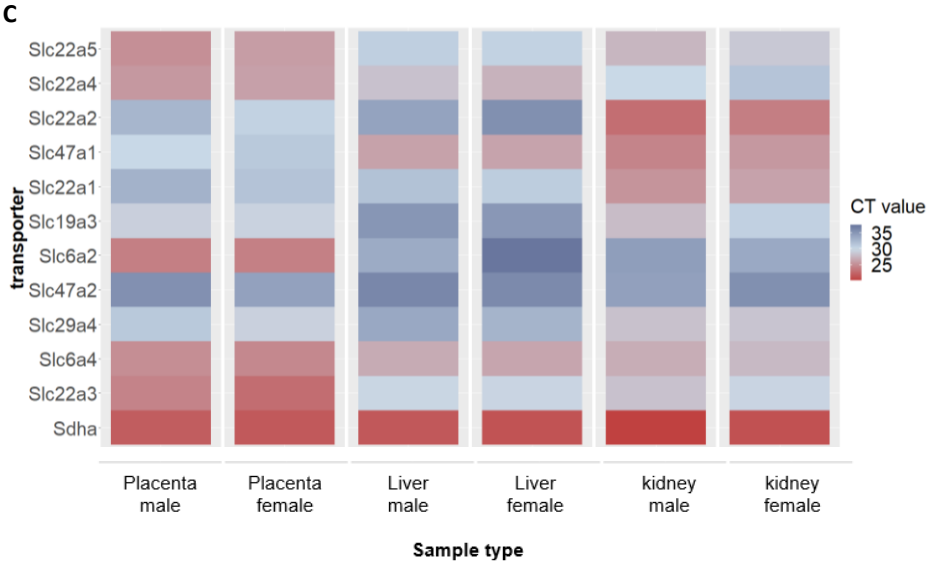
A



B



C



D

Sample type (E18.5)	metformin (mean ± SD)
fetal kidney	189.3 ± 207.7 nmol/g
fetal liver	17.9 ± 21.57 nmol/g
placenta	109.7 ± 125.4 nmol/g
amniotic fluid	21.89 ± 28.22 nmol/ml
Maternal serum	1.67 ± 2.05 nmol/ml
Fetal plasma	2.06 ± 2.33 nmol/ml

Figure 1

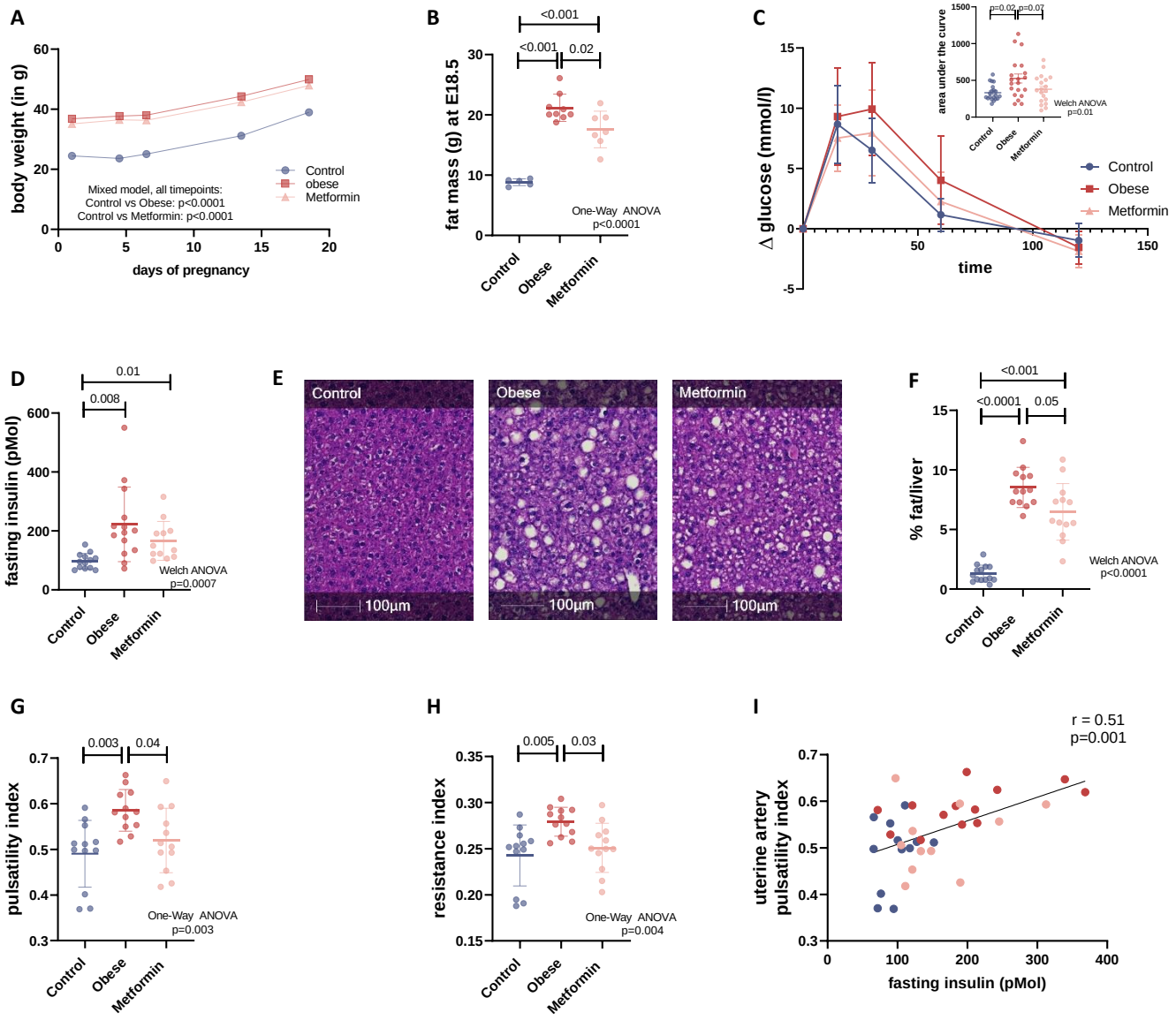

A
body weight (in g)
days of pregnancy
Control
obese
Metformin
Mixed model, all timepoints:
Control vs Obese: p<0.0001
Control vs Metformin: p<0.0001
B
fat mass (g) at E18.5
<0.001
<0.001
0.02
One-Way ANOVA
p<0.0001
Control
Obese
Metformin
C
Δ glucose (mmol/l)
time
area under the curve
p=0.02
p=0.07
Welch ANOVA
p=0.01
Control
Obese
Metformin
D
fasting insulin (pMol)
0.01
0.008
Welch ANOVA
p=0.0007
Control
Obese
Metformin
E
Control
Obese
Metformin
100µm
100µm
100µm
F
% fat/liver
<0.001
<0.0001
0.05
Welch ANOVA
p<0.0001
Control
Obese
Metformin
G
pulsatility index
0.003
0.04
One-Way ANOVA
p=0.003
Control
Obese
Metformin
H
resistance index
0.005
0.03
One-Way ANOVA
p=0.004
Control
Obese
Metformin
I
uterine artery
pulsatility index
fasting insulin (pMol)
r = 0.51
p=0.001

Figure 2

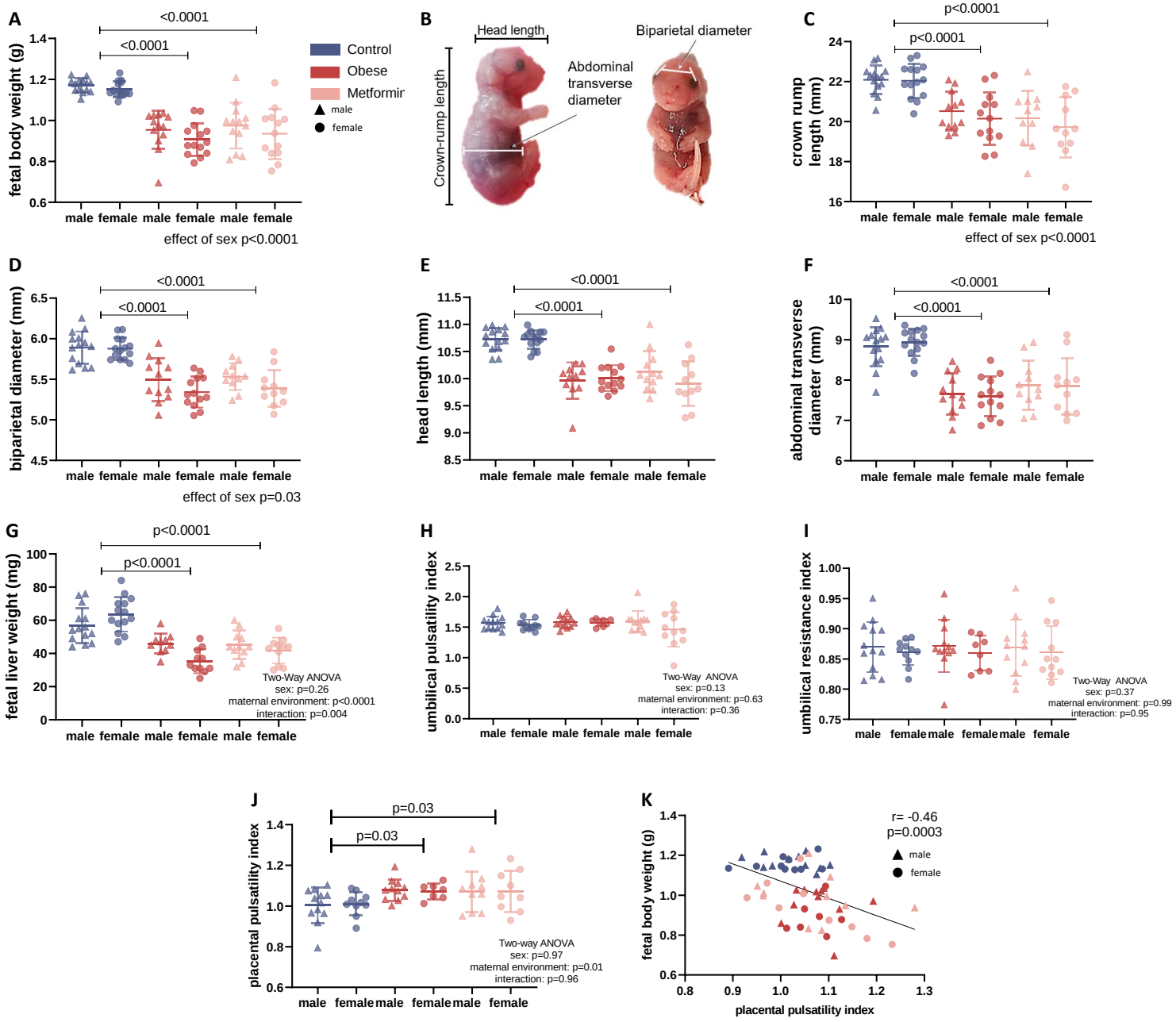

A
fetal body weight (g)
<0.0001
<0.0001
Control
Obese
Metformir
male
female
male female male female male female
effect of sex p<0.0001
B
Head length
Biparietal diameter
Abdominal transverse diameter
Crown-rump length
C
crown rump length (mm)
p<0.0001
p<0.0001
male female male female male female
effect of sex p<0.0001
D
biparietal diameter (mm)
<0.0001
<0.0001
male female male female male female
effect of sex p=0.03
E
head length (mm)
<0.0001
<0.0001
male female male female male female
F
abdominal transverse diameter (mm)
<0.0001
<0.0001
male female male female male female
G
fetal liver weight (mg)
p<0.0001
p<0.0001
Two-Way ANOVA
sex: p=0.26
maternal environment: p<0.0001
interaction: p=0.004
male female male female male female
H
umbilical pulsatility index
Two-Way ANOVA
sex: p=0.13
maternal environment: p=0.63
interaction: p=0.36
male female male female male female
I
umbilical resistance index
Two-Way ANOVA
sex: p=0.37
maternal environment: p=0.99
interaction: p=0.95
male female male female male female
J
placental pulsatility index
p=0.03
p=0.03
Two-way ANOVA
sex: p=0.97
maternal environment: p=0.01
interaction: p=0.96
male female male female male female
K
fetal body weight (g)
placental pulsatility index
r= -0.46
p=0.0003
male
female

Figure 3

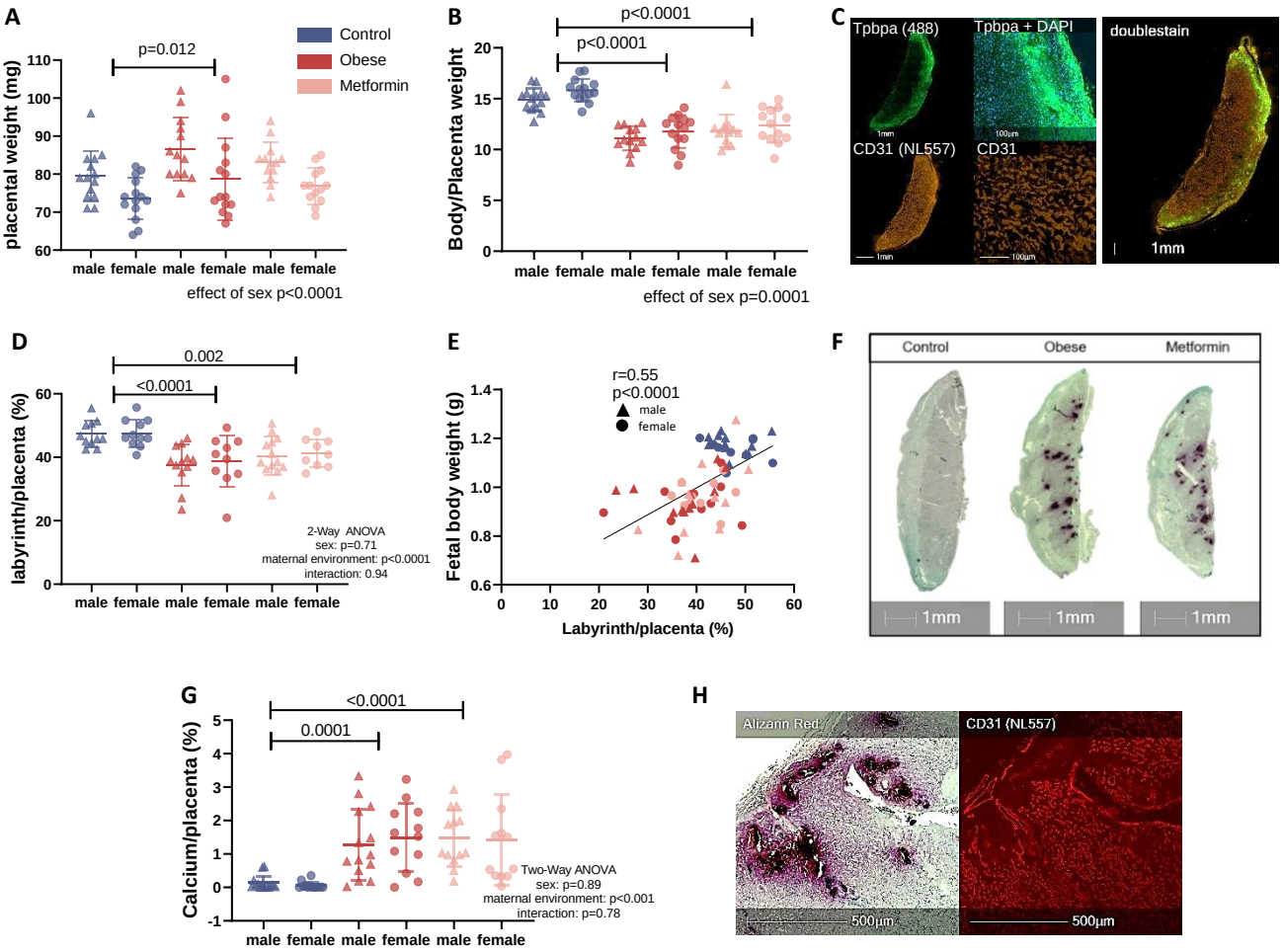

A
placental weight (mg)
p=0.012
Control
Obese
Metformin
male female male female male female
effect of sex p<0.0001
B
Body/Placenta weight
p<0.0001
p<0.0001
male female male female male female
effect of sex p=0.0001
C
Tpbpa (488)
Tpbpa + DAPI
doublestain
CD31 (NL557)
CD31
1mm
D
labyrinth/placenta (%)
0.002
<0.0001
2-Way ANOVA
sex: p=0.71
maternal environment: p<0.0001
interaction: 0.94
male female male female male female
E
Fetal body weight (g)
r=0.55
p<0.0001
male
female
Labyrinth/placenta (%)
F
Control
Obese
Metformin
1mm
1mm
1mm
G
Calcium/placenta (%)
<0.0001
0.0001
Two-Way ANOVA
sex: p=0.89
maternal environment: p<0.001
interaction: p=0.78
male female male female male female
H
Alizarin Red
CD31 (NL557)
500µm
500µm

Figure 4