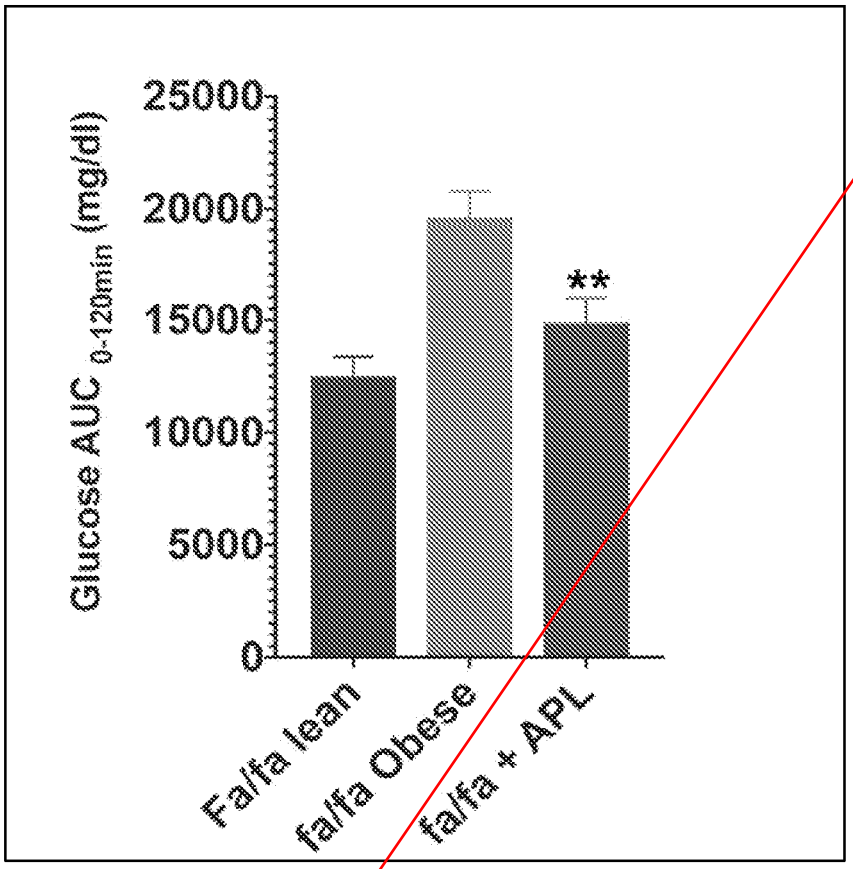
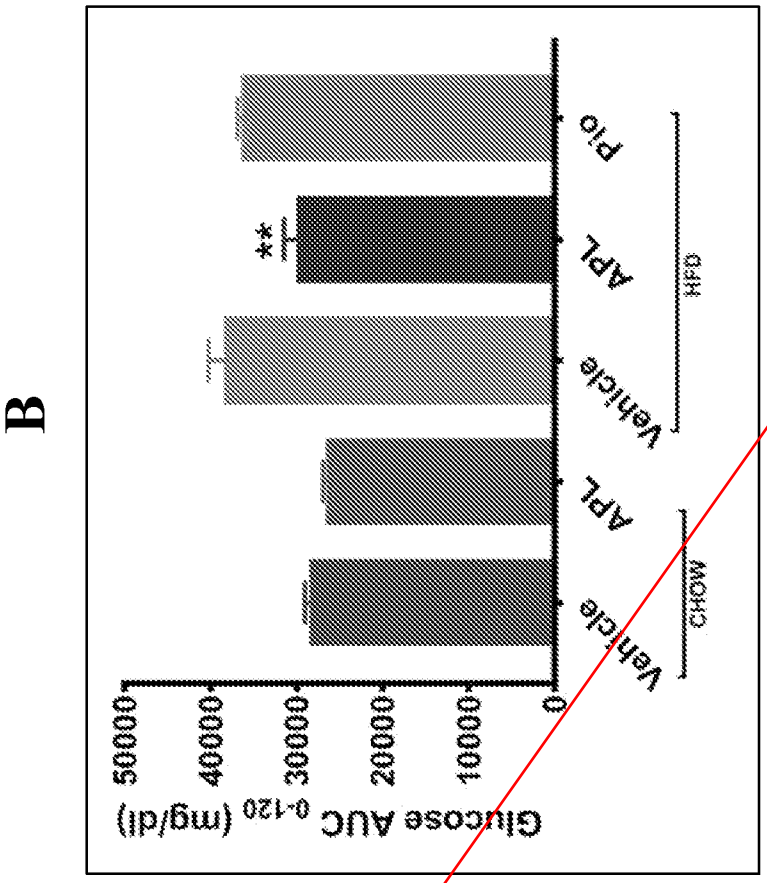
FIGURE 1


Glucose AUC 0-120min (mg/dl)
25000
20000
15000
10000
5000
0
**
Fa/fa lean
fa/fa Obese
fa/fa + APL


B
Glucose AUC 0-120 (mg/dl)
50000
40000
30000
20000
10000
0
Vehicle
APL
Vehicle
APL
Pio
CHOW
HFD
**

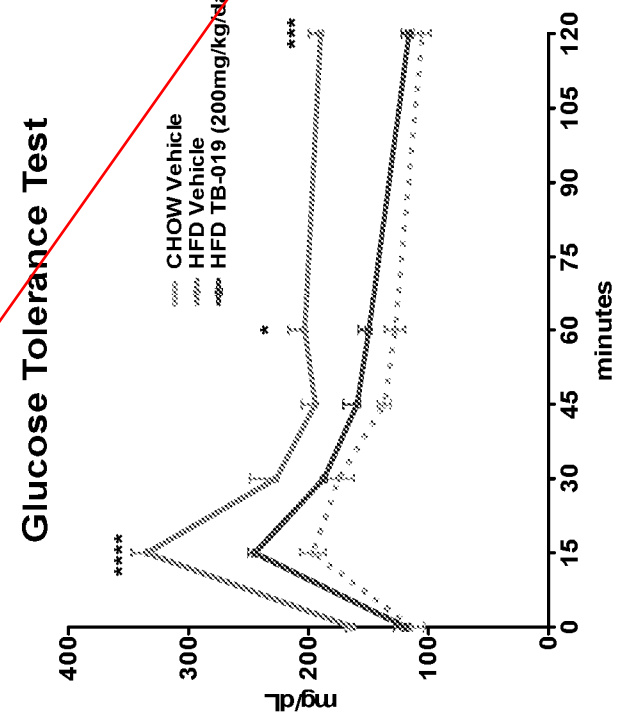

A
Glucose Tolerance Test
CHOW Vehicle
HFD Vehicle
HFD TB-019 (200mg/kg/day)
mg/dL
400
300
200
100
0
0
15
30
45
60
75
90
105
120
minutes
****
*
***

Figure 2

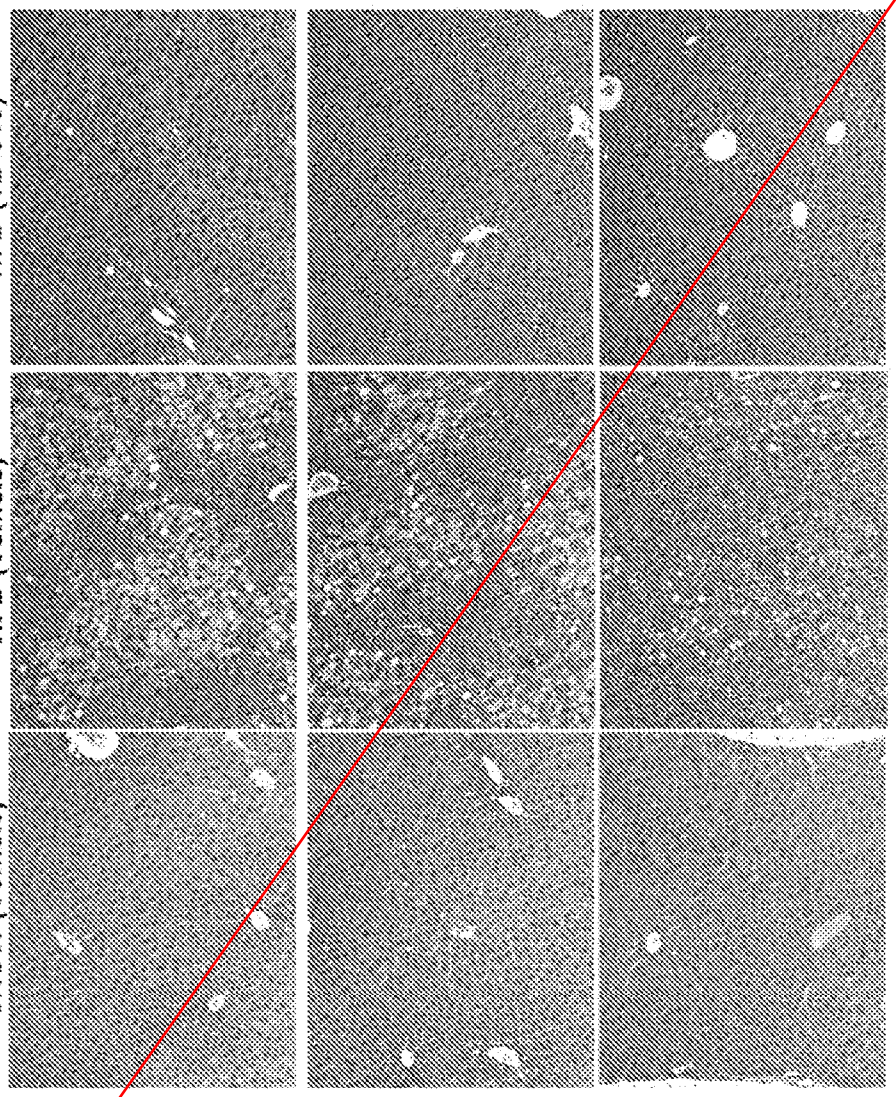


FIGURE 3

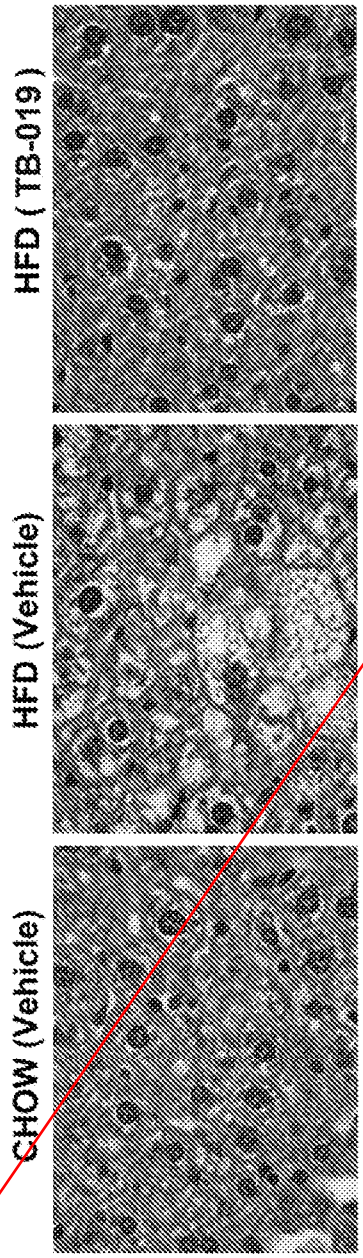


FIGURE 4

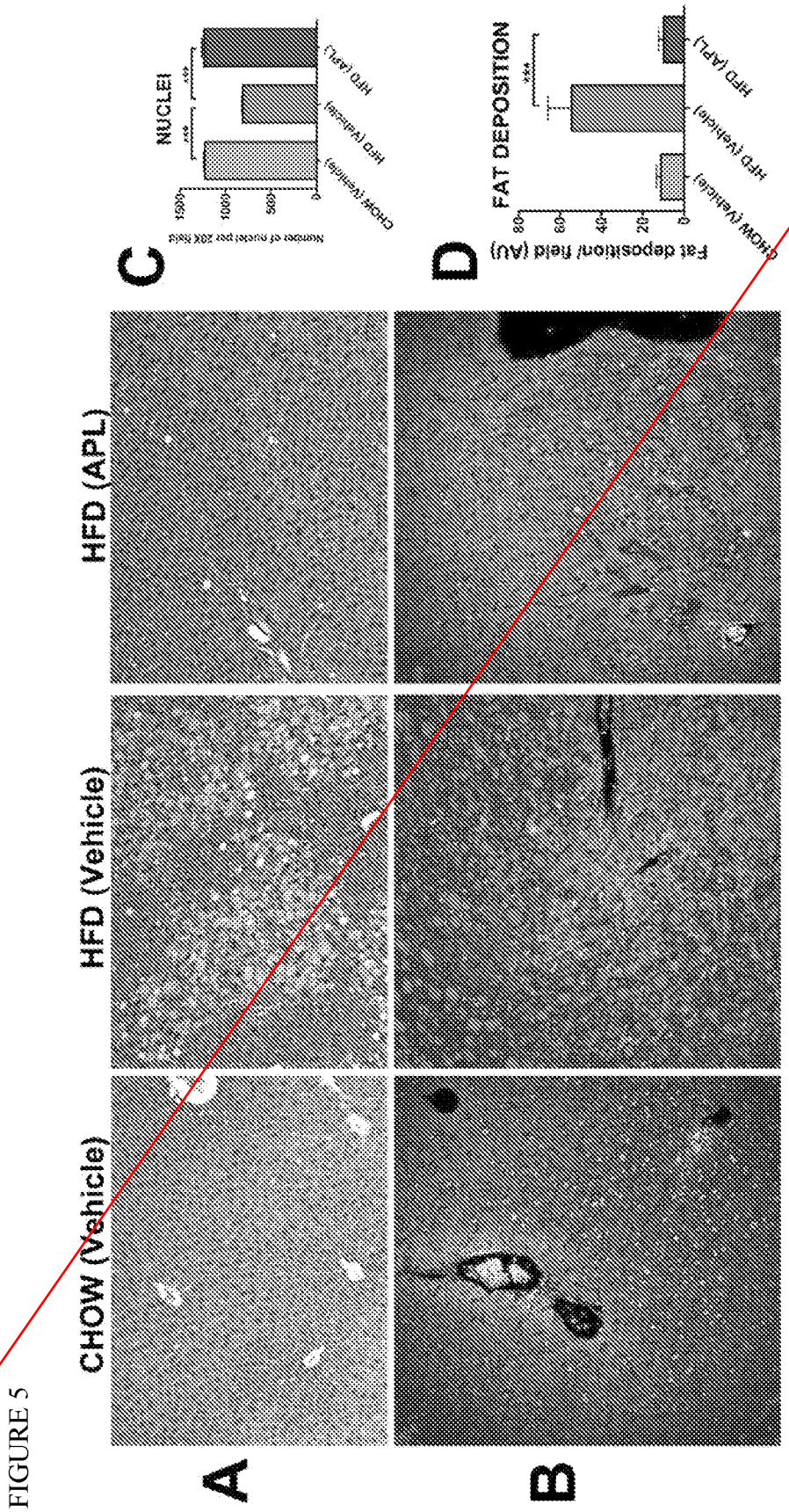

A
B
C
D
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)
NUCLEI
FAT DEPOSITION
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)

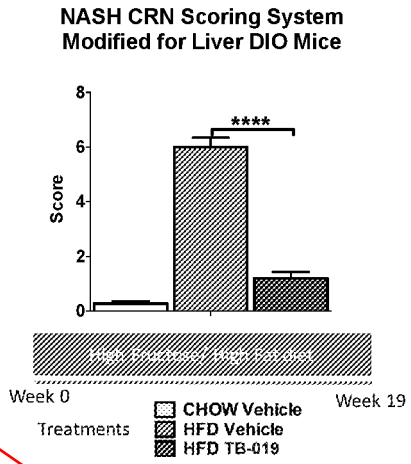
FIGURE 5

FIGURE 6

A
CHOW Vehicle
HFD Vehicle
HFD APL
1
2
3
4
B
NAS Score from DIO Liver Mice
Score
0
1
2
3
4
***
***
***
1 Macrovesicular steatosis
2 Microvesicular steatosis
3 Hypertrophy
4 Inflammatory foci
Week 0
Week 19
Treatments
CHOW Vehicle
HFD Vehicle
HFD APL

FIGURE 7

A


NASH CRN Scoring System
Modified for Liver DIO Mice
Score
8
6
4
2
0
****
High Fructose/ High Fat diet
Week 0
Week 19
Treatments
CHOW Vehicle
HFD Vehicle
HFD TB-019

B

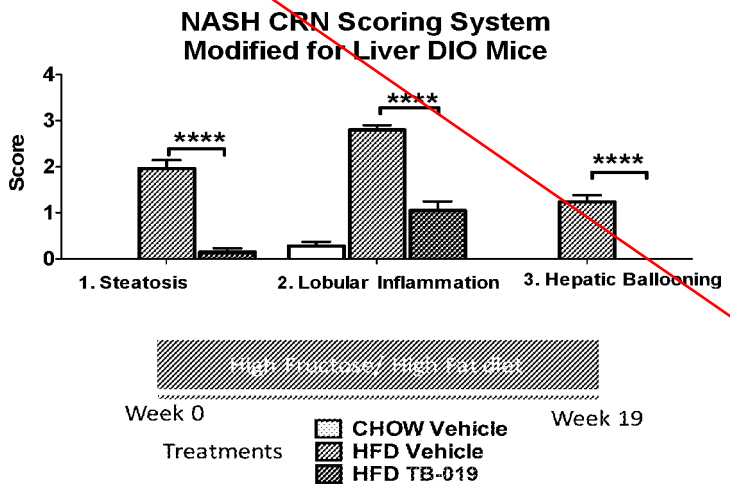
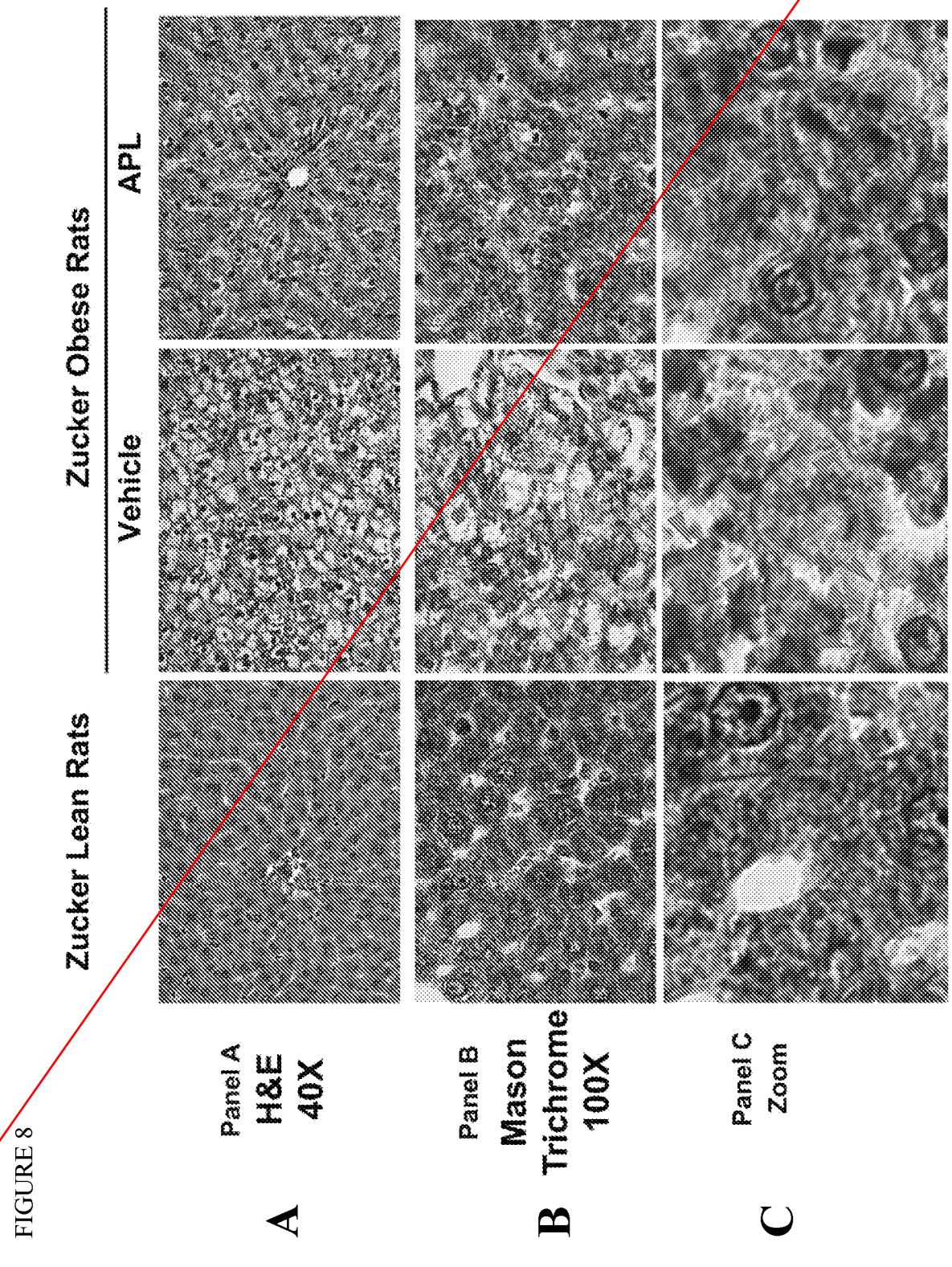

NASH CRN Scoring System
Modified for Liver DIO Mice
Score
4
3
2
1
0
****
****
****
1. Steatosis
2. Lobular Inflammation
3. Hepatic Ballooning
High Fructose/ High Fat diet
Week 0
Week 19
Treatments
CHOW Vehicle
HFD Vehicle
HFD TB-019

FIGURE 8


Zucker Lean Rats
Zucker Obese Rats
Vehicle
APL
A
Panel A
H&E
40X
B
Panel B
Mason
Trichrome
100X
C
Panel C
Zoom

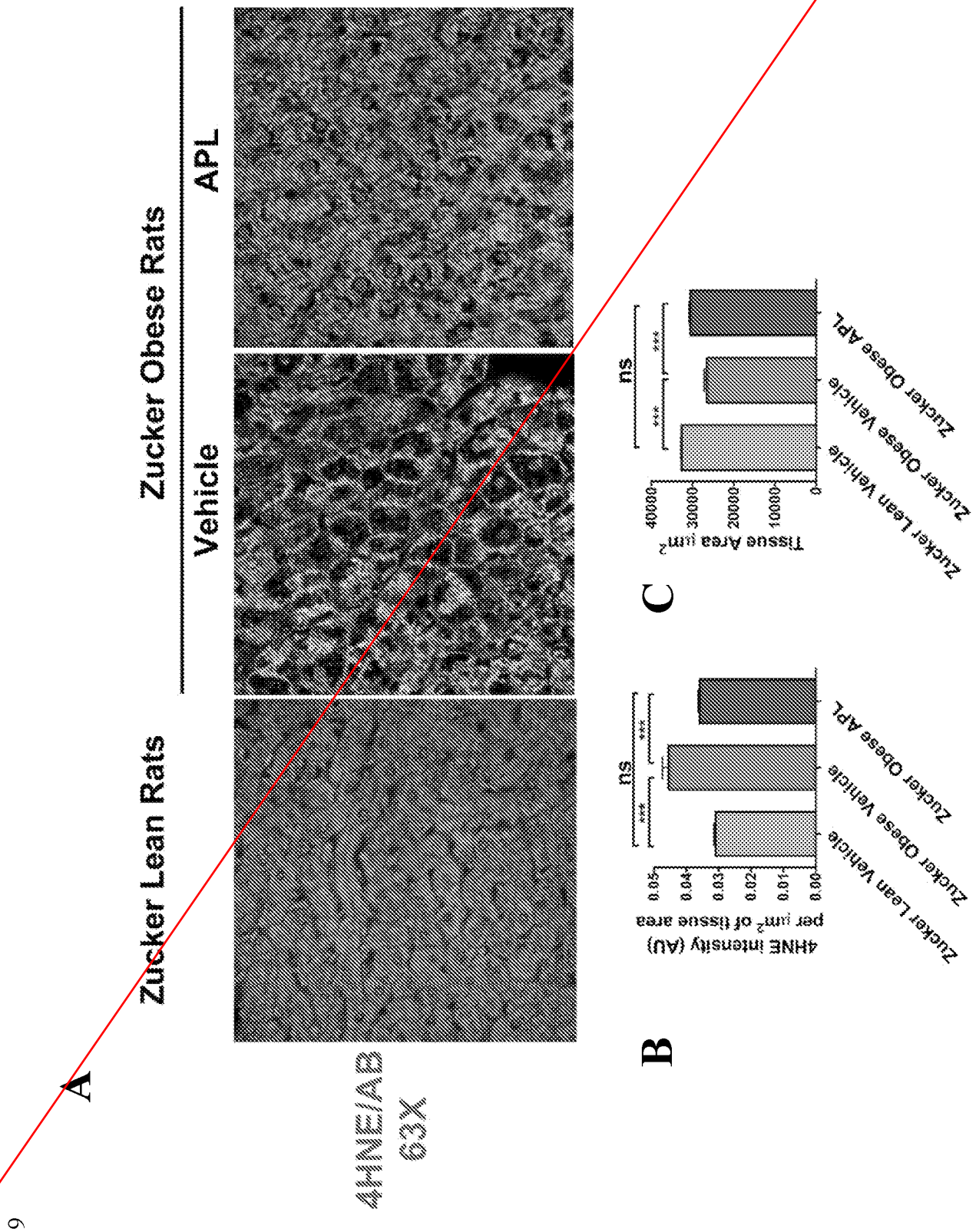

A
Zucker Lean Rats
Zucker Obese Rats
Vehicle
APL
4HNE/AB
63X
B
4HNE intensity (AU)
per μm² of tissue area
0.05
0.04
0.03
0.02
0.01
0.00
ns
***
***
Zucker Lean Vehicle
Zucker Obese Vehicle
Zucker Obese APL
C
Tissue Area μm²
40000
30000
20000
10000
0
ns
***
***
Zucker Lean Vehicle
Zucker Obese Vehicle
Zucker Obese APL

FIGURE 9

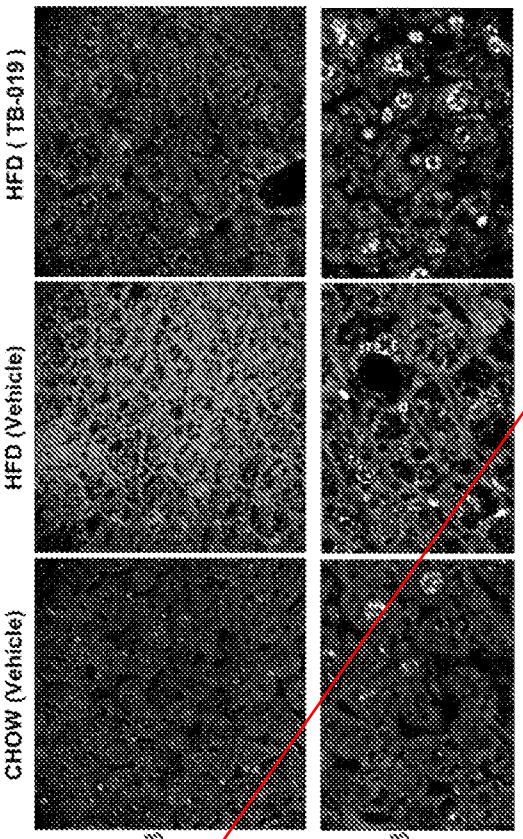

A
CHOW (Vehicle)
HFD (Vehicle)
HFD (TB-019)
4HNE/AB
10X
4HNE/AB
63 X
B
4HNE Intensity/μm²
0
1
2
3
4
5
***
***
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)

FIGURE 10

FIGURE 11

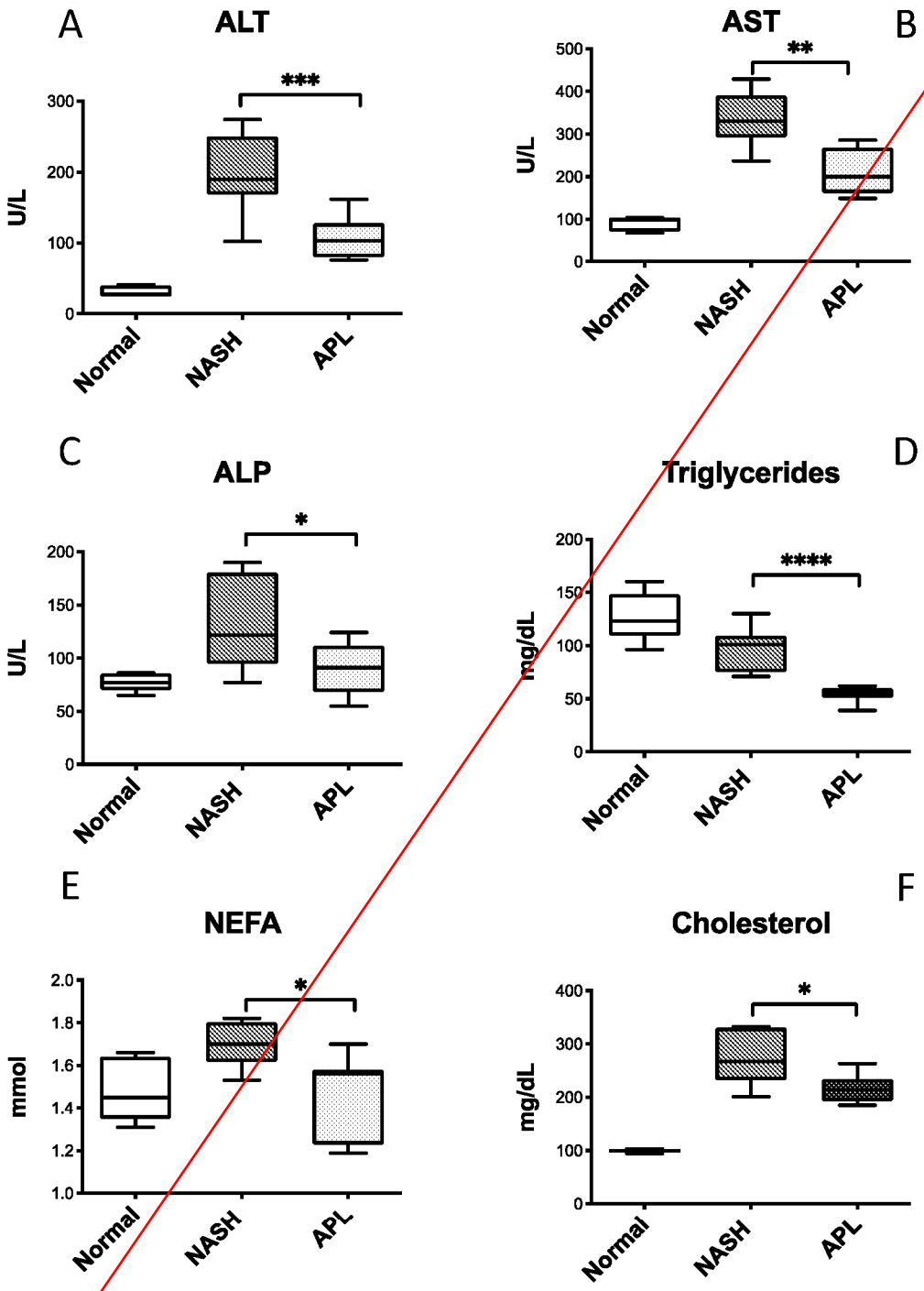

A
ALT
U/L
300
200
100
0
***
Normal
NASH
APL
B
AST
U/L
500
400
300
200
100
0
**
Normal
NASH
APL
C
ALP
U/L
200
150
100
50
0
*
Normal
NASH
APL
D
Triglycerides
mg/dL
200
150
100
50
0
****
Normal
NASH
APL
E
NEFA
mmol
2.0
1.8
1.6
1.4
1.2
1.0
*
Normal
NASH
APL
F
Cholesterol
mg/dL
400
300
200
100
0
*
Normal
NASH
APL

FIGURE 12

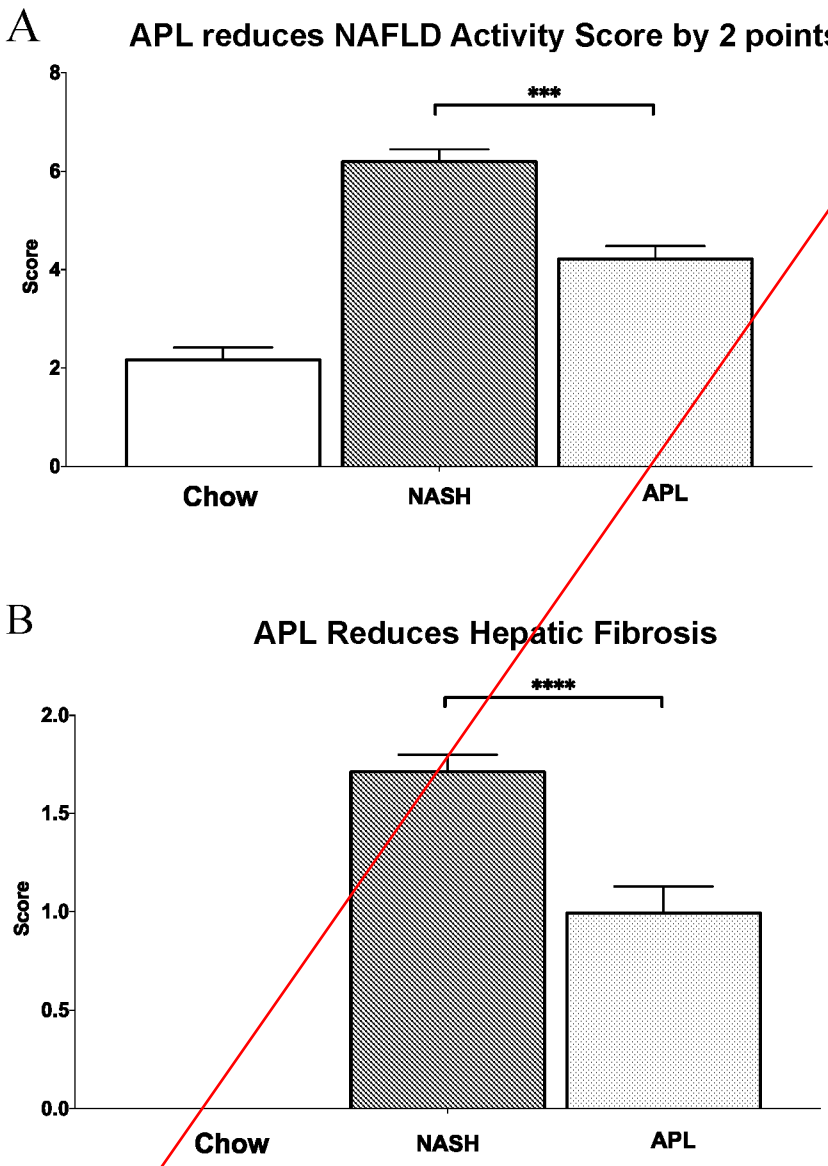

A
APL reduces NAFLD Activity Score by 2 points
***
Score
8
6
4
2
0
Chow
NASH
APL
B
APL Reduces Hepatic Fibrosis
****
Score
2.0
1.5
1.0
0.5
0.0
Chow
NASH
APL

FIGURE 1

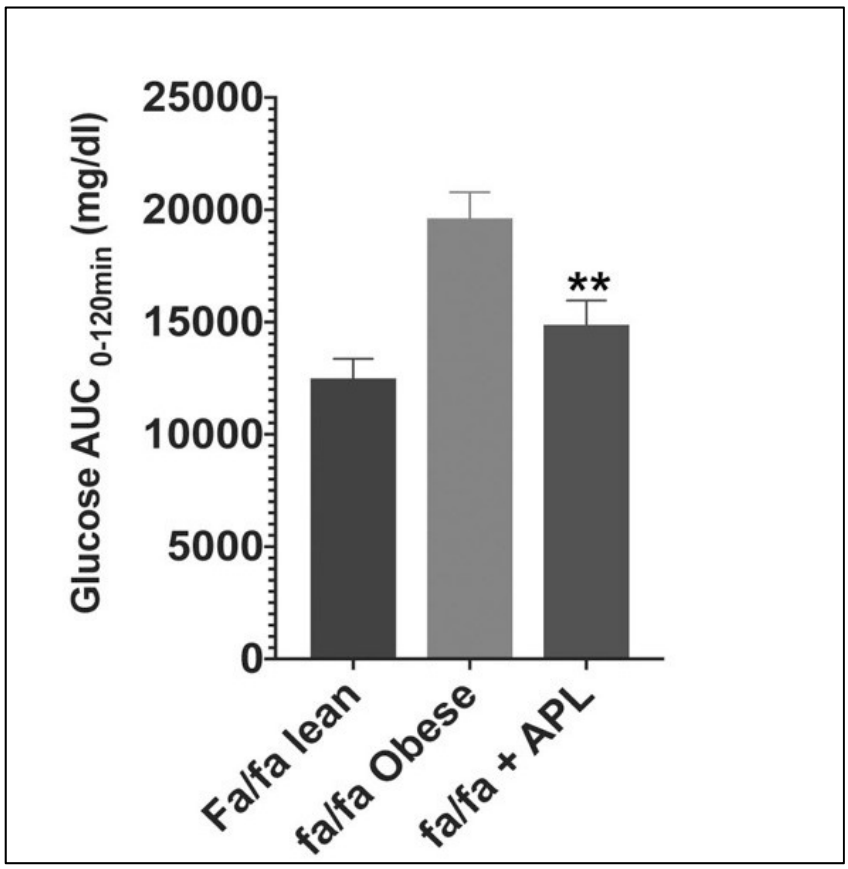
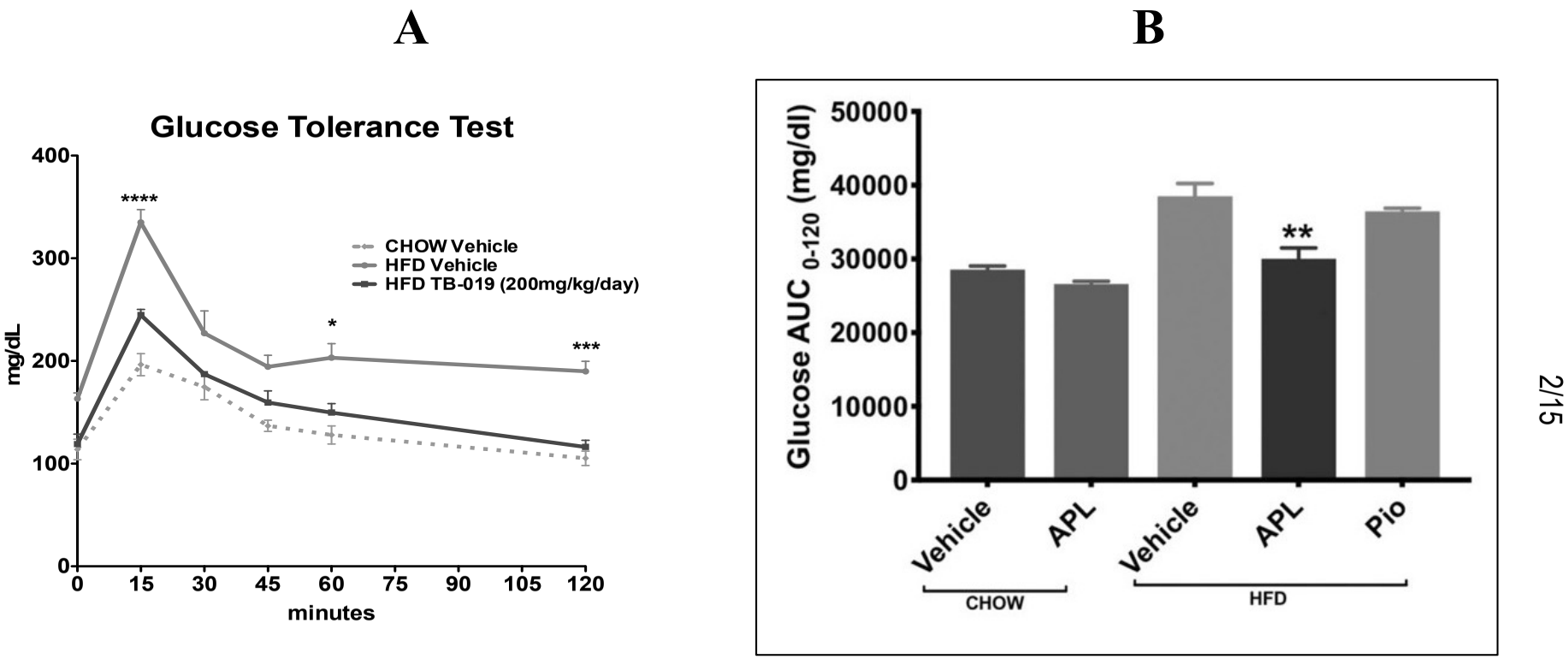

Glucose AUC 0-120min (mg/dl)
25000
20000
15000
10000
5000
0
**
Fa/fa lean
fa/fa Obese
fa/fa + APL

Figure 2


A
Glucose Tolerance Test
400
300
200
100
0
mg/dL
****
*
***
CHOW Vehicle
HFD Vehicle
HFD TB-019 (200mg/kg/day)
0
15
30
45
60
75
90
105
120
minutes
B
Glucose AUC 0-120 (mg/dl)
50000
40000
30000
20000
10000
0
**
Vehicle
APL
Vehicle
APL
Pio
CHOW
HFD

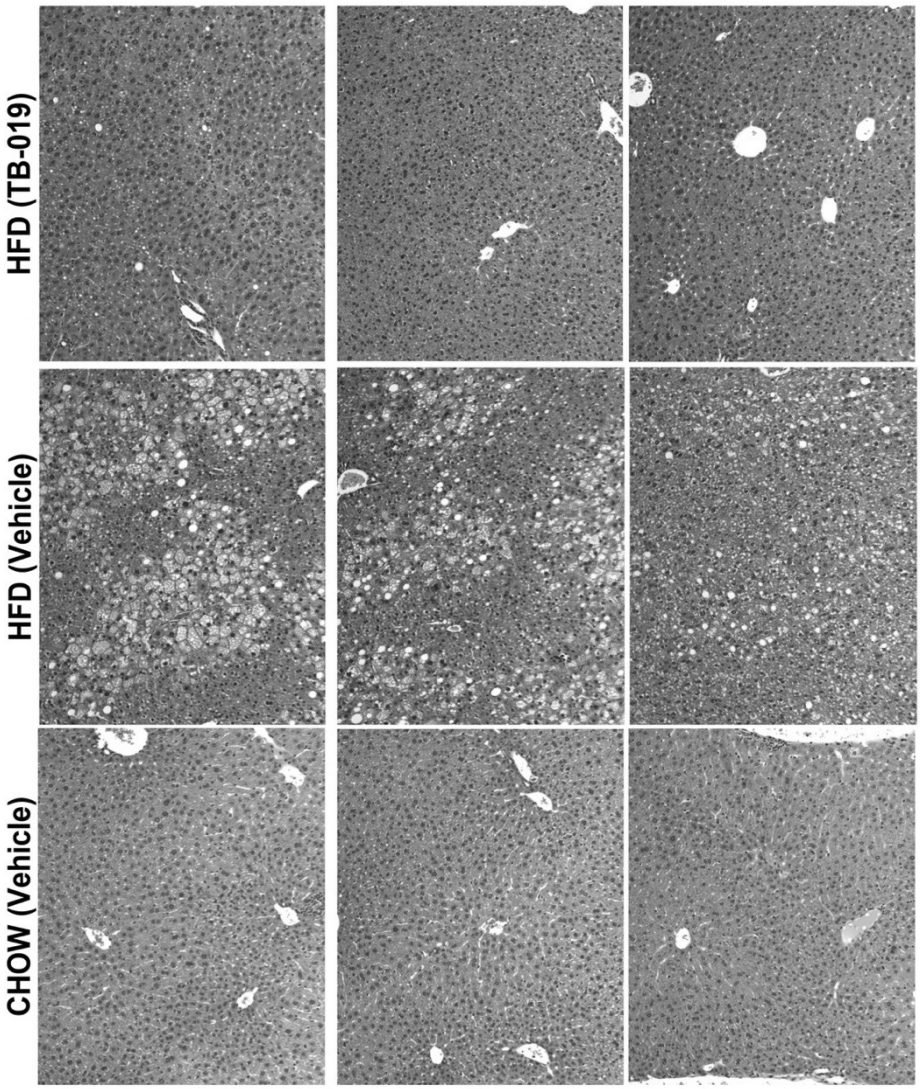


FIGURE 3

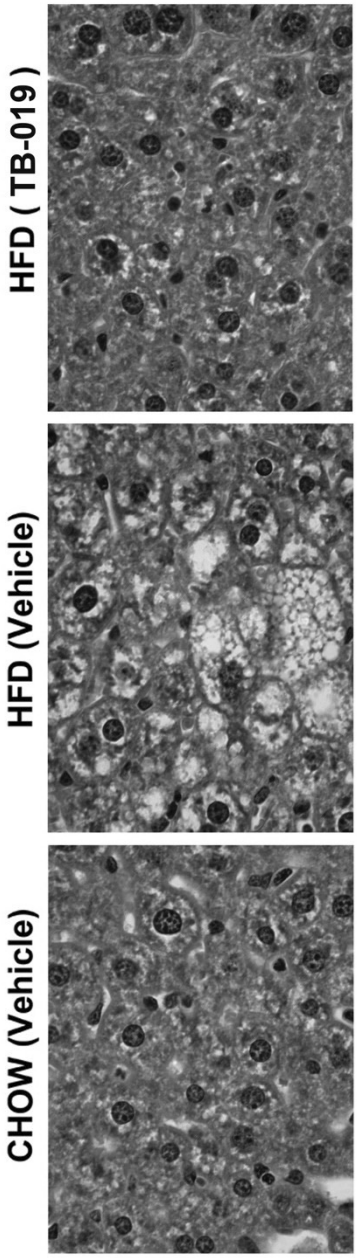


FIGURE 4

FIGURE 5

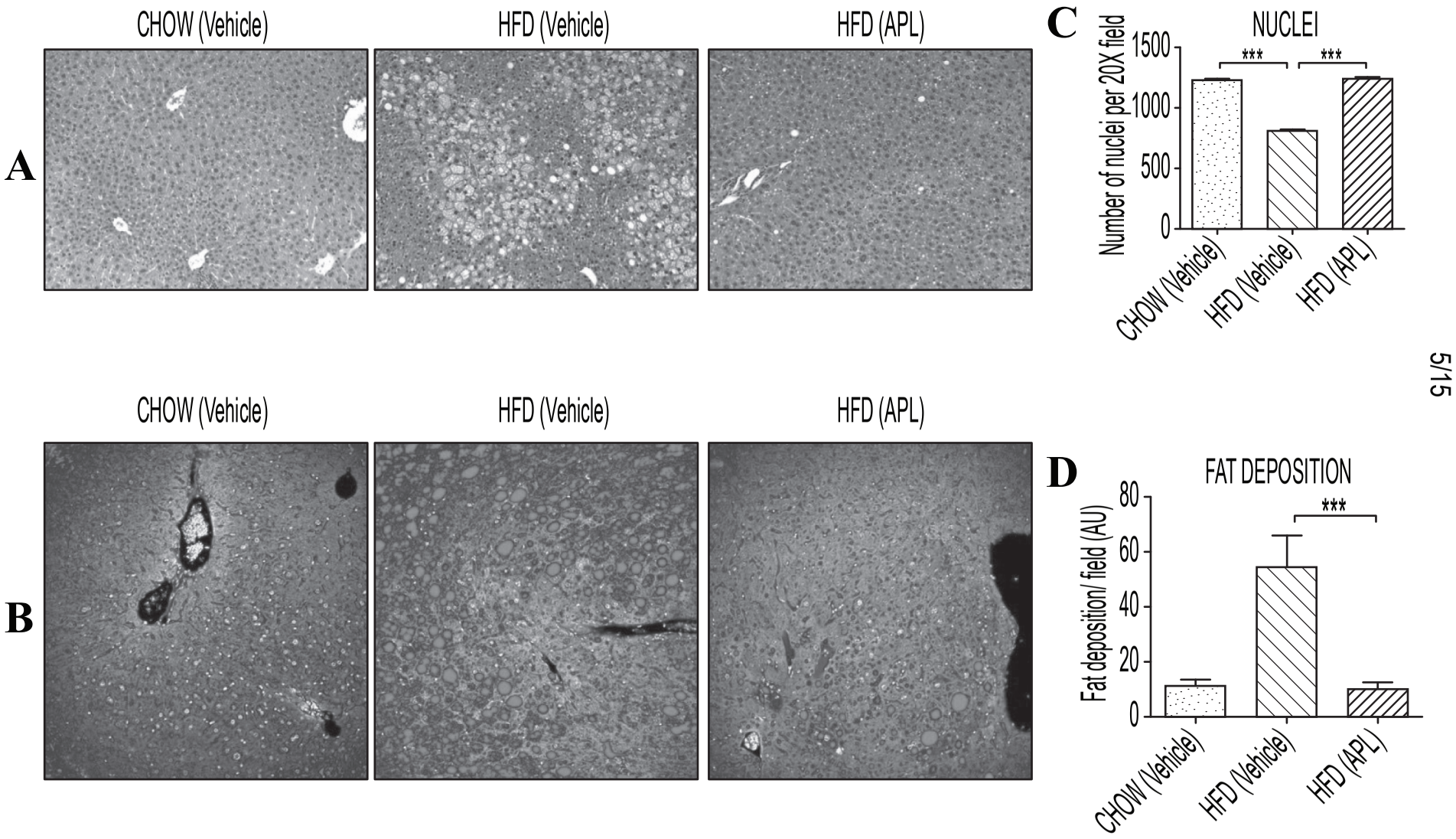

A
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)
B
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)
C
NUCLEI
Number of nuclei per 20X field
1500
1000
500
0
***
***
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)
D
FAT DEPOSITION
Fat deposition/ field (AU)
80
60
40
20
0
***
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)

FIGURE 6

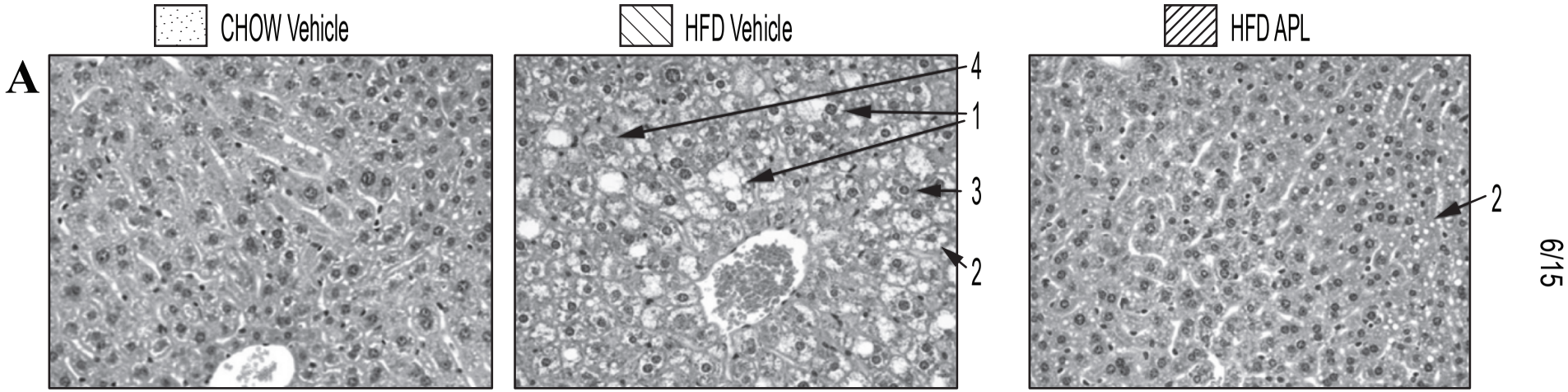


FIGURE 6

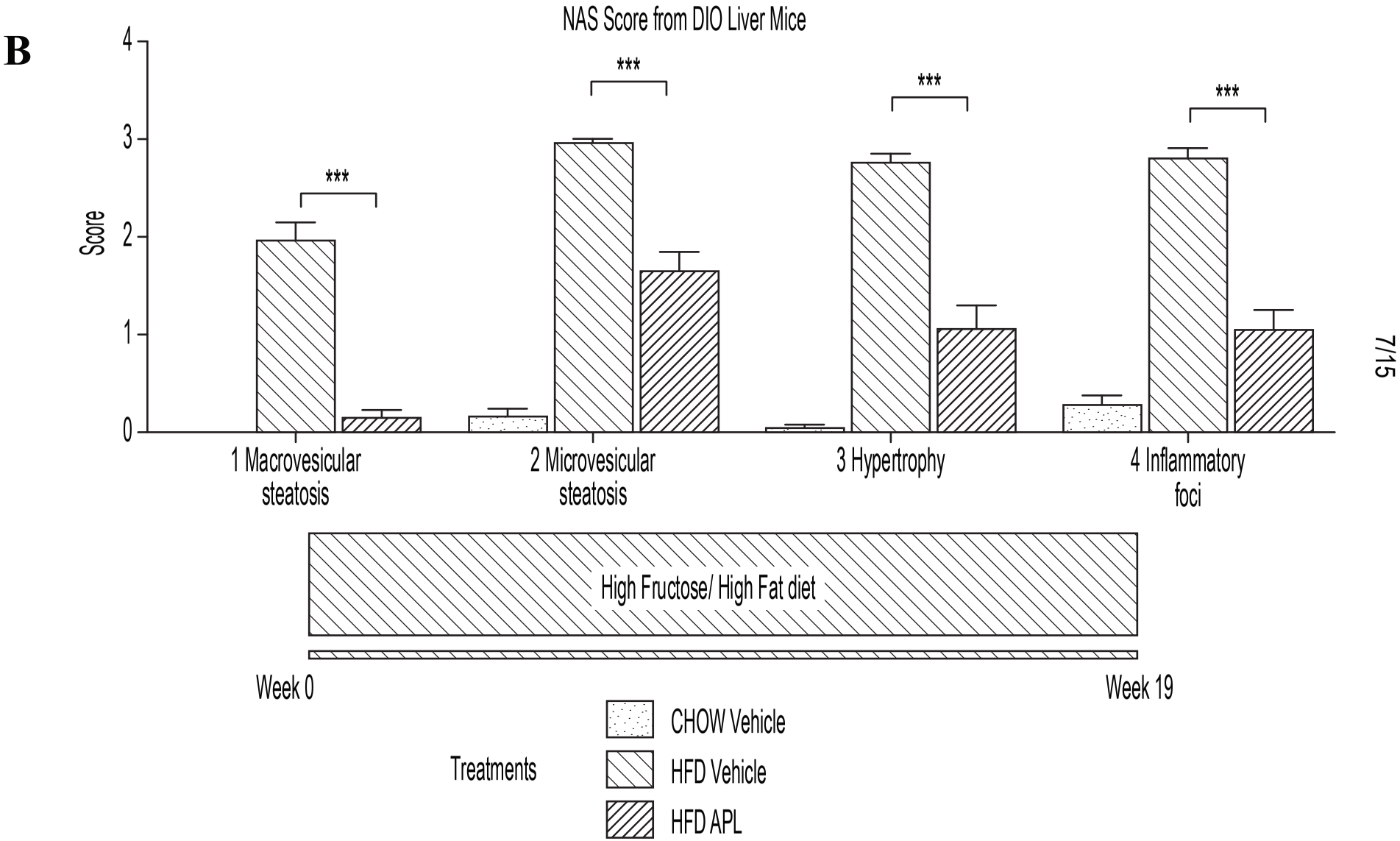

B
NAS Score from DIO Liver Mice
Score
4
3
2
1
0
***
***
***
***
1 Macrovesicular steatosis
2 Microvesicular steatosis
3 Hypertrophy
4 Inflammatory foci
High Fructose/ High Fat diet
Week 0
Week 19
Treatments
CHOW Vehicle
HFD Vehicle
HFD APL

FIGURE 7

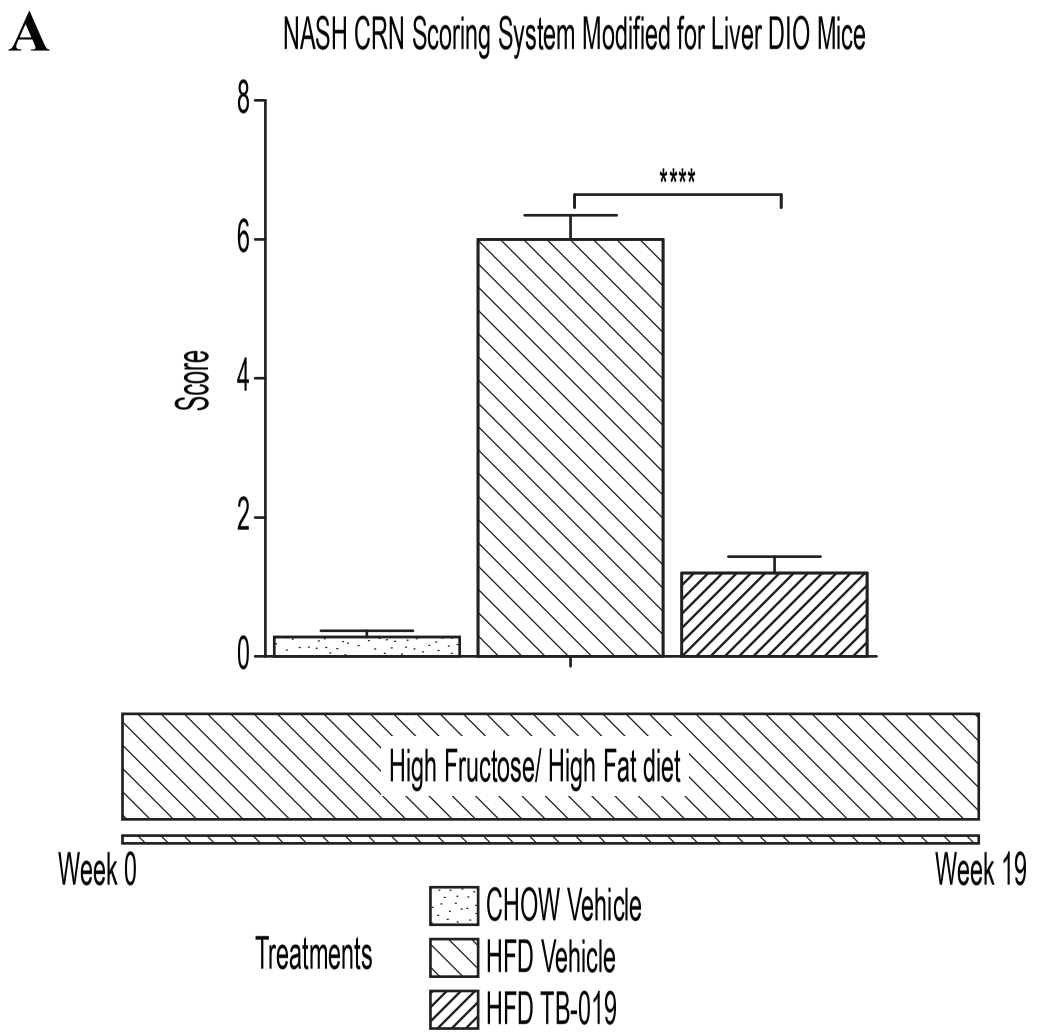

A
NASH CRN Scoring System Modified for Liver DIO Mice
Score
8
6
4
2
0
****
High Fructose/ High Fat diet
Week 0
Week 19
Treatments
CHOW Vehicle
HFD Vehicle
HFD TB-019

FIGURE 7

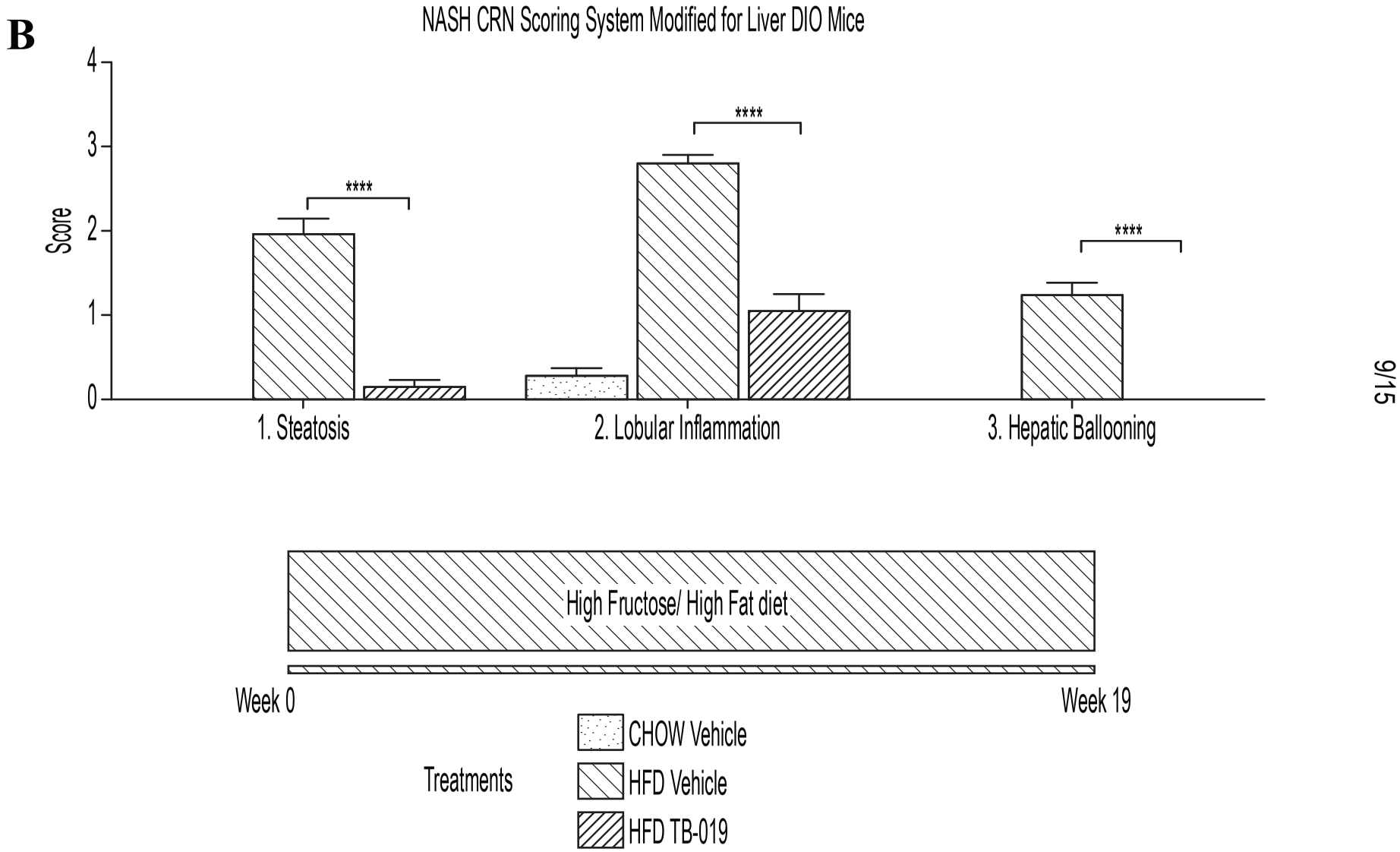

B
NASH CRN Scoring System Modified for Liver DIO Mice
Score
4
3
2
1
0
****
****
****
1. Steatosis
2. Lobular Inflammation
3. Hepatic Ballooning
High Fructose/ High Fat diet
Week 0
Week 19
Treatments
CHOW Vehicle
HFD Vehicle
HFD TB-019

FIGURE 8

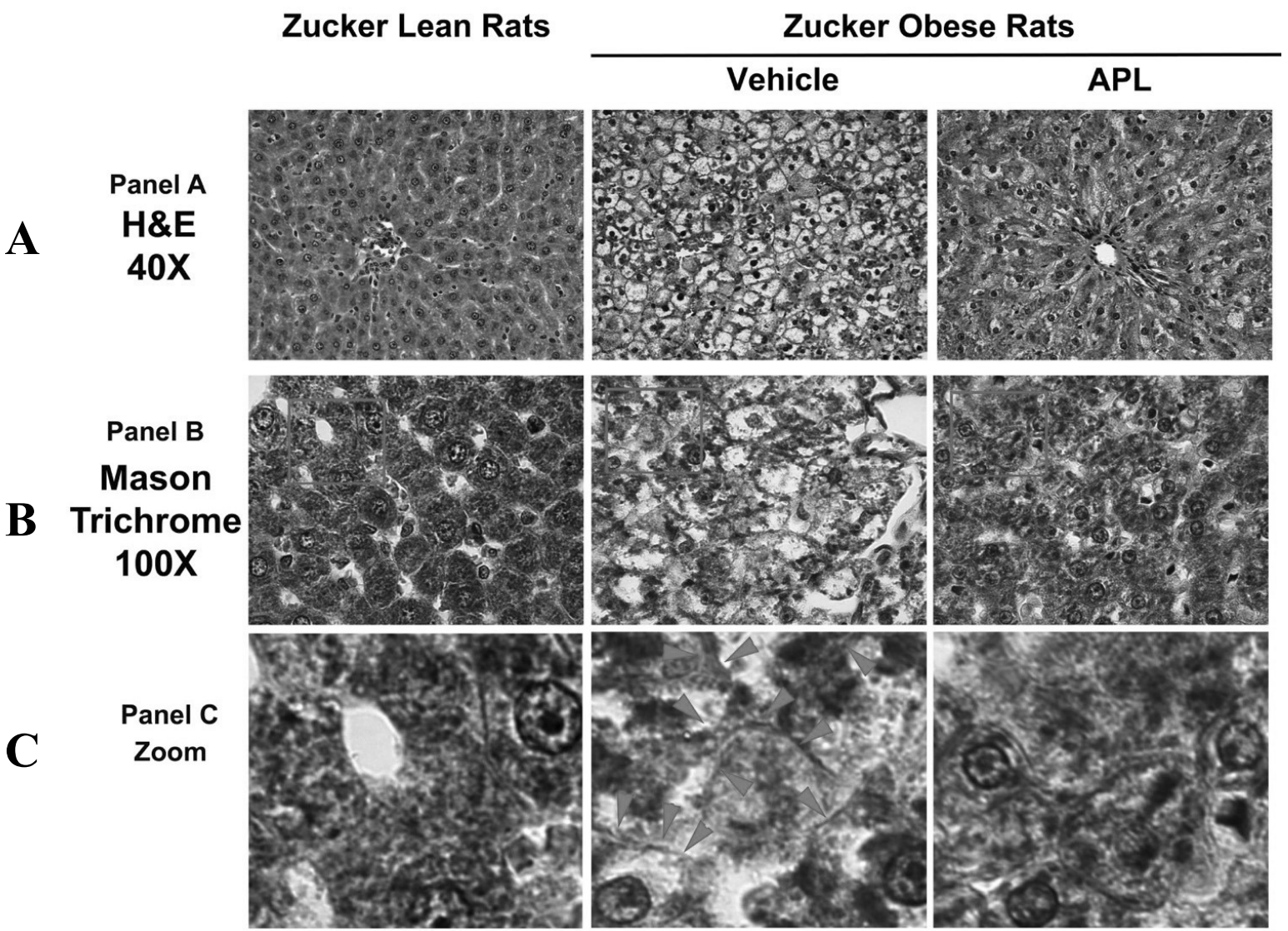

Zucker Lean Rats
Zucker Obese Rats
Vehicle
APL
A
Panel A
H&E
40X
B
Panel B
Mason
Trichrome
100X
C
Panel C
Zoom

FIGURE 9

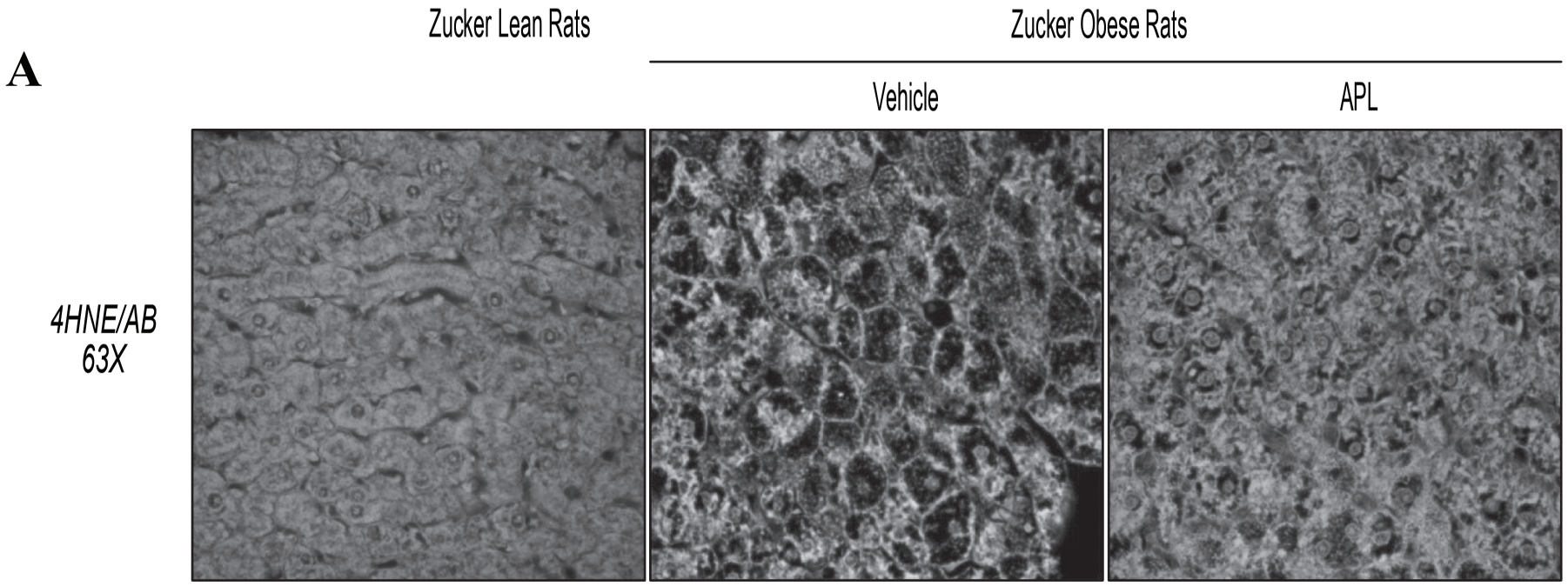


FIGURE 9

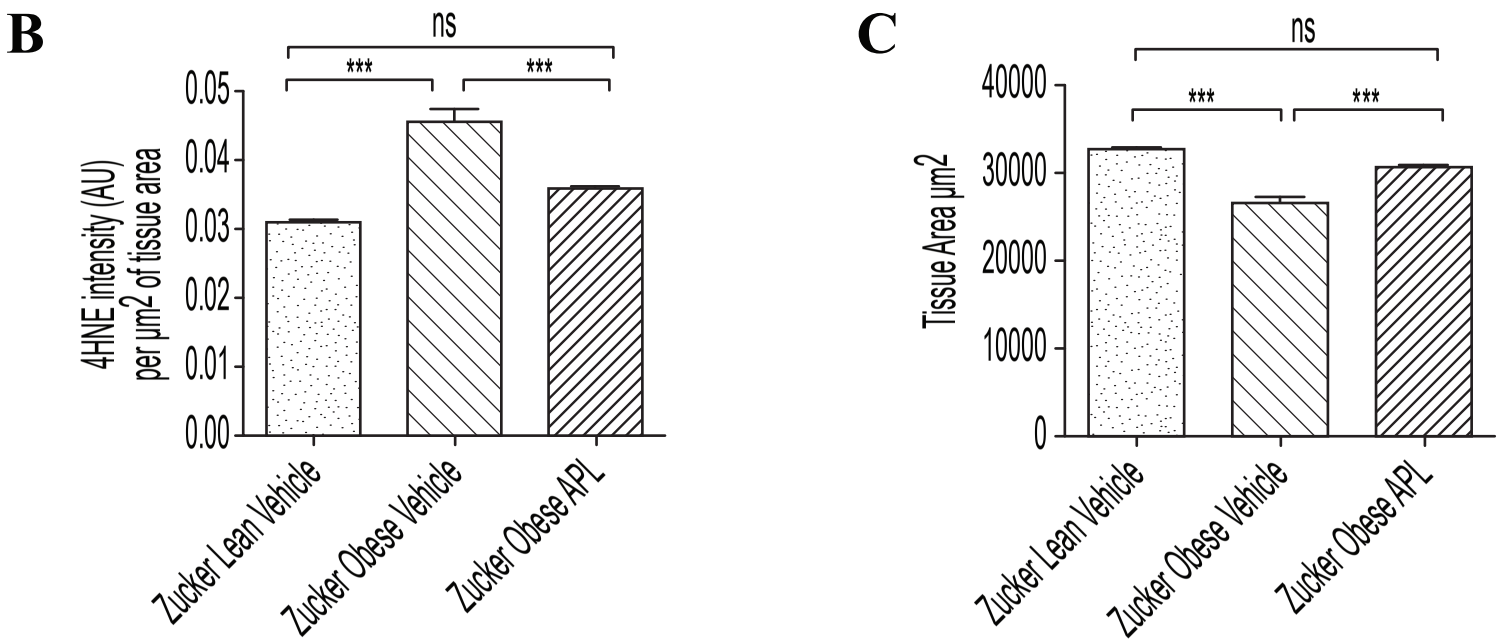

B
ns
***
***
0.05
0.04
0.03
0.02
0.01
0.00
4HNE intensity (AU)
per µm2 of tissue area
Zucker Lean Vehicle
Zucker Obese Vehicle
Zucker Obese APL
C
ns
***
***
40000
30000
20000
10000
0
Tissue Area µm2
Zucker Lean Vehicle
Zucker Obese Vehicle
Zucker Obese APL

FIGURE 10

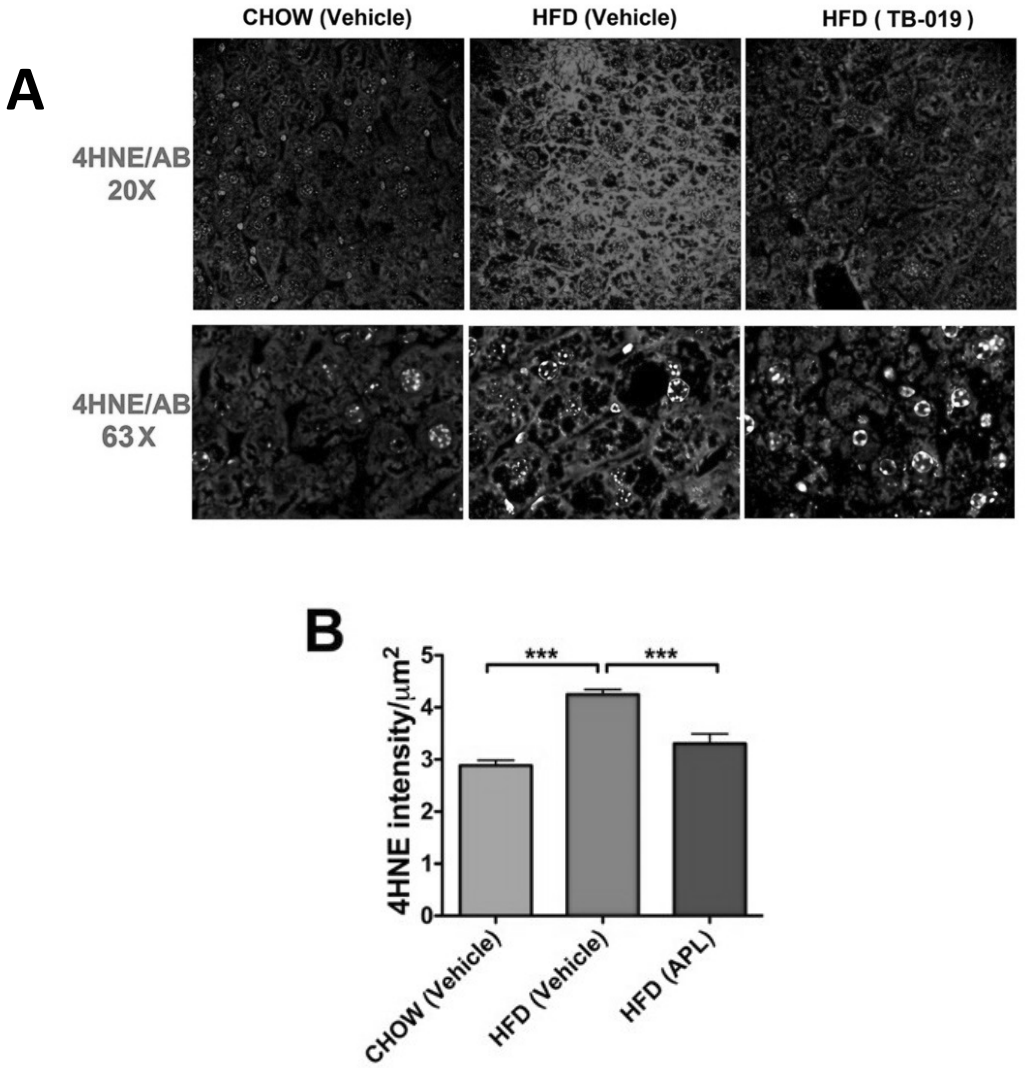

A
CHOW (Vehicle)
HFD (Vehicle)
HFD (TB-019)
4HNE/AB
20X
4HNE/AB
63X
B
4HNE intensity/μm2
0
1
2
3
4
5
***
***
CHOW (Vehicle)
HFD (Vehicle)
HFD (APL)

FIGURE 11

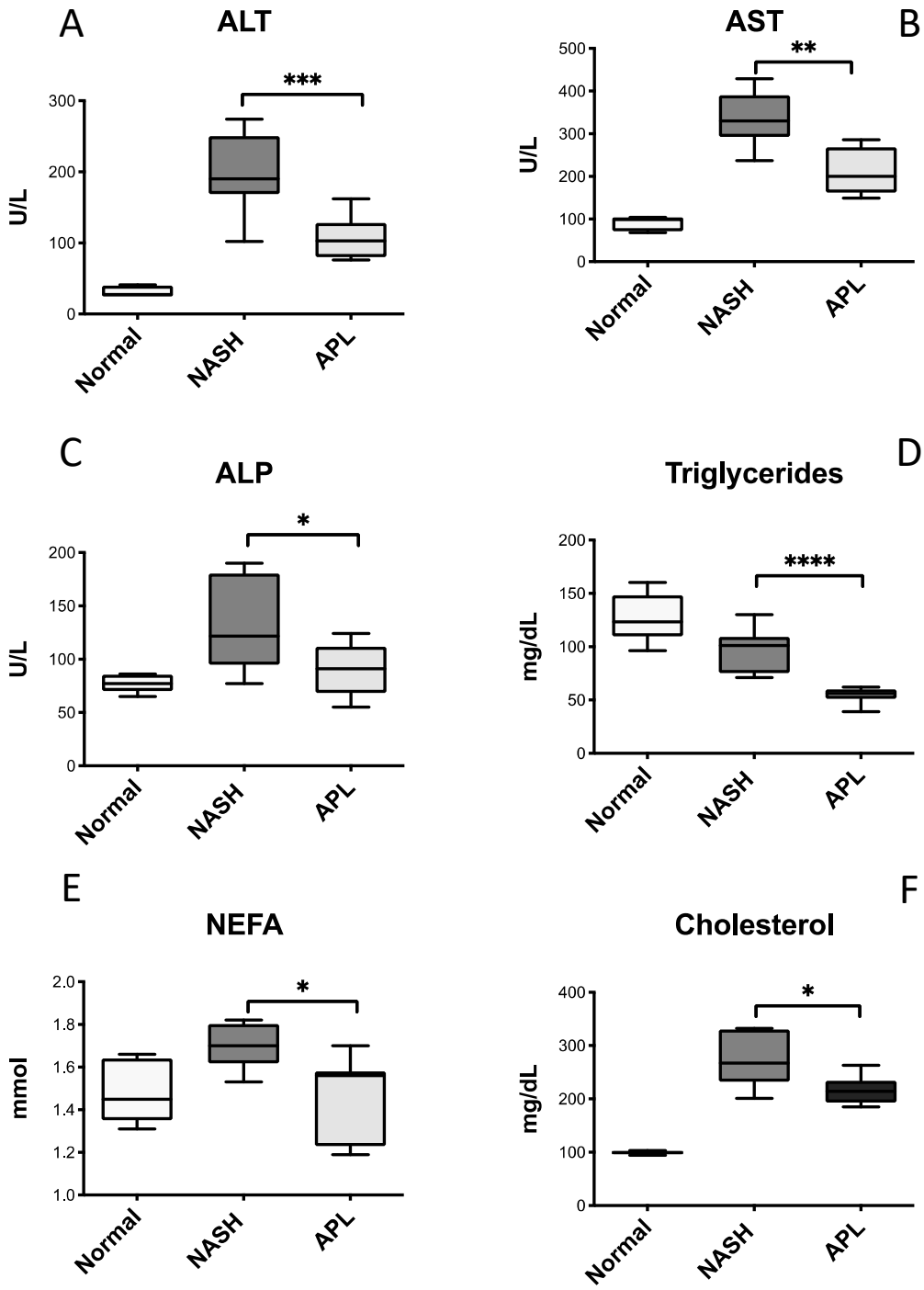
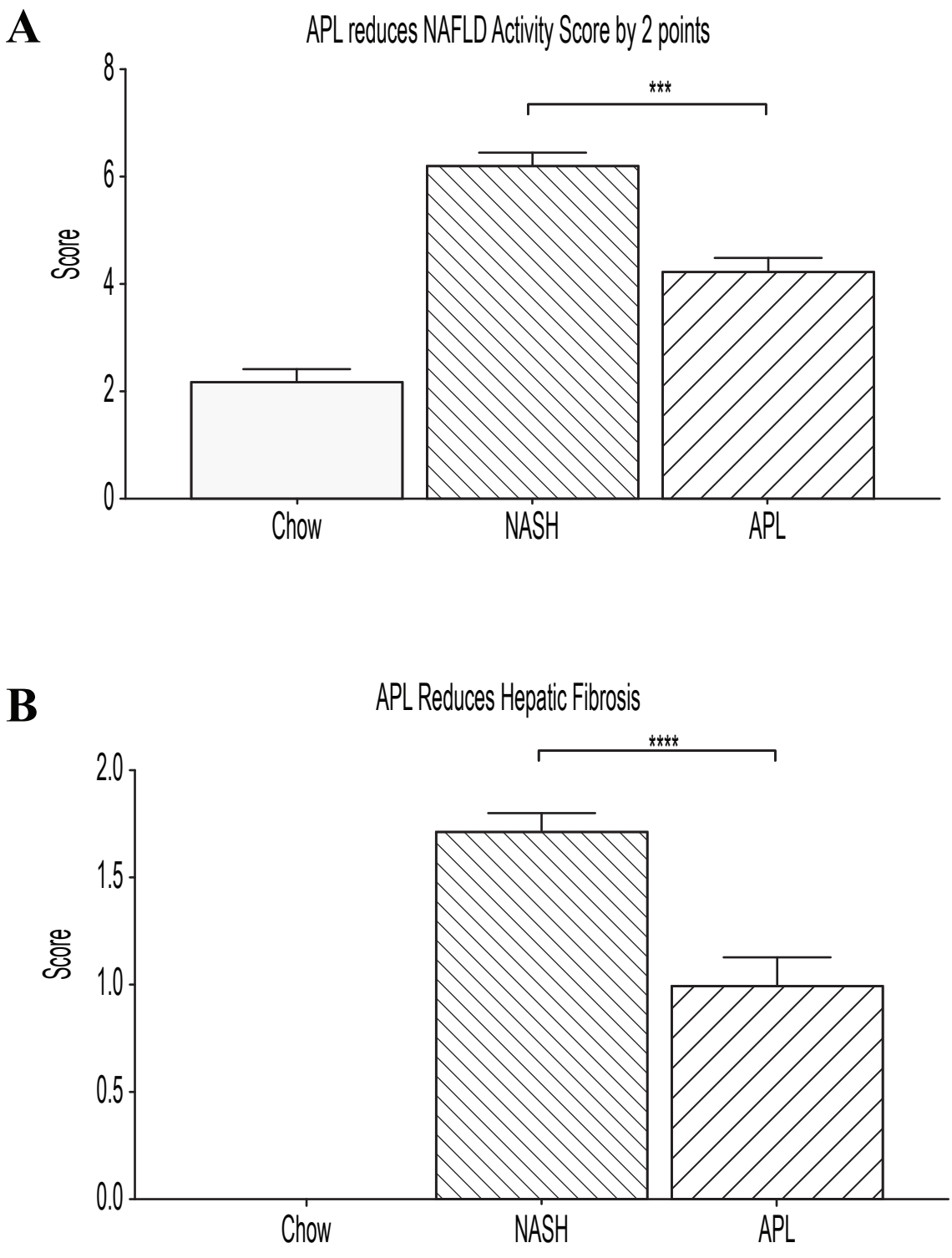

A
ALT
***
U/L
300
200
100
0
Normal
NASH
APL
B
AST
**
U/L
500
400
300
200
100
0
Normal
NASH
APL
C
ALP
*
U/L
200
150
100
50
0
Normal
NASH
APL
D
Triglycerides
****
mg/dL
200
150
100
50
0
Normal
NASH
APL
E
NEFA
*
mmol
2.0
1.8
1.6
1.4
1.2
1.0
Normal
NASH
APL
F
Cholesterol
*
mg/dL
400
300
200
100
0
Normal
NASH
APL

FIGURE 12


A
APL reduces NAFLD Activity Score by 2 points
***
Score
8
6
4
2
0
Chow
NASH
APL
B
APL Reduces Hepatic Fibrosis
****
Score
2.0
1.5
1.0
0.5
0.0
Chow
NASH
APL