FIG. 1

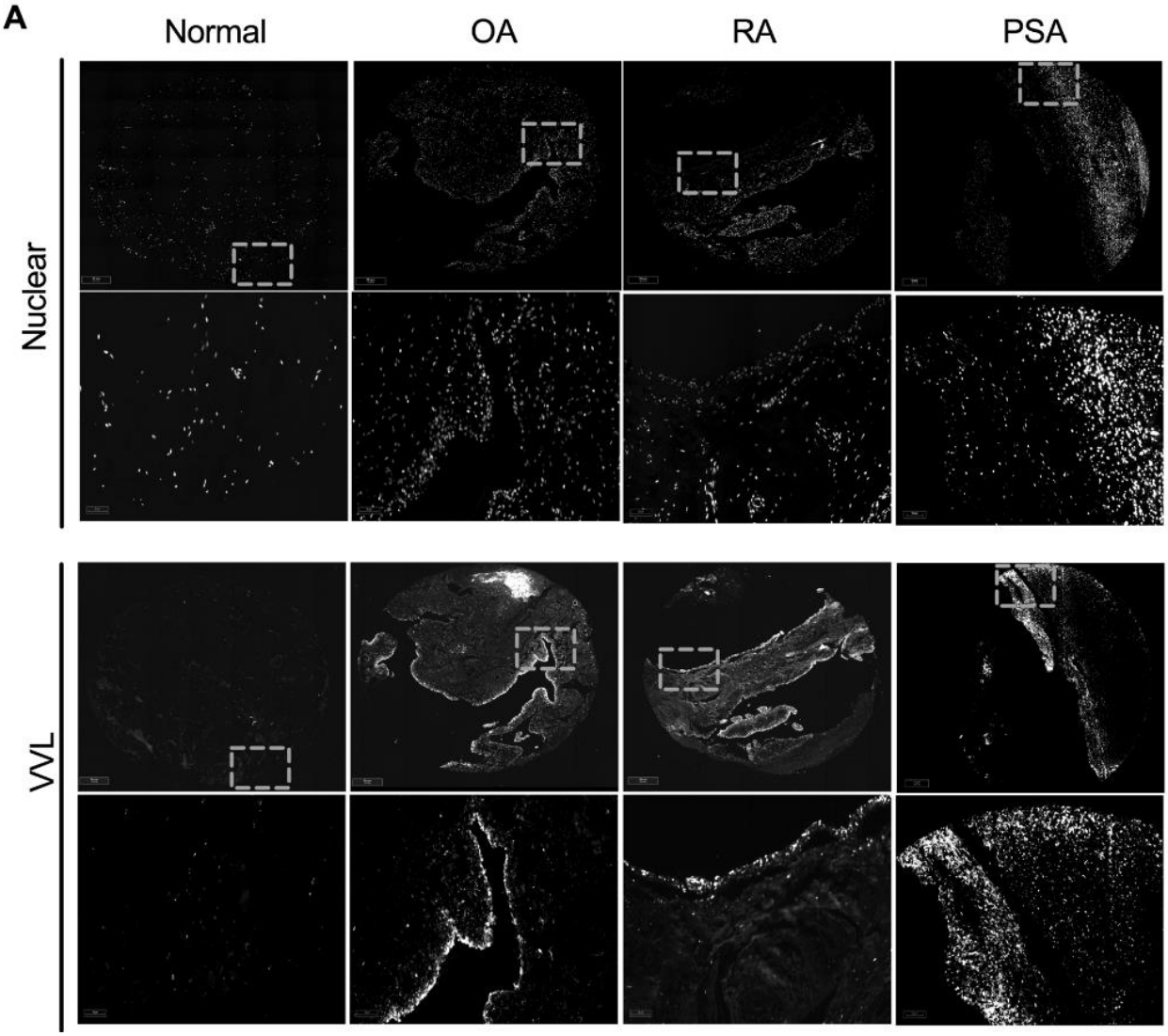


FIG. 1 continued

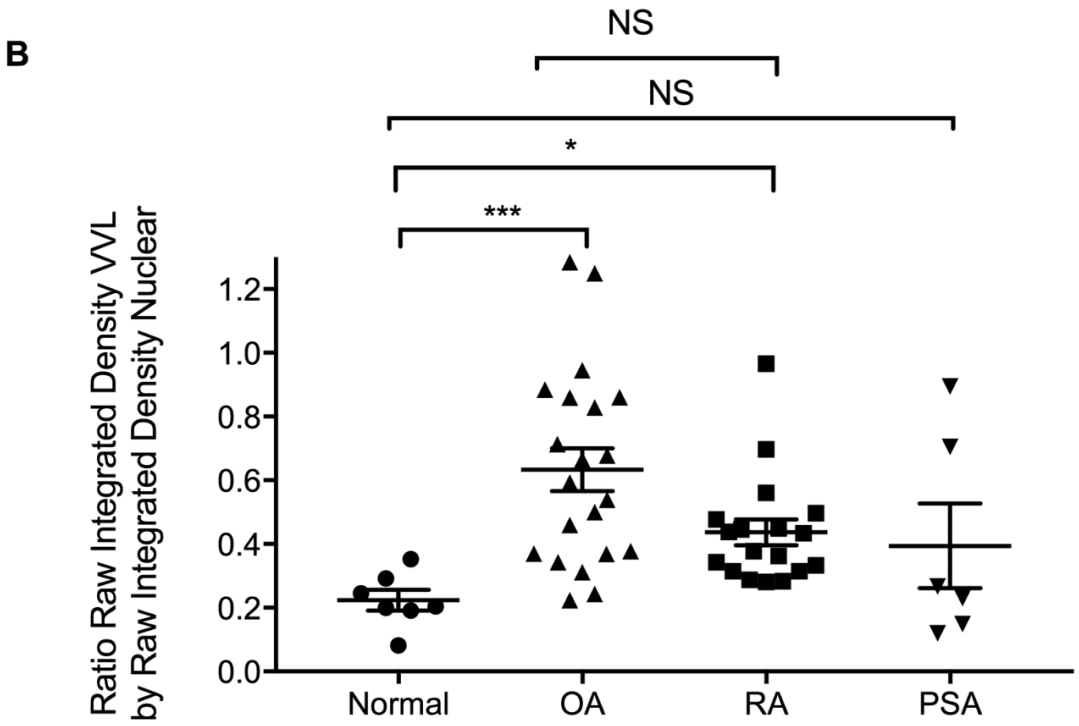
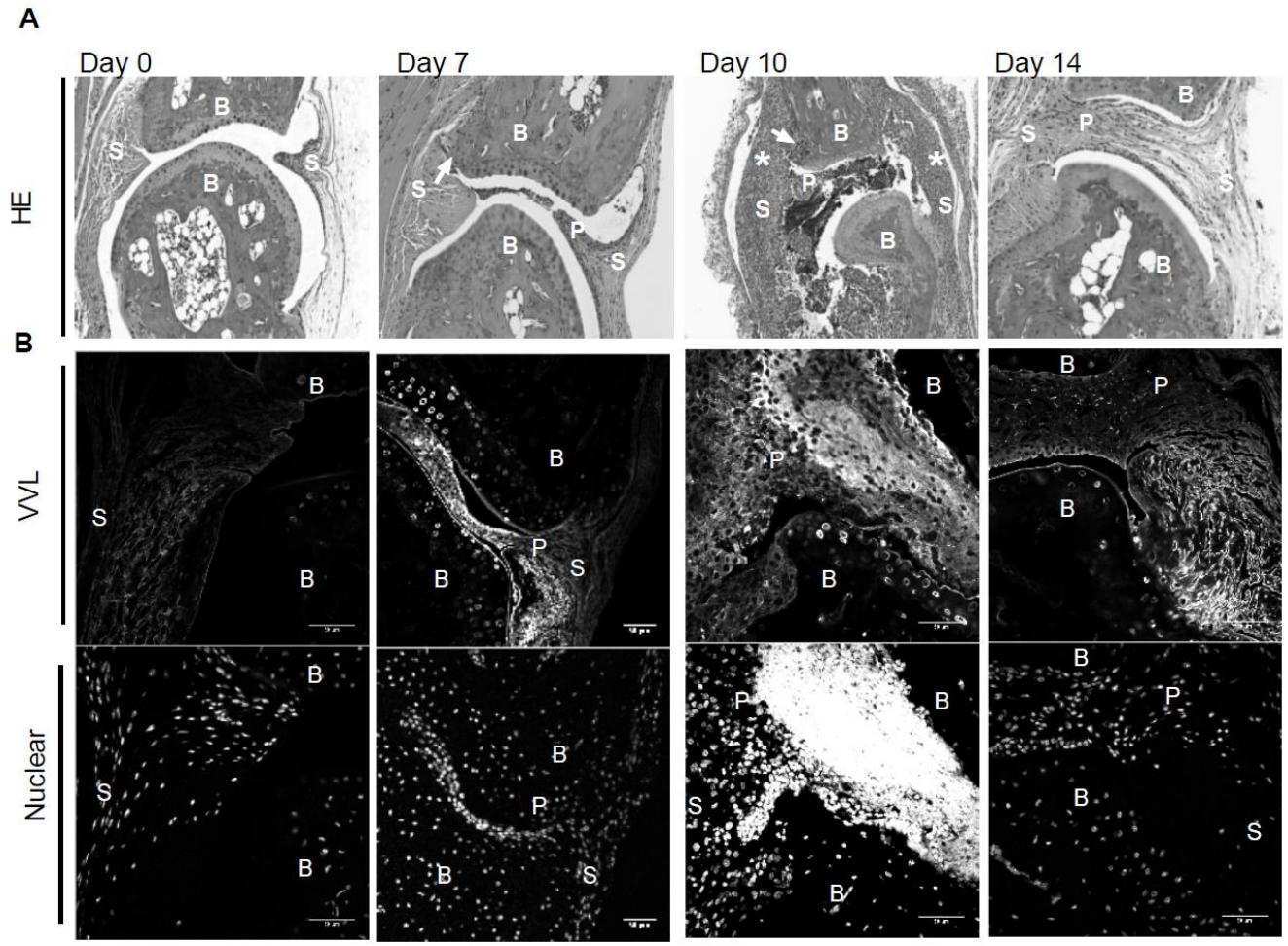


FIG. 2


A
Day 0
Day 7
Day 10
Day 14
HE
B
VVL
Nuclear
B
S
P

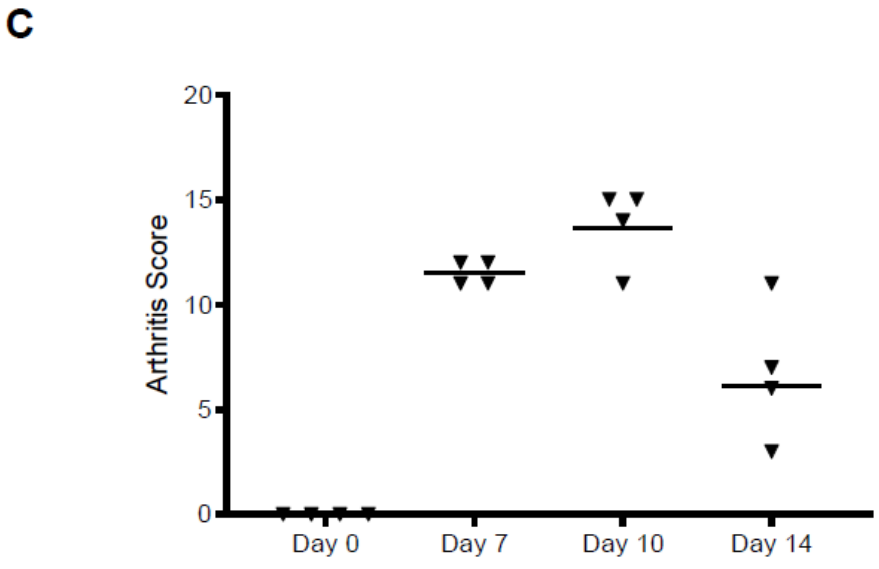

C
Arthritis Score
20
15
10
5
0
Day 0
Day 7
Day 10
Day 14

FIG. 2 continued

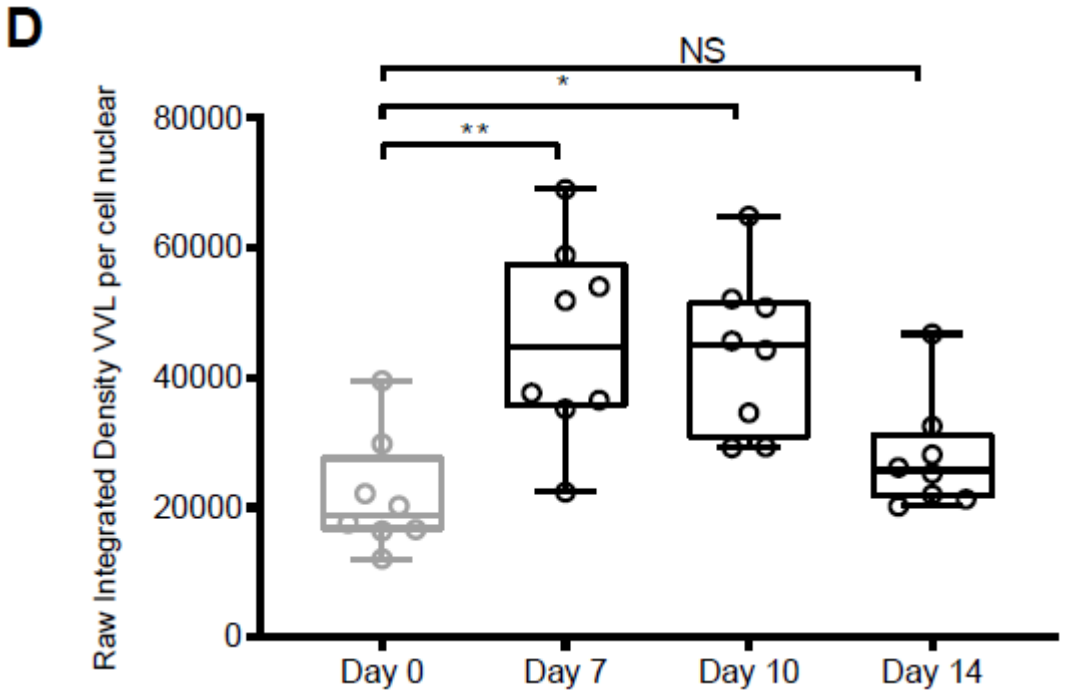


FIG. 3

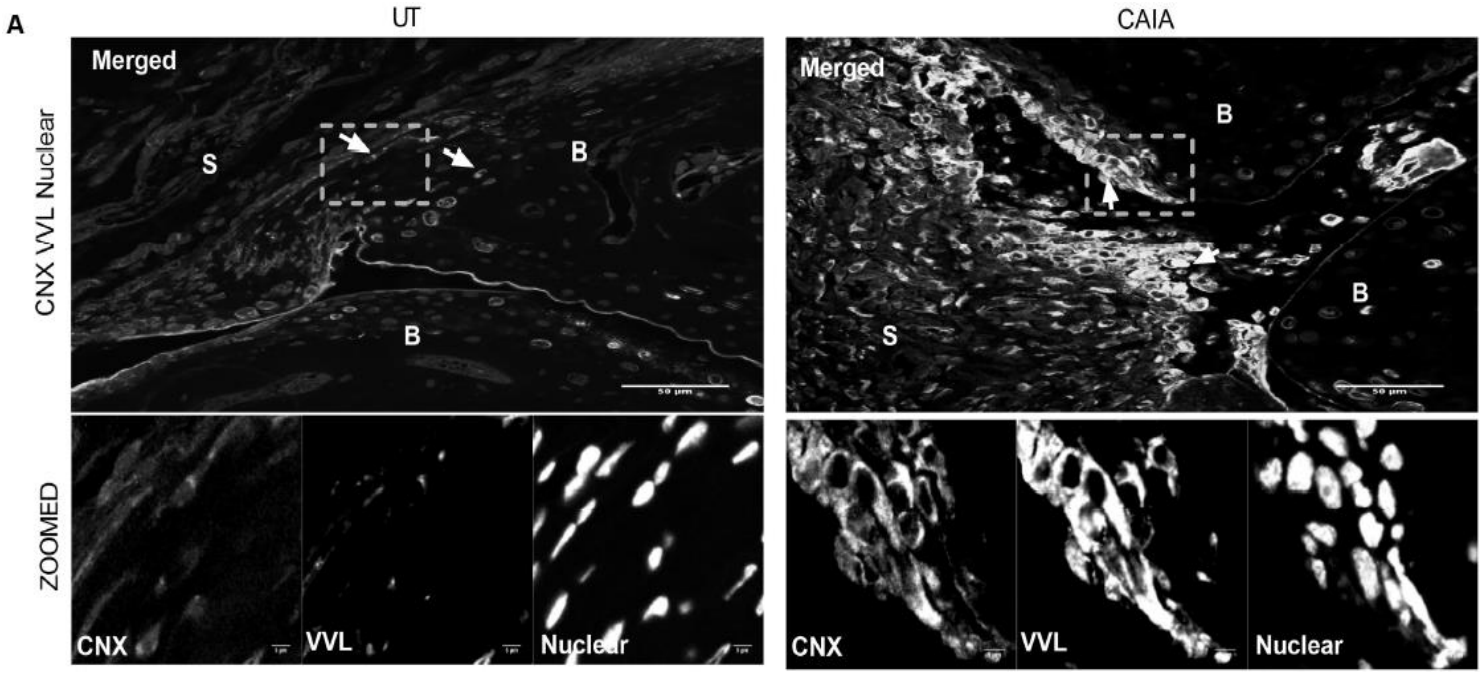


FIG. 3 continued

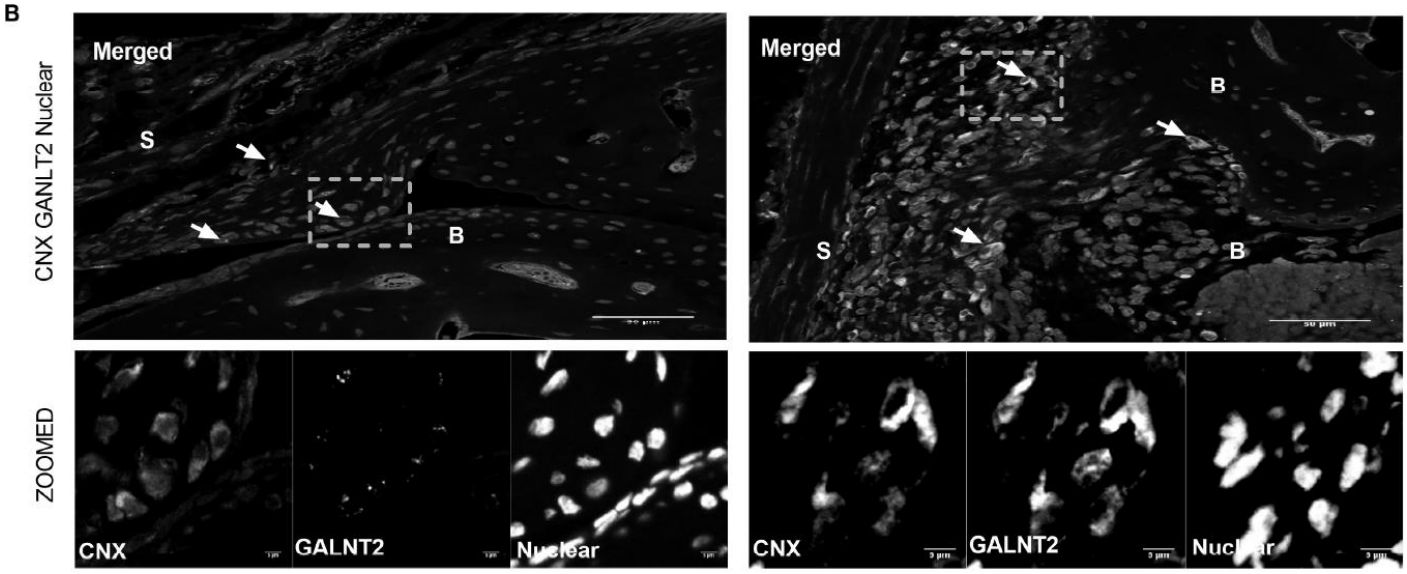


FIG. 4

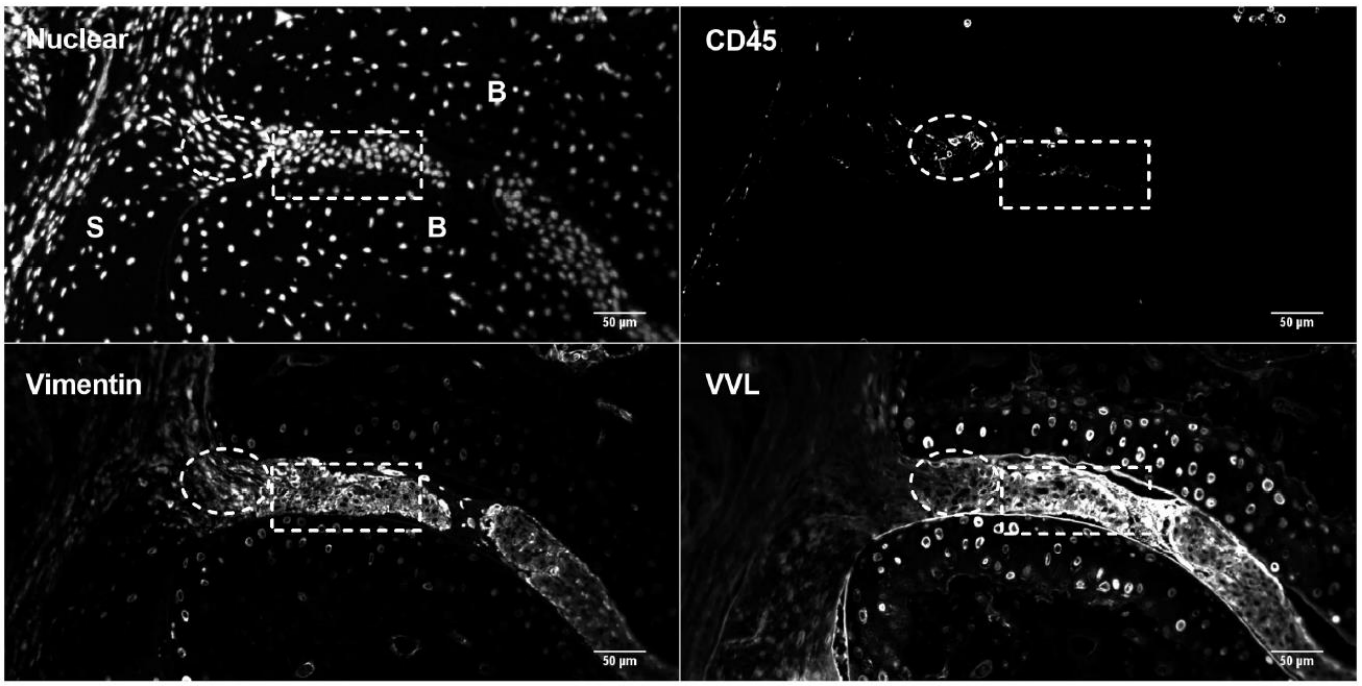


FIG. 5

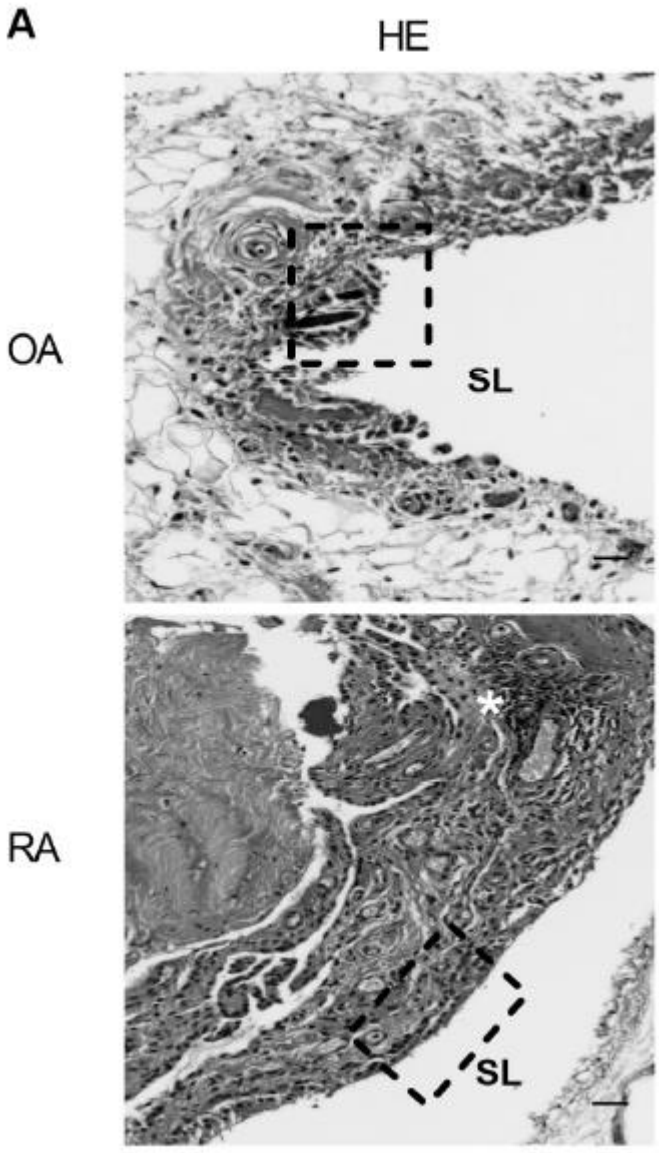


FIG. 5 continued

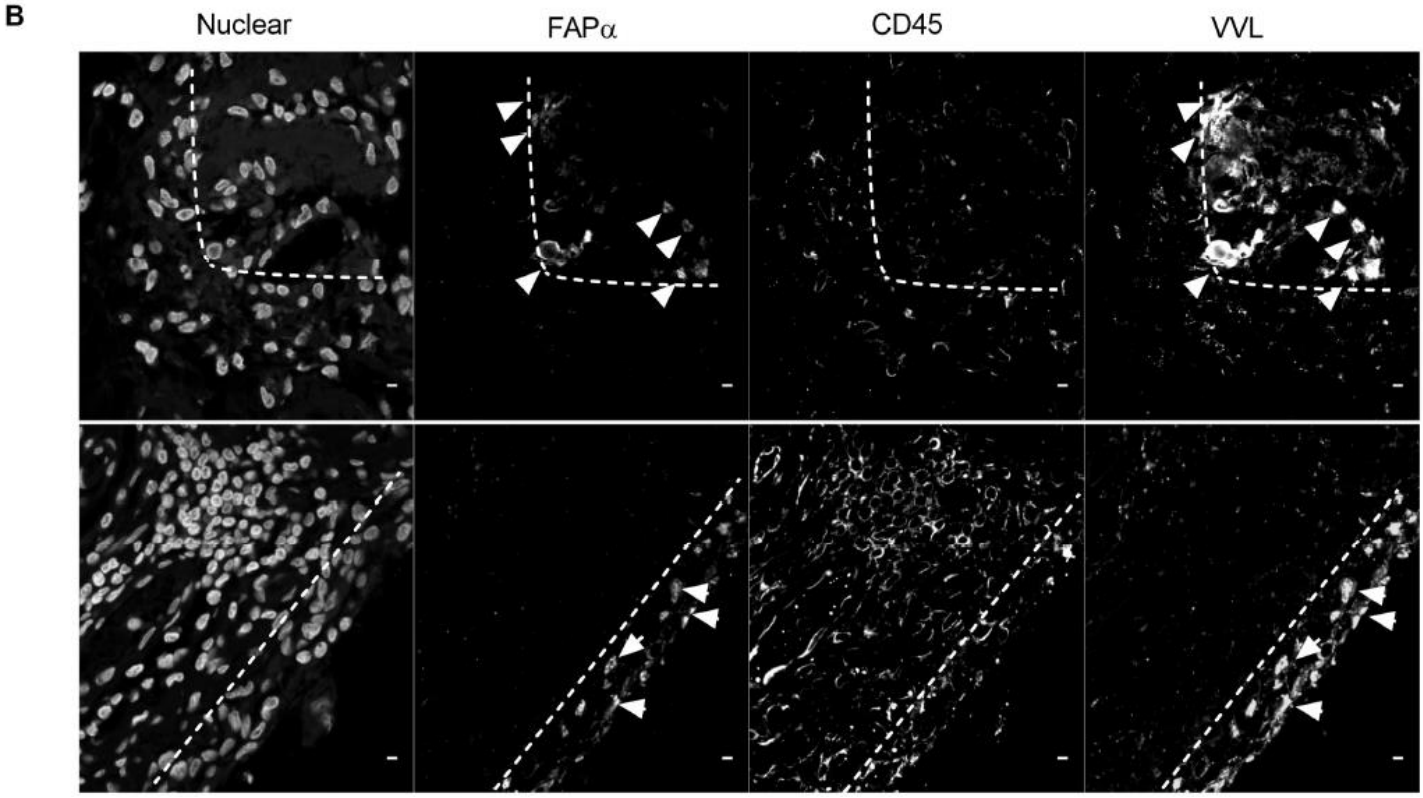


FIG. 6

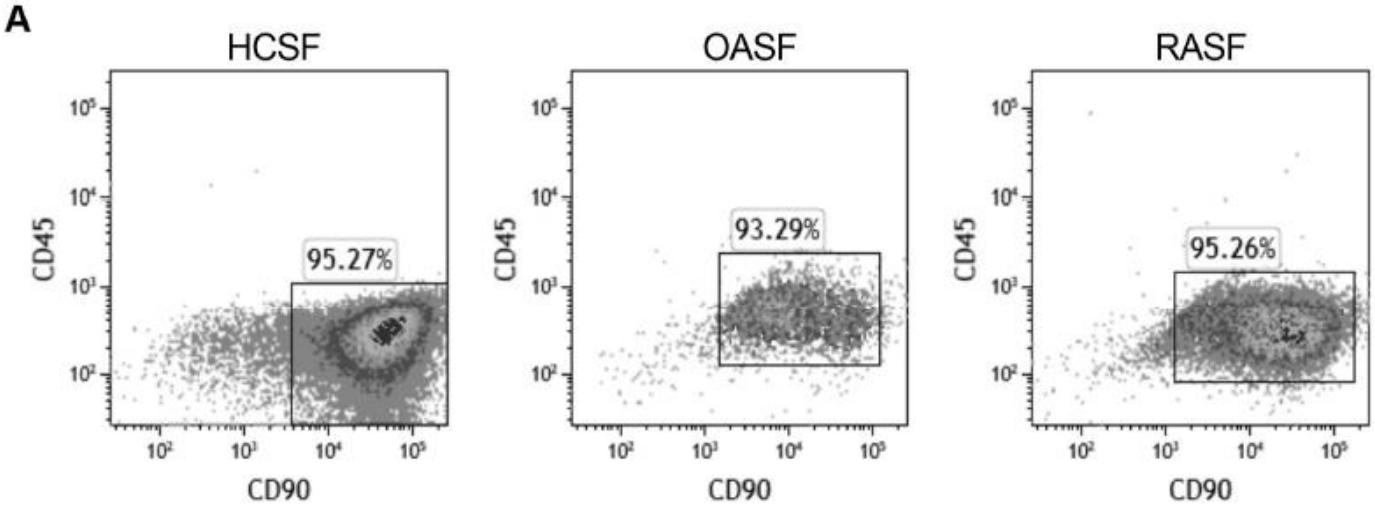
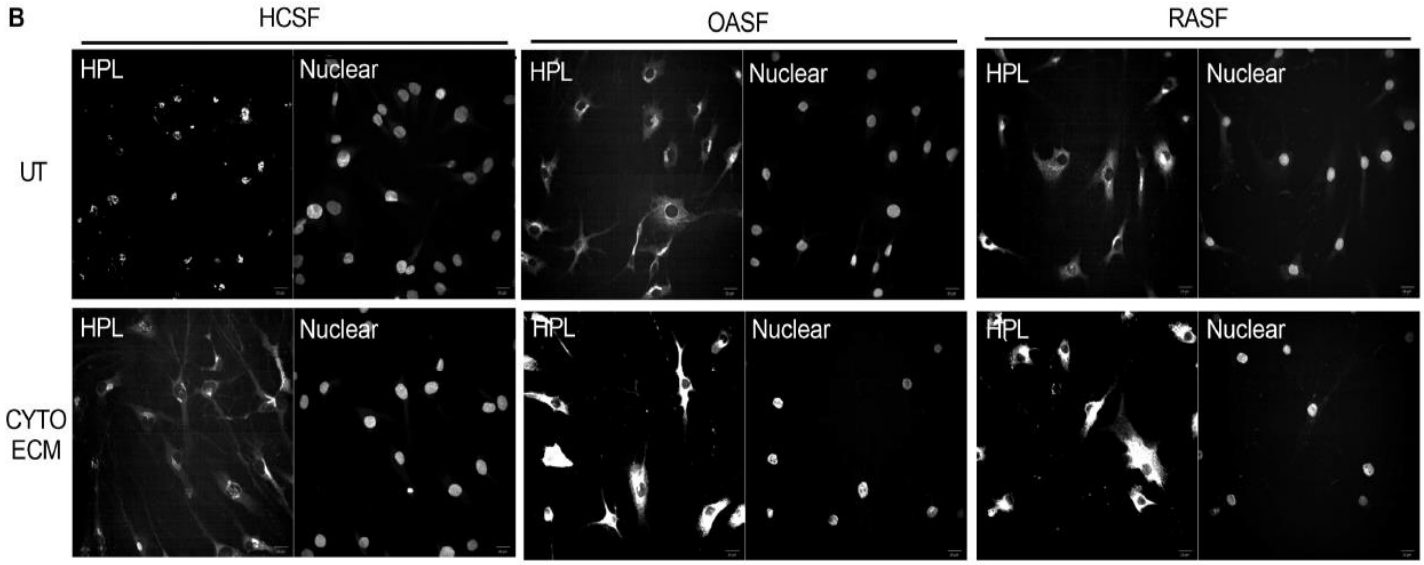


FIG. 6 continued



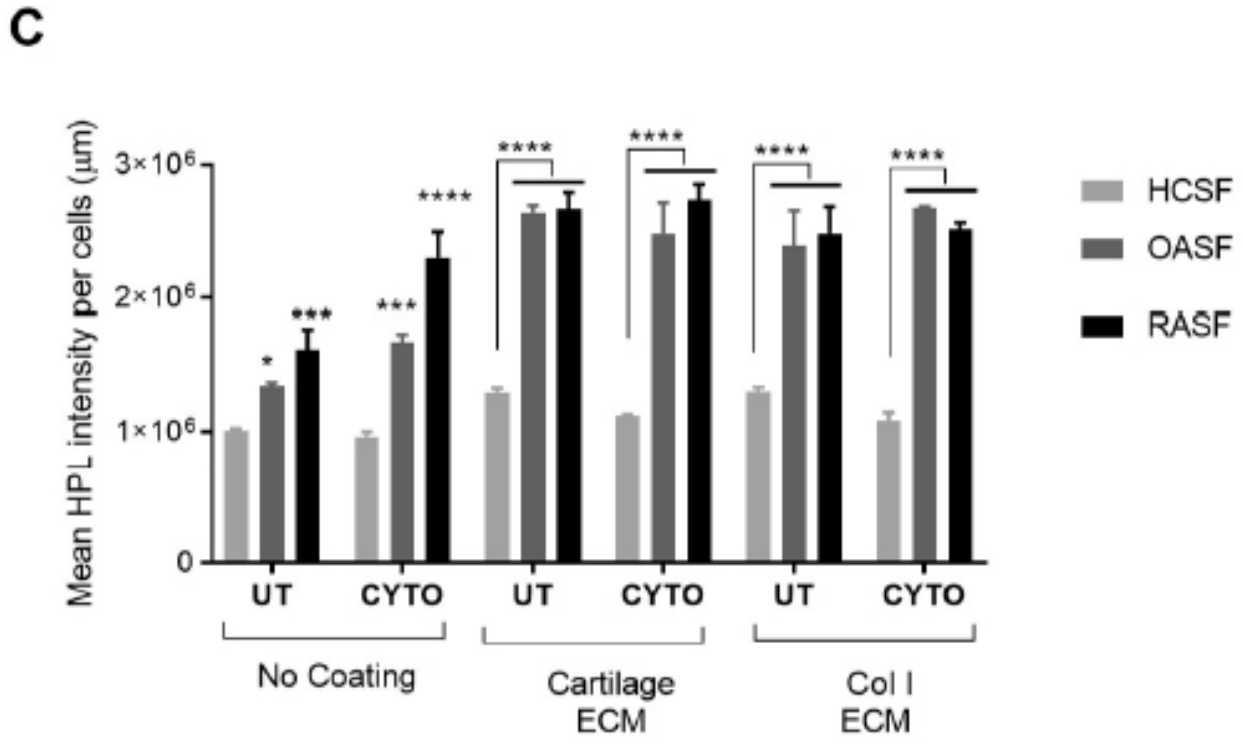


FIG. 7

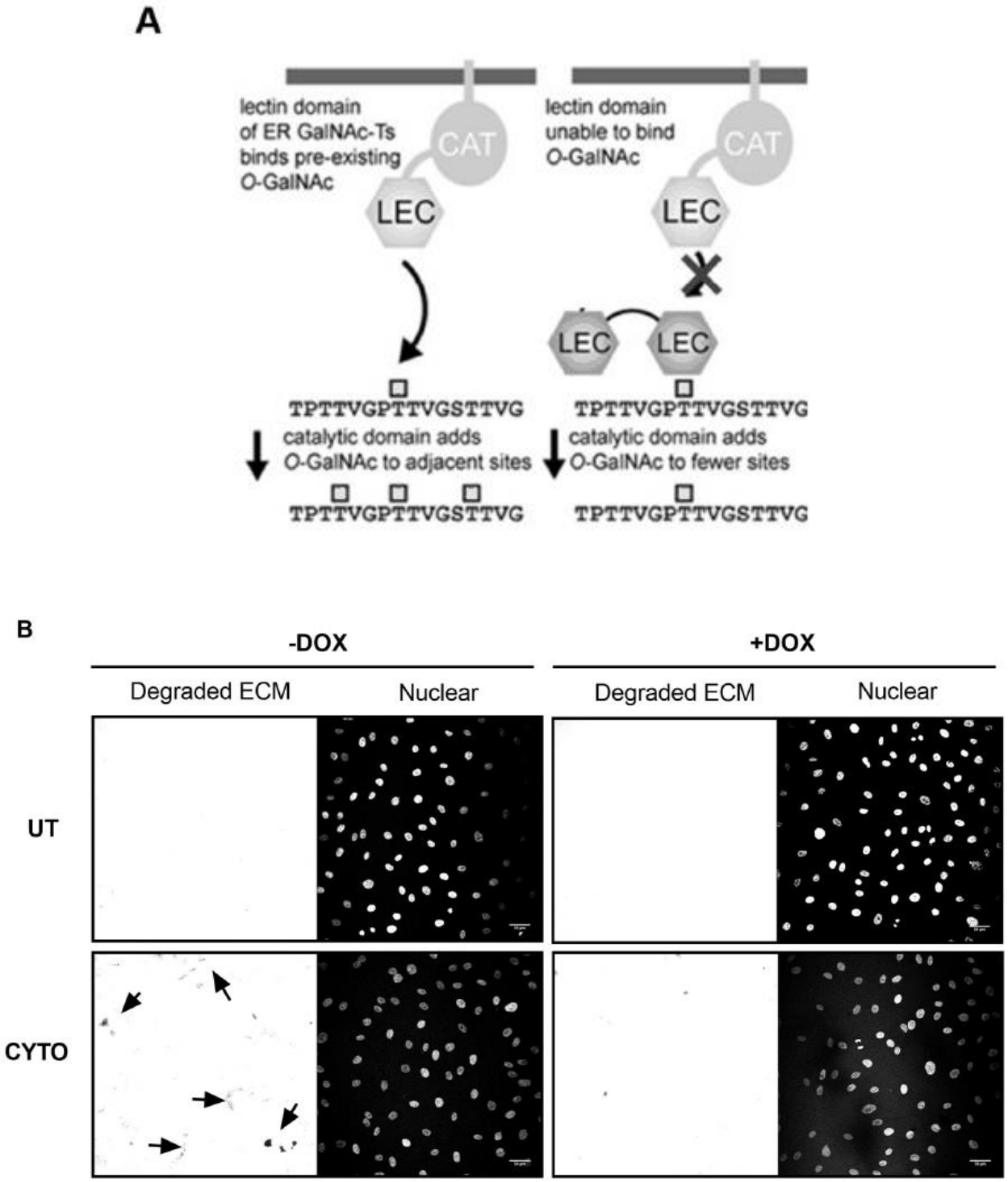

A
lectin domain
of ER GalNAc-Ts
binds pre-existing
O-GalNAc
CAT
LEC
lectin domain
unable to bind
O-GalNAc
CAT
LEC
LEC
LEC
TPTTVGPTTVGSTTVG
TPTTVGPTTVGSTTVG
catalytic domain adds
O-GalNAc to adjacent sites
catalytic domain adds
O-GalNAc to fewer sites
TPTTVGPTTVGSTTVG
TPTTVGPTTVGSTTVG
B
-DOX
+DOX
Degraded ECM
Nuclear
Degraded ECM
Nuclear
UT
CYTO

FIG. 7 continued

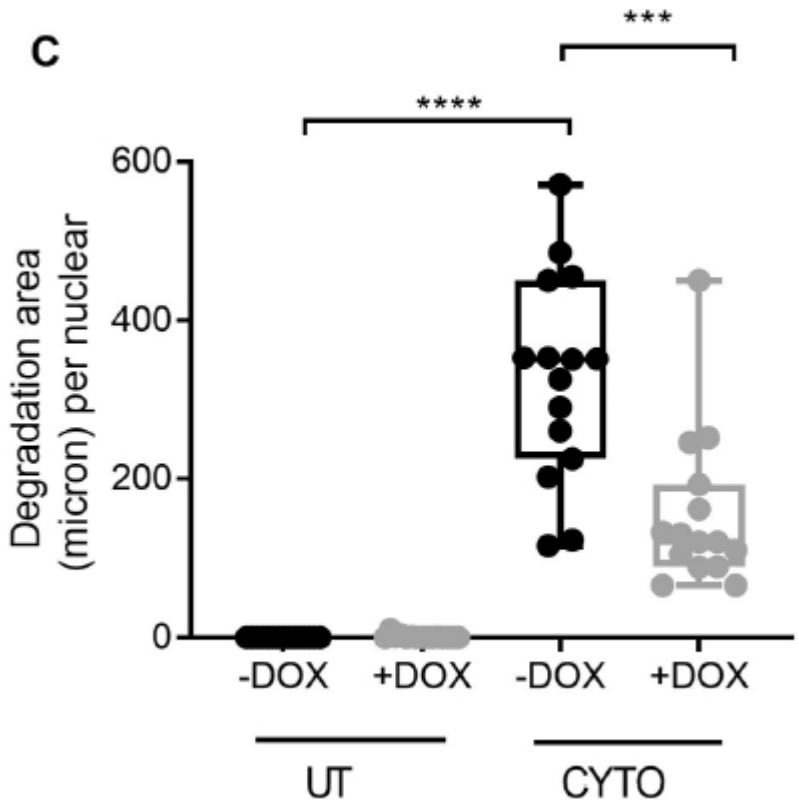


FIG. 8

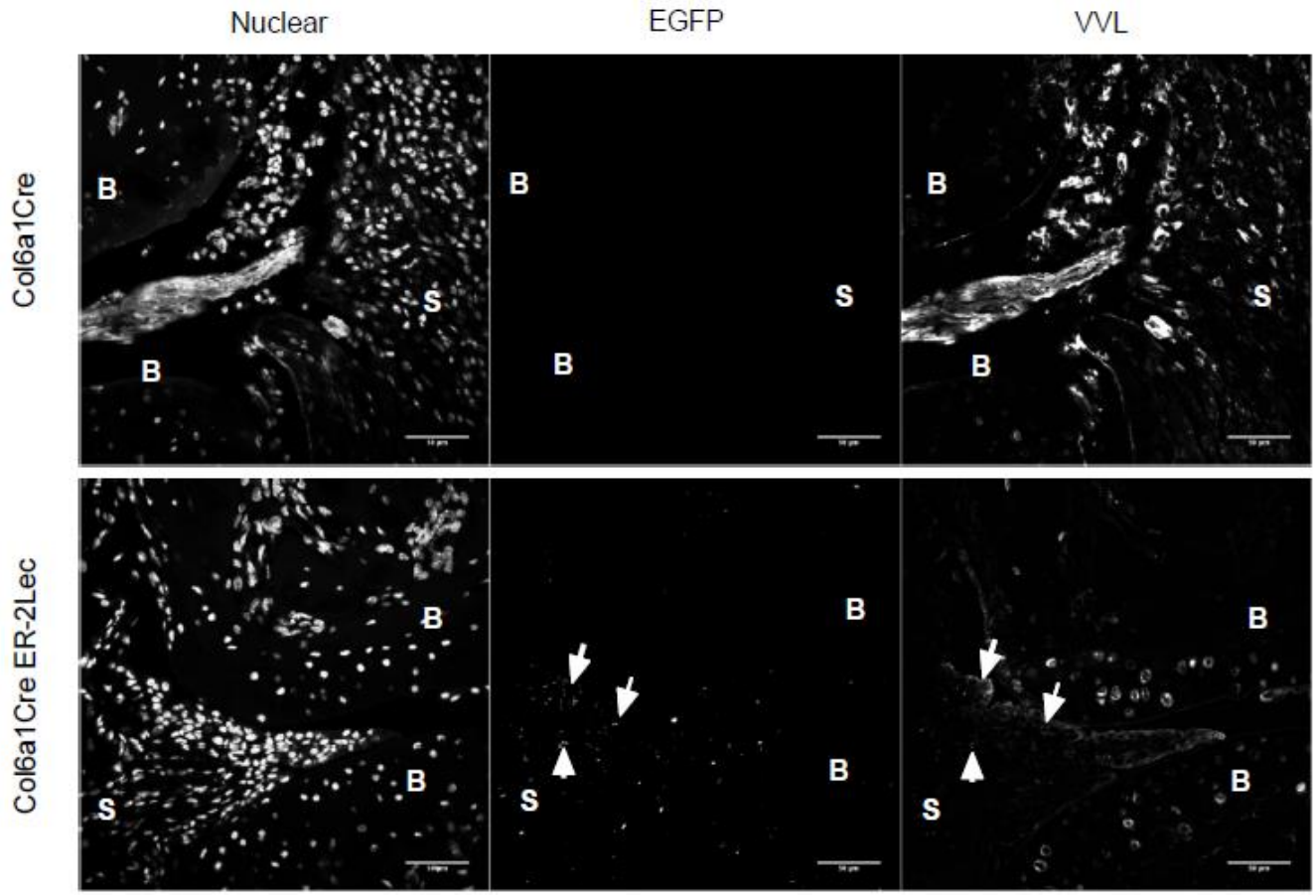

Nuclear
EGFP
VVL
Col6a1Cre
Col6a1Cre ER-2Lec
B
S

FIG. 9

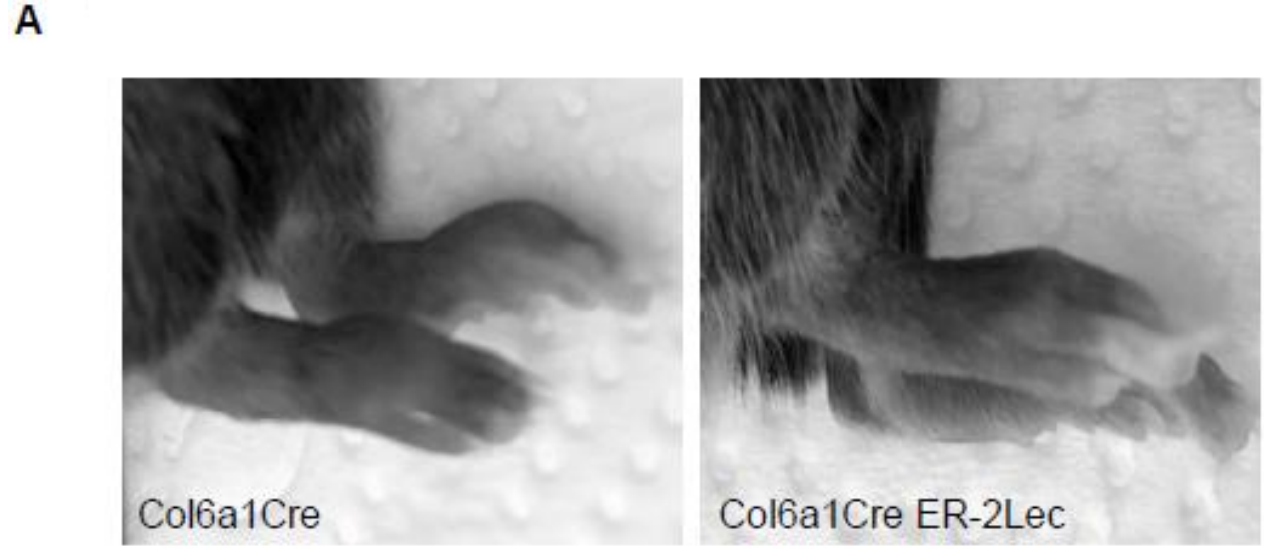

A
Col6a1Cre
Col6a1Cre ER-2Lec

FIG. 9 continued

B

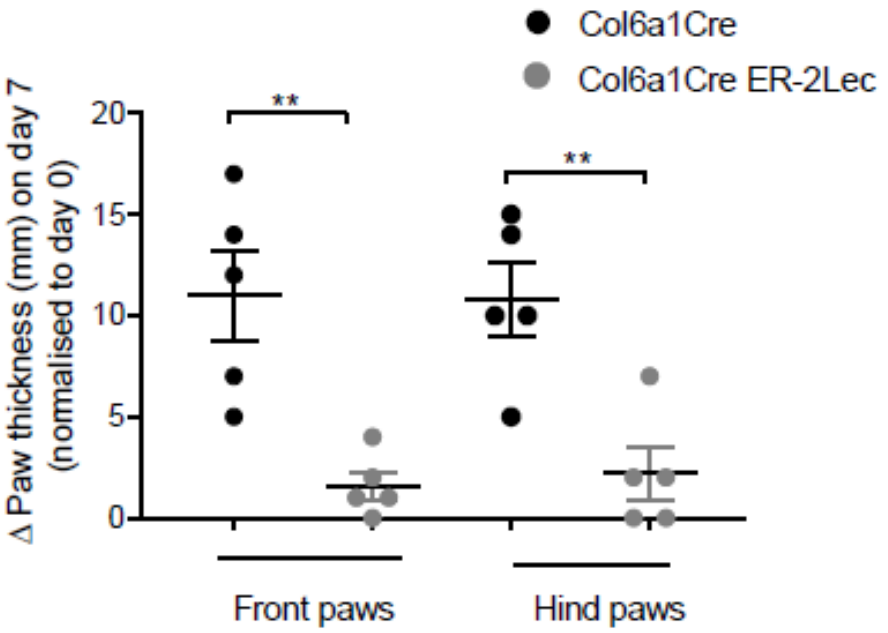


FIG. 10

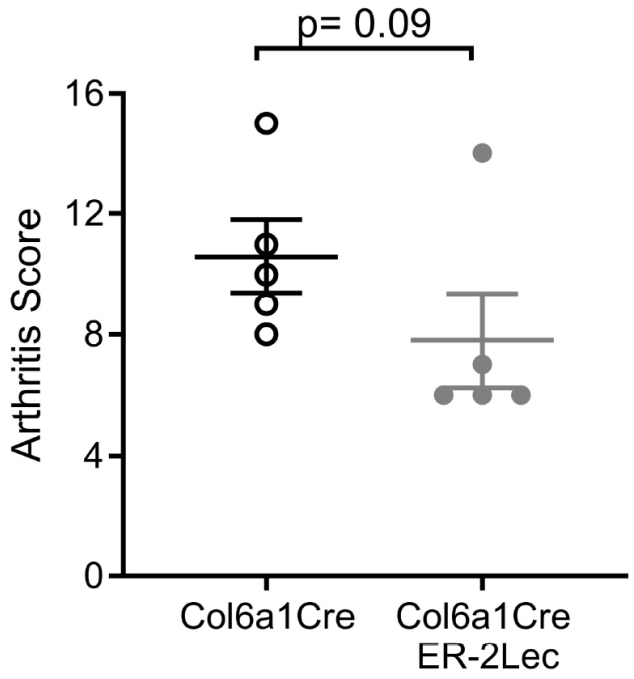


FIG. 11

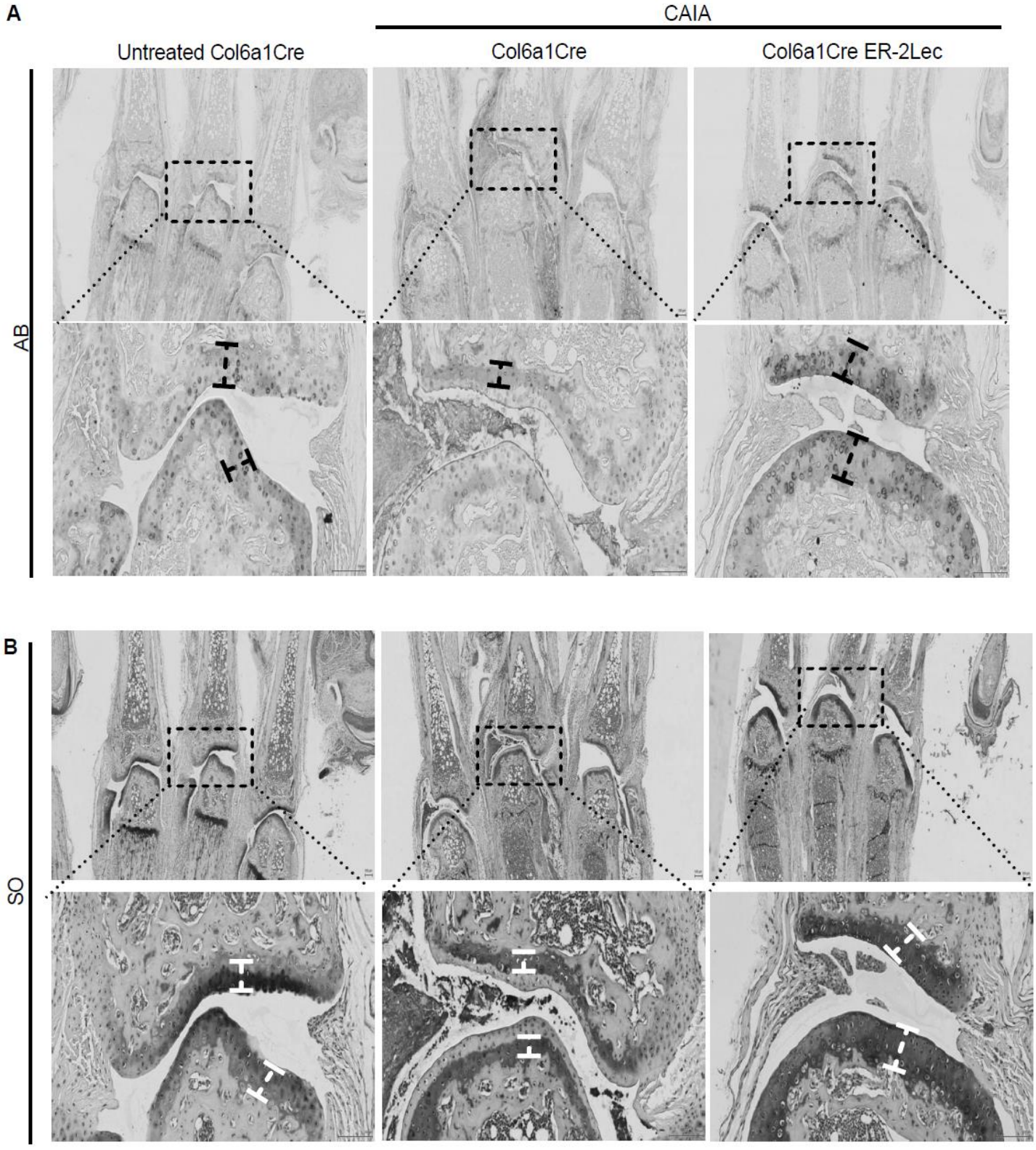

A
CAIA
Untreated Col6a1Cre
Col6a1Cre
Col6a1Cre ER-2Lec
AB
B
SO

FIG. 11 continued

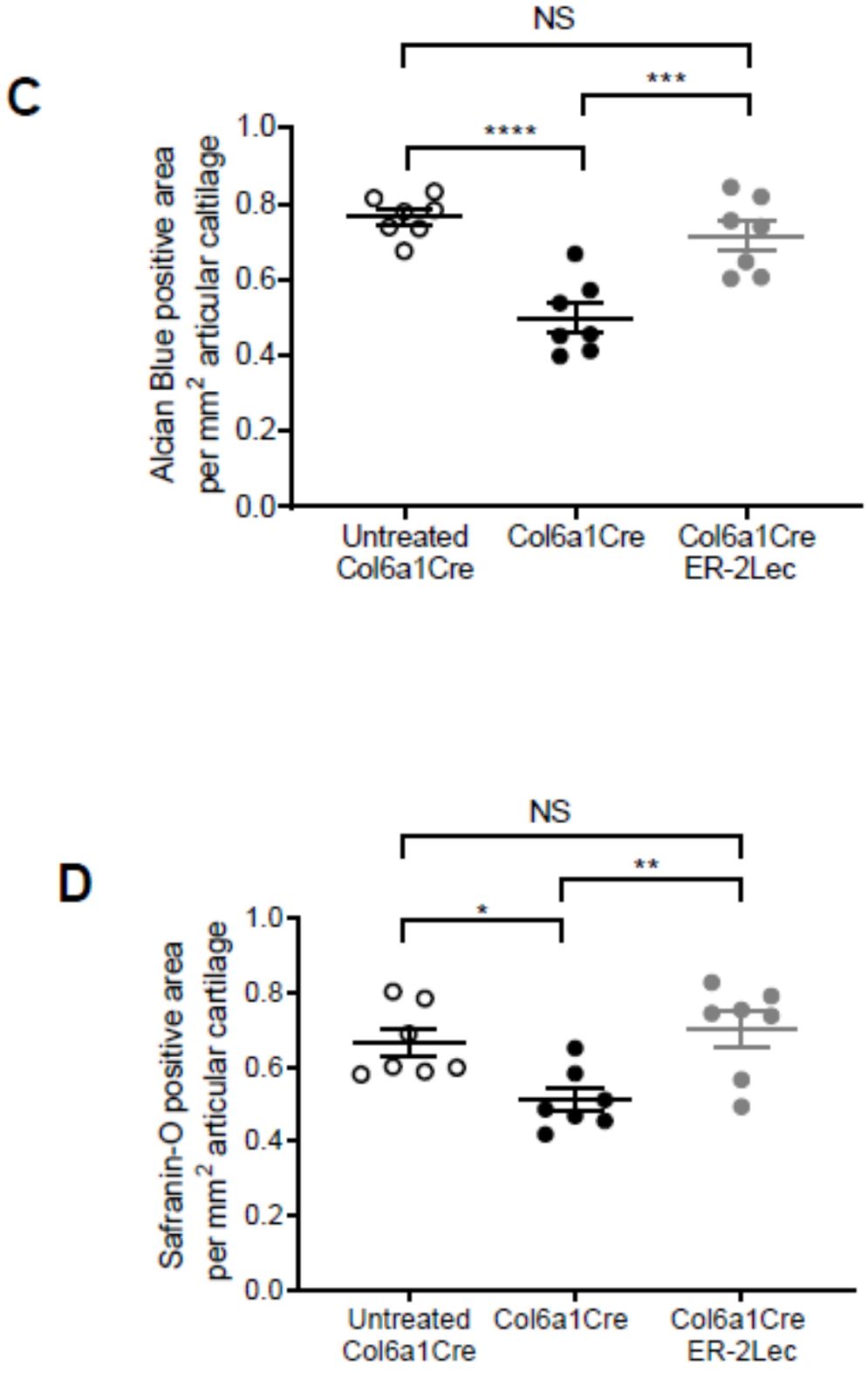


FIG. 12

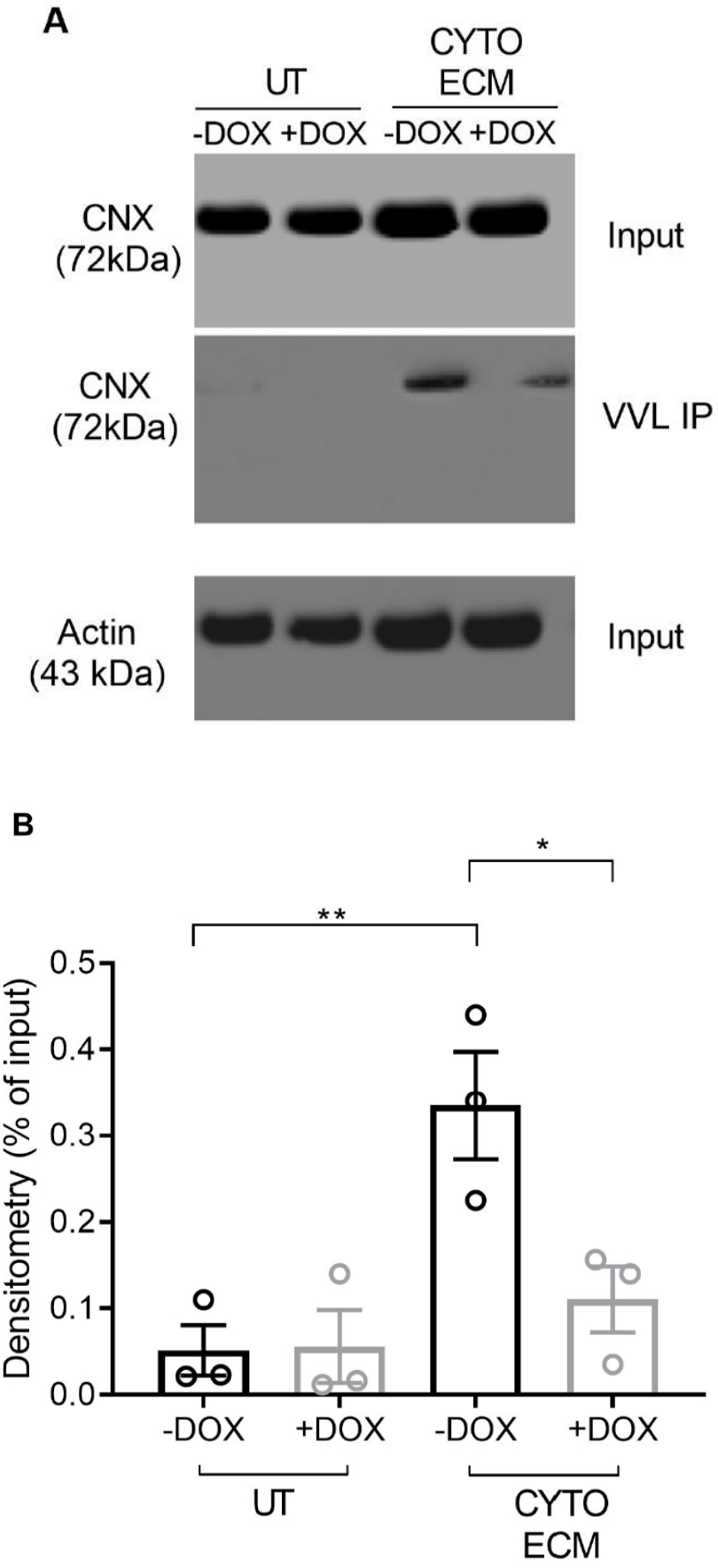

A
UT
CYTO ECM
-DOX +DOX -DOX +DOX
CNX (72kDa)
Input
CNX (72kDa)
VVL IP
Actin (43 kDa)
Input
B
*
**
Densitometry (% of input)
0.5
0.4
0.3
0.2
0.1
0.0
-DOX
+DOX
-DOX
+DOX
UT
CYTO ECM

FIG. 13

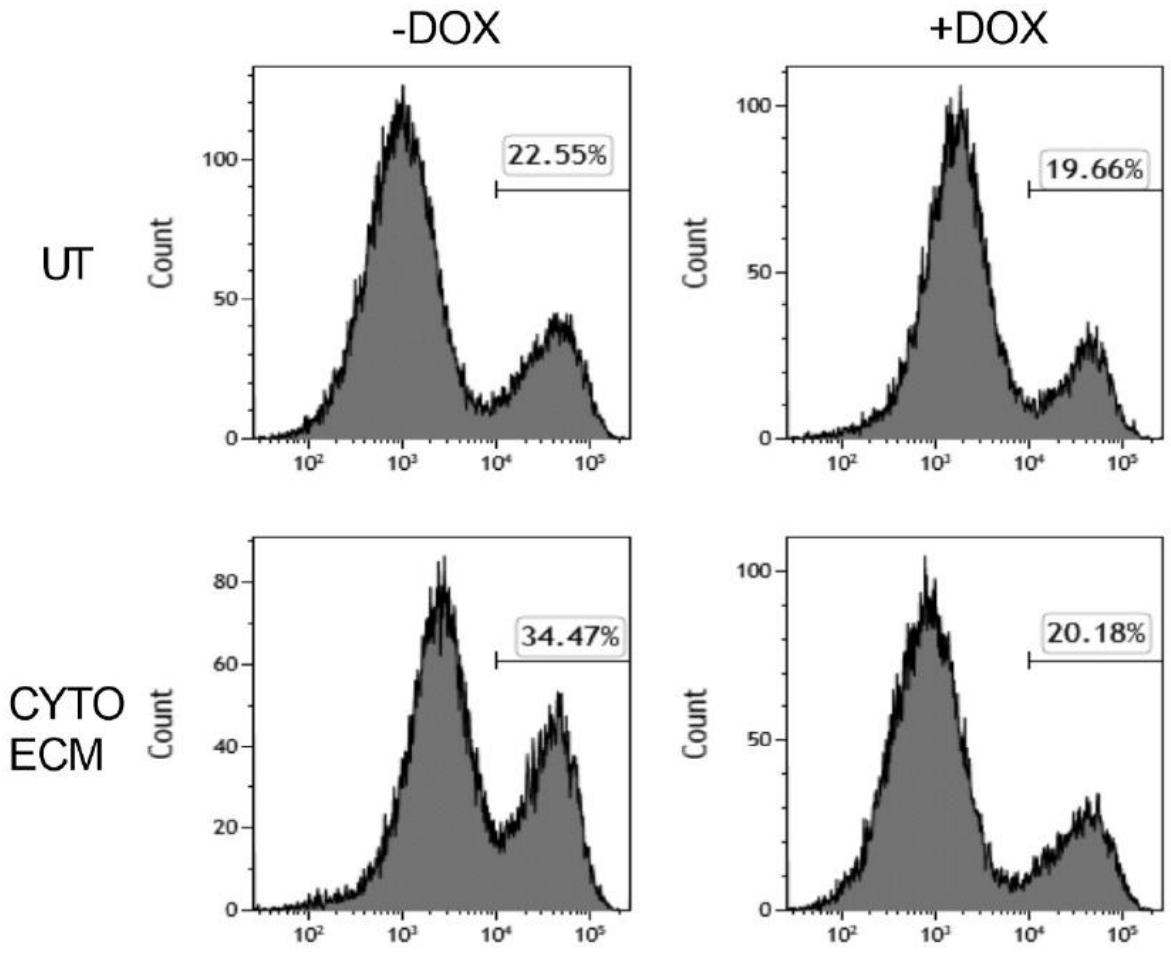


FIG. 13 continued

B

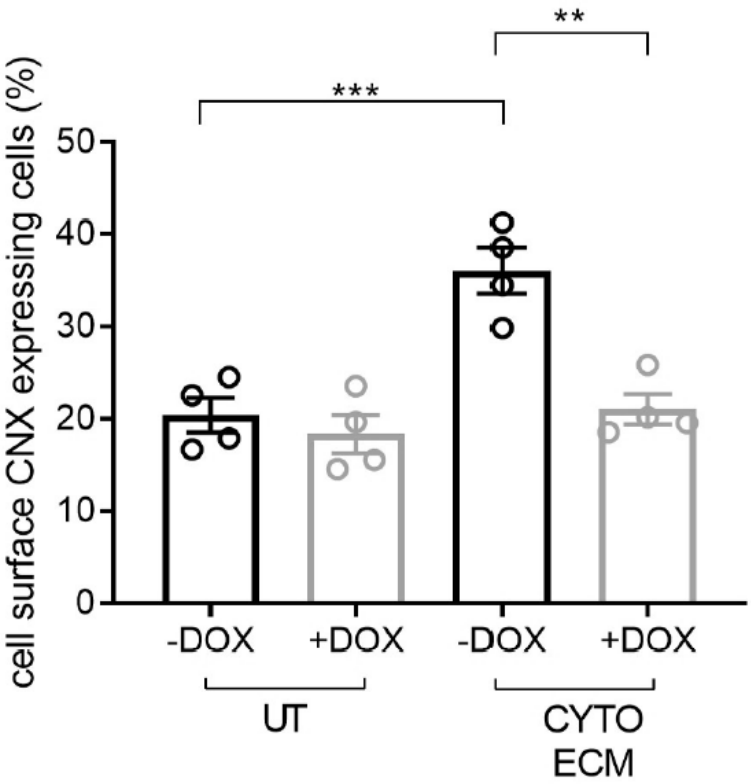


FIG. 14

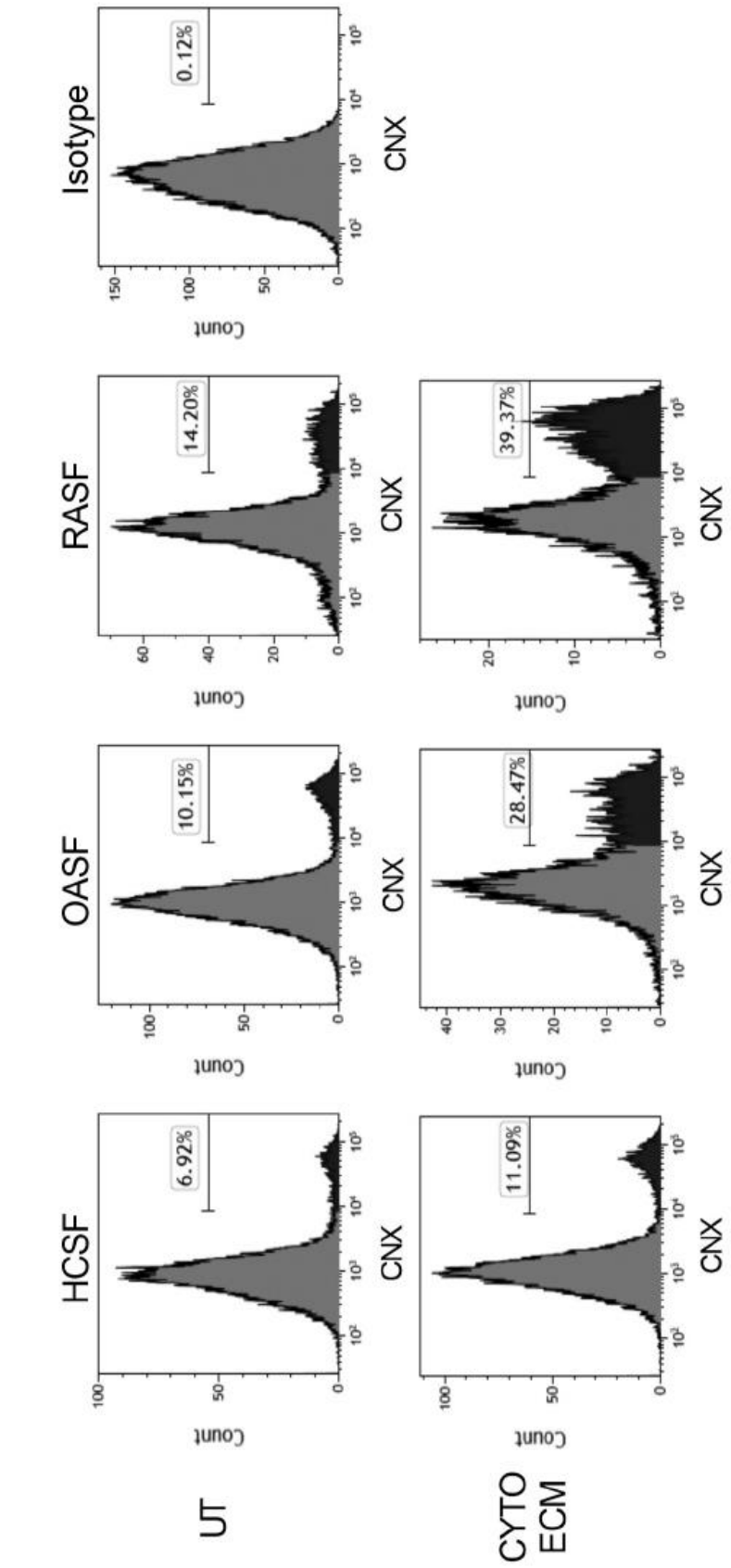

A
UT
CYTO ECM
HCSF
OASF
RASF
Isotype
CNX
Count
6.92%
10.15%
14.20%
0.12%
11.09%
28.47%
39.37%

FIG. 14 continued

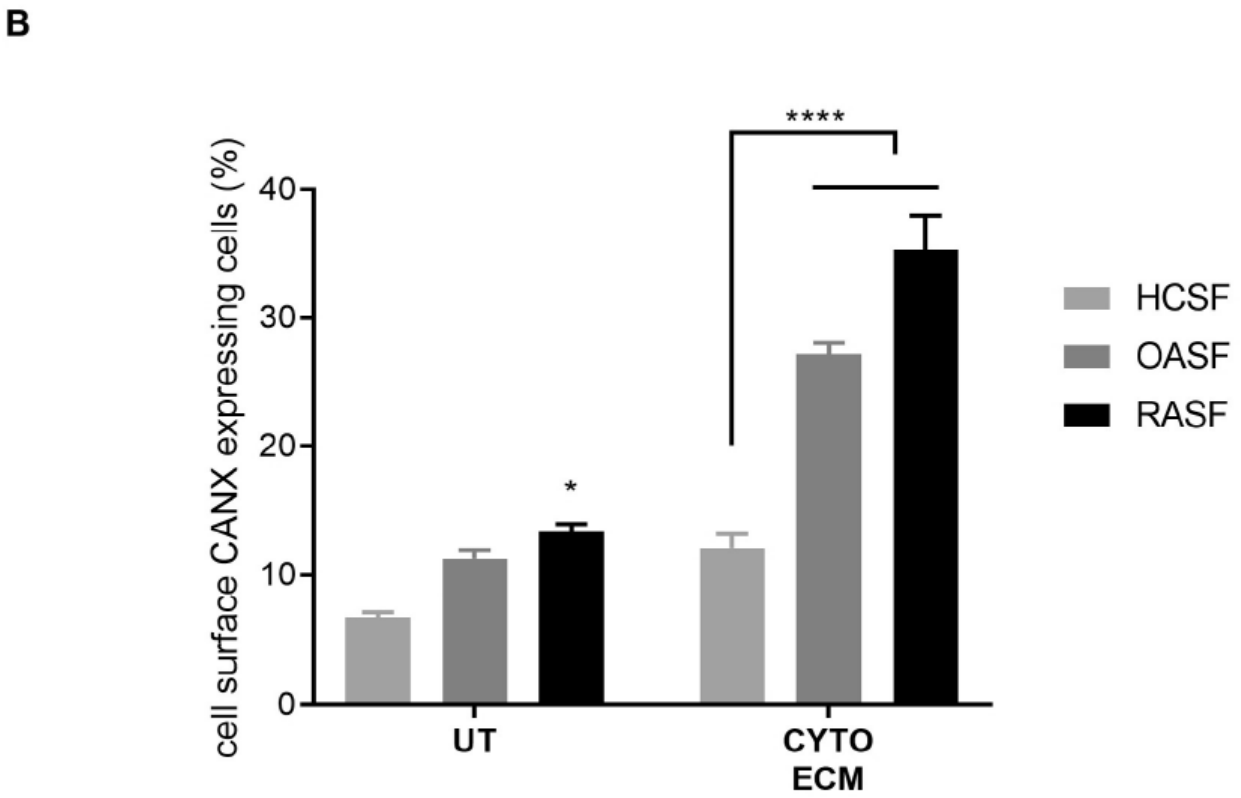


FIG. 15

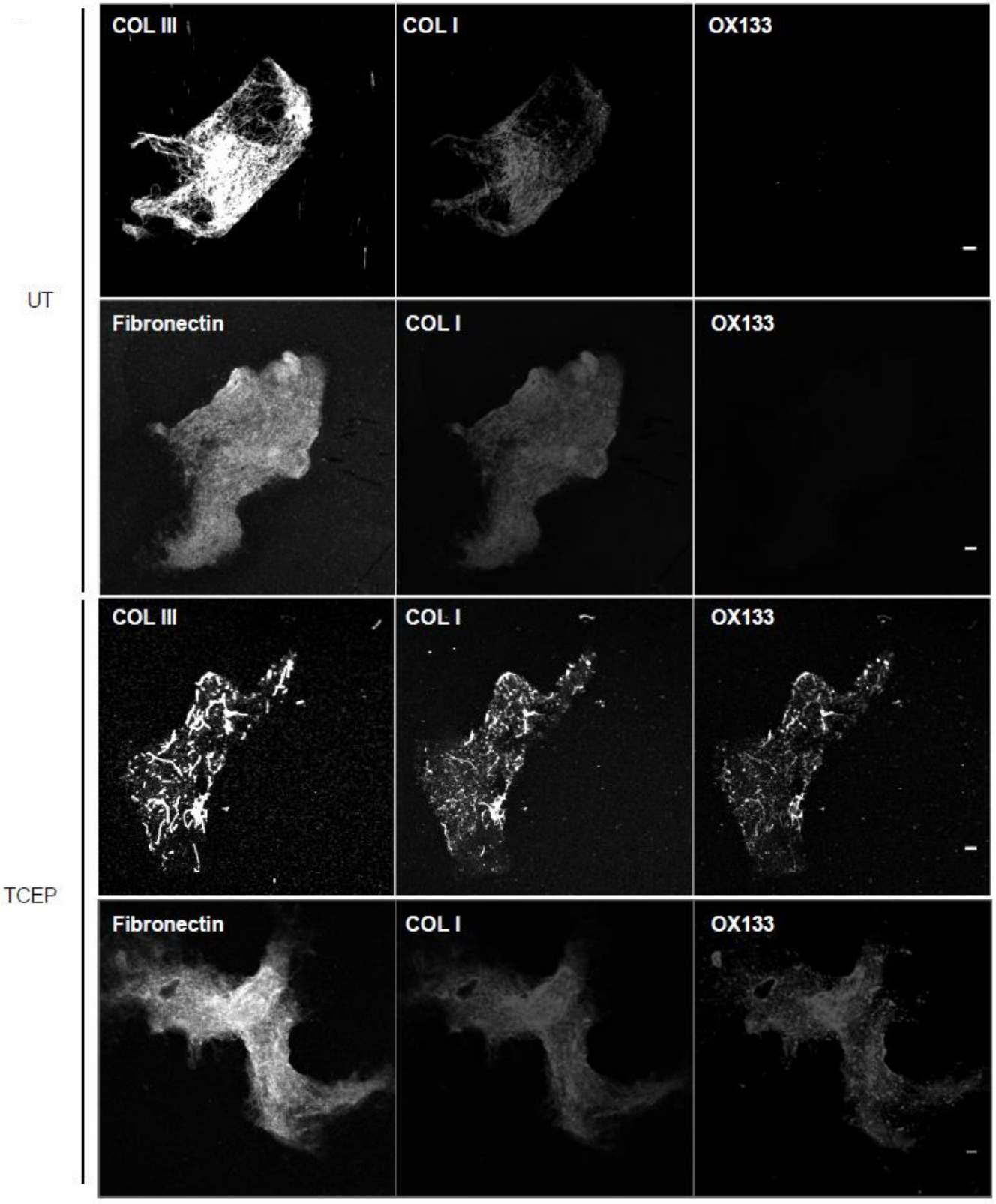

UT
TCEP
COL III
COL I
OX133
Fibronectin
COL I
OX133
COL III
COL I
OX133
Fibronectin
COL I
OX133

FIG. 16

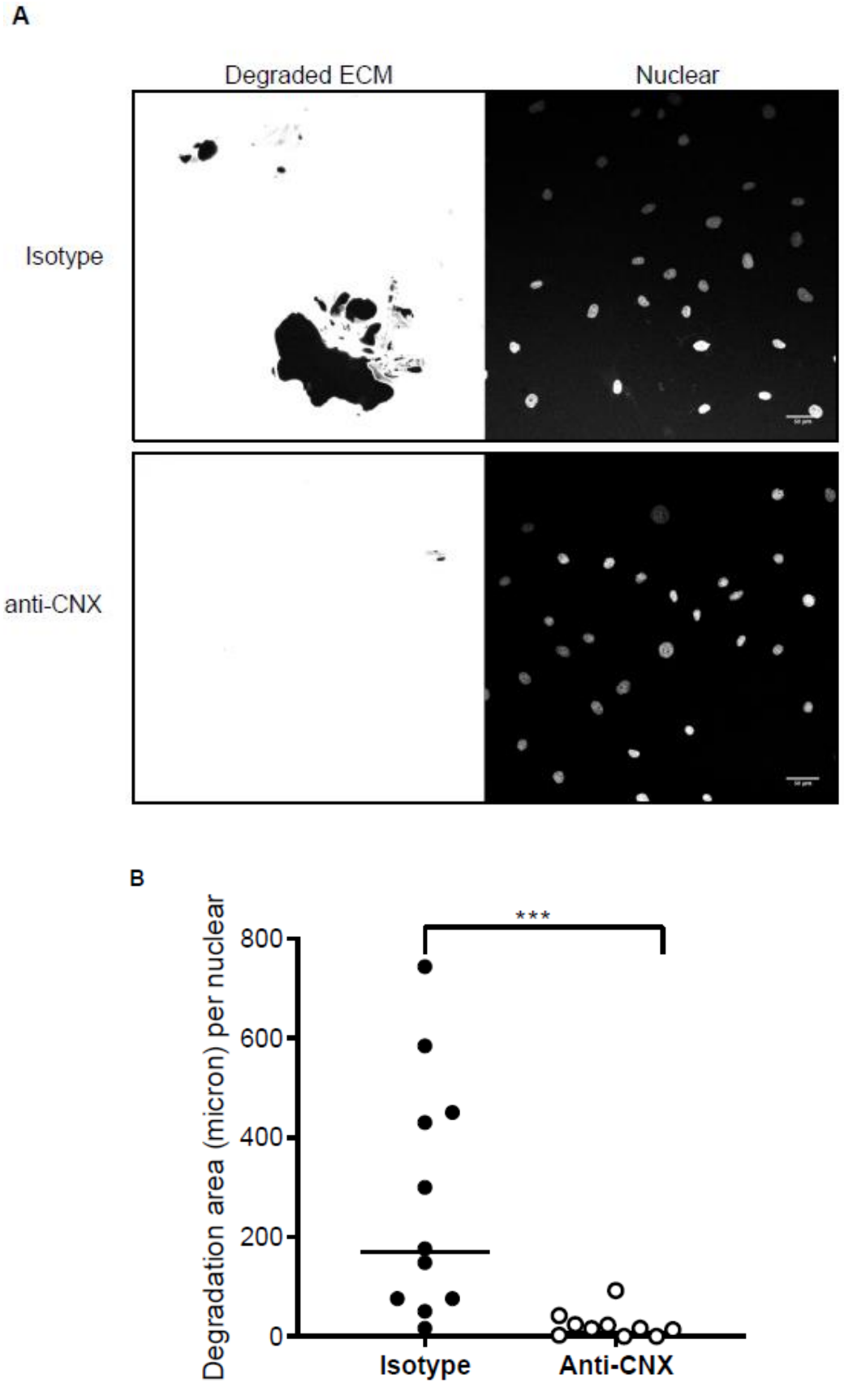

A
Degraded ECM
Nuclear
Isotype
anti-CNX
B
***
Degradation area (micron) per nuclear
800
600
400
200
0
Isotype
Anti-CNX

FIG. 17

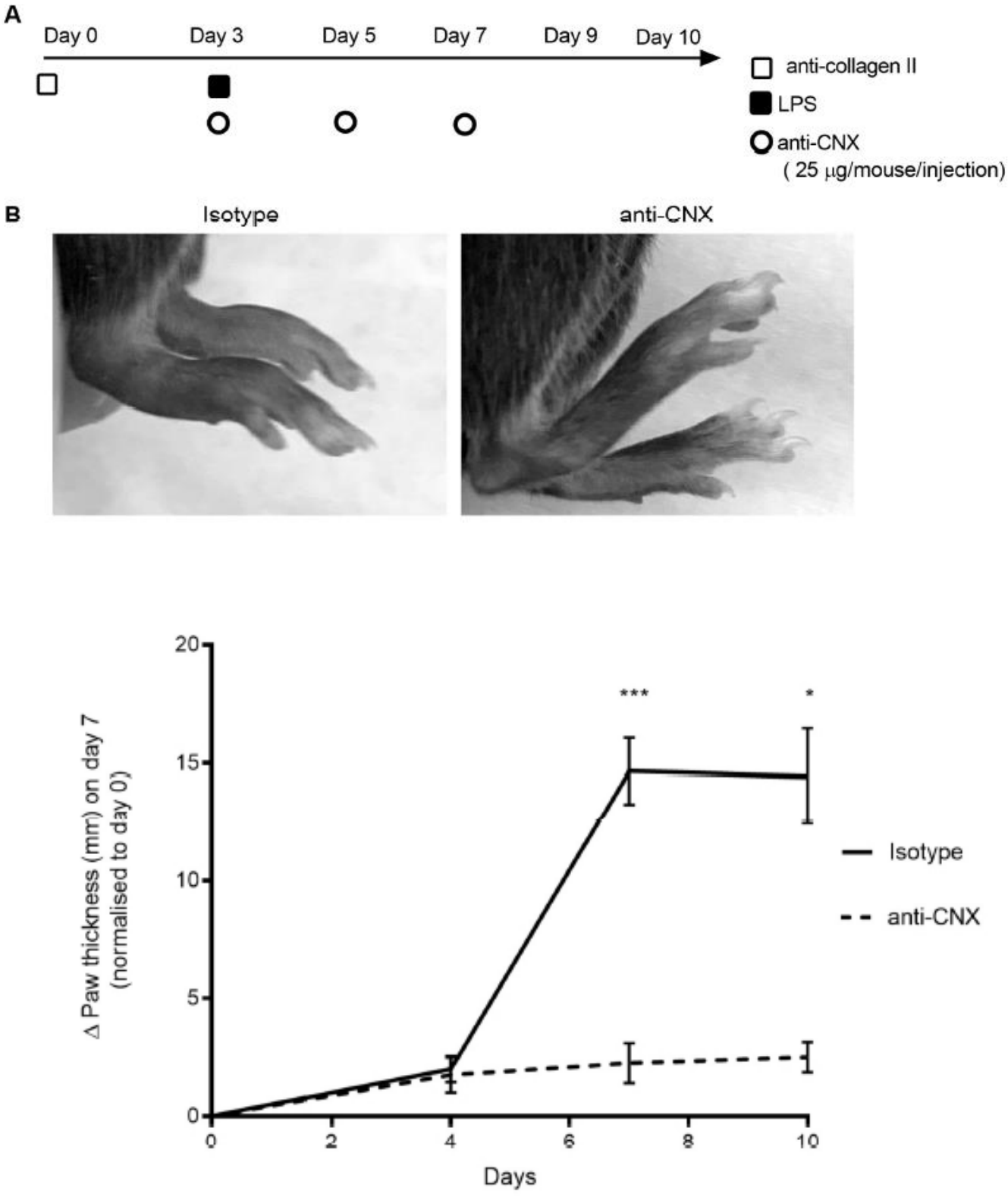

A
Day 0
Day 3
Day 5
Day 7
Day 9
Day 10
anti-collagen II
LPS
anti-CNX
(25 μg/mouse/injection)
B
Isotype
anti-CNX
C
Δ Paw thickness (mm) on day 7
(normalised to day 0)
20
15
10
5
0
0
2
4
6
8
10
Days
***
*
Isotype
anti-CNX

FIG. 18

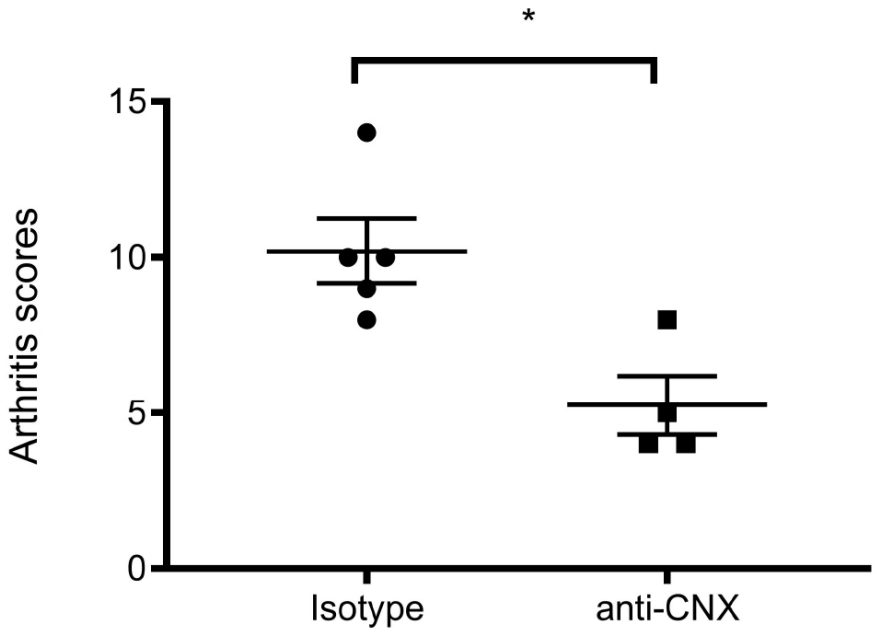

*
15
10
5
0
Arthritis scores
Isotype
anti-CNX

FIG. 19

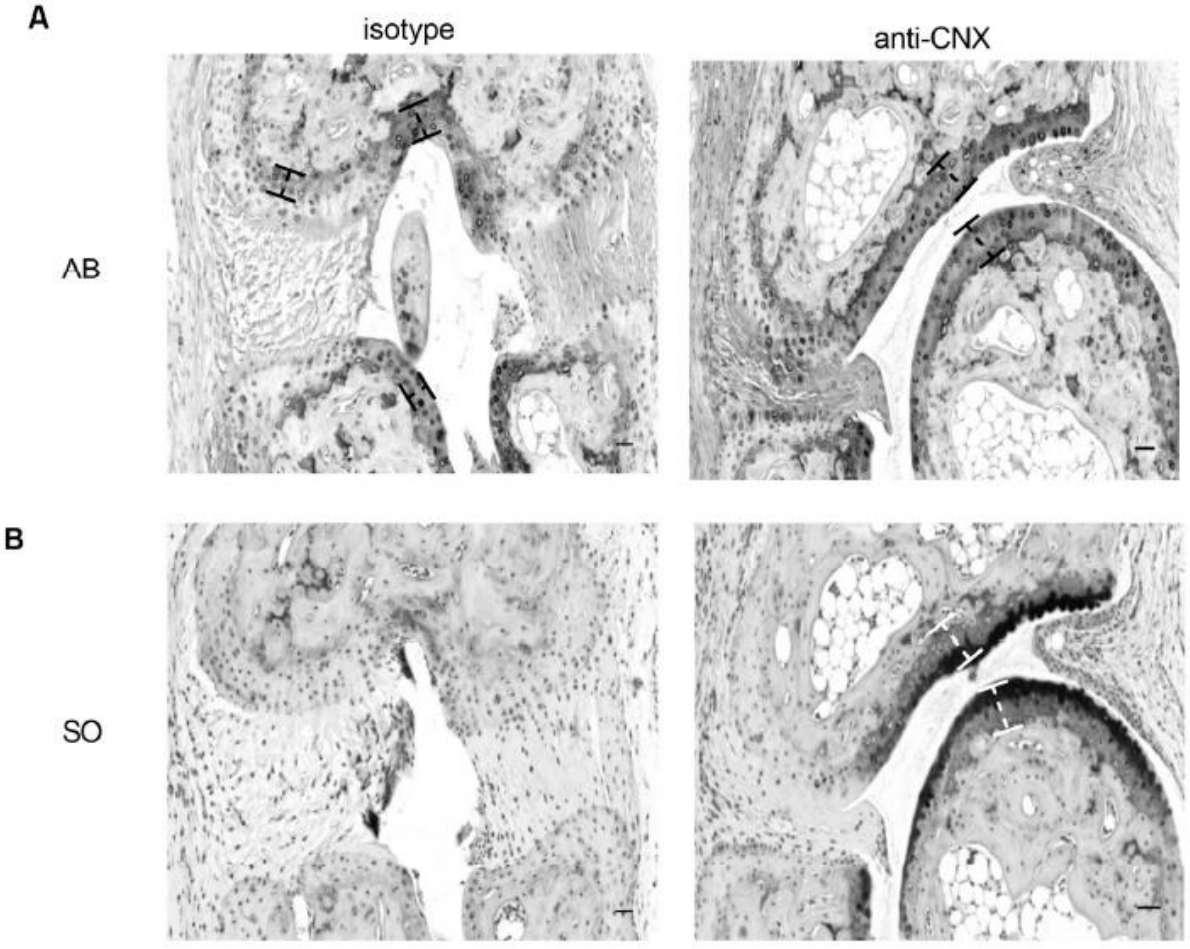

A
isotype
anti-CNX
AB
B
SO

FIG. 19 continued

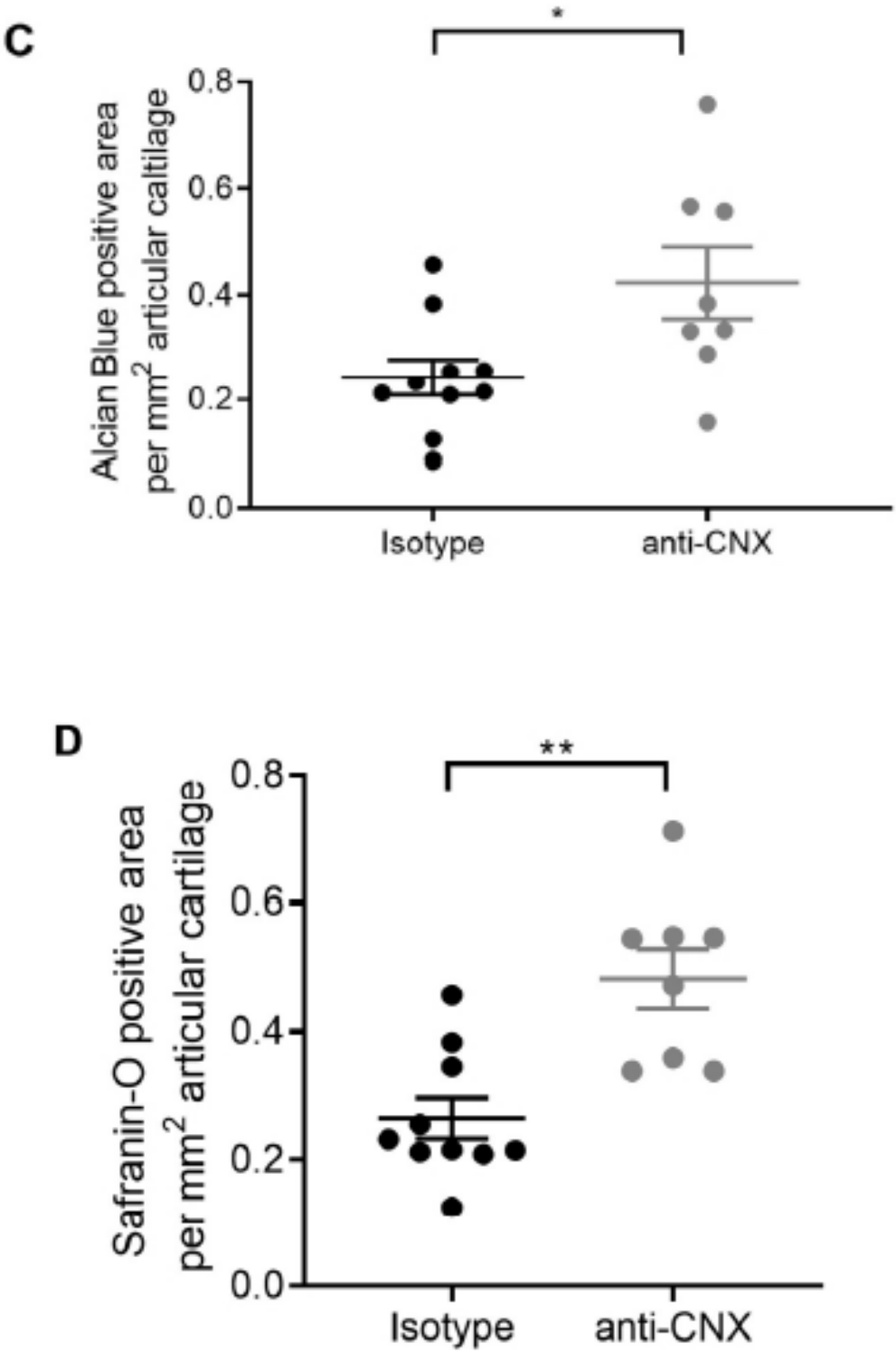


FIG. 20

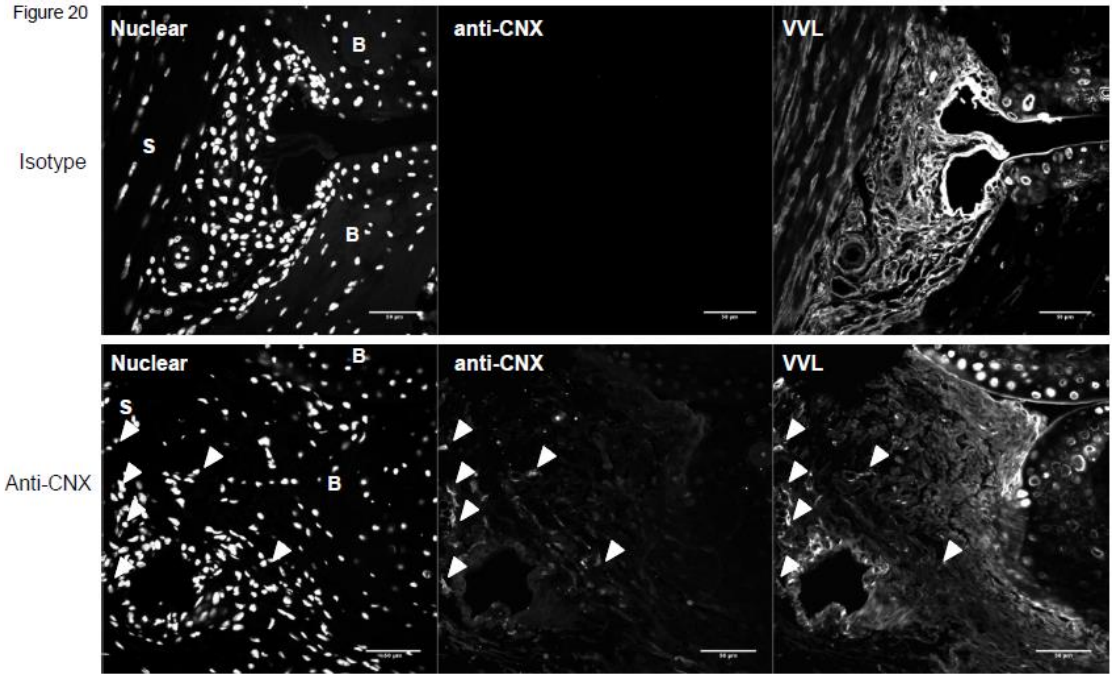


Figure 20
Nuclear
anti-CNX
VVL
Isotype
Anti-CNX
B
S

FIG. 21

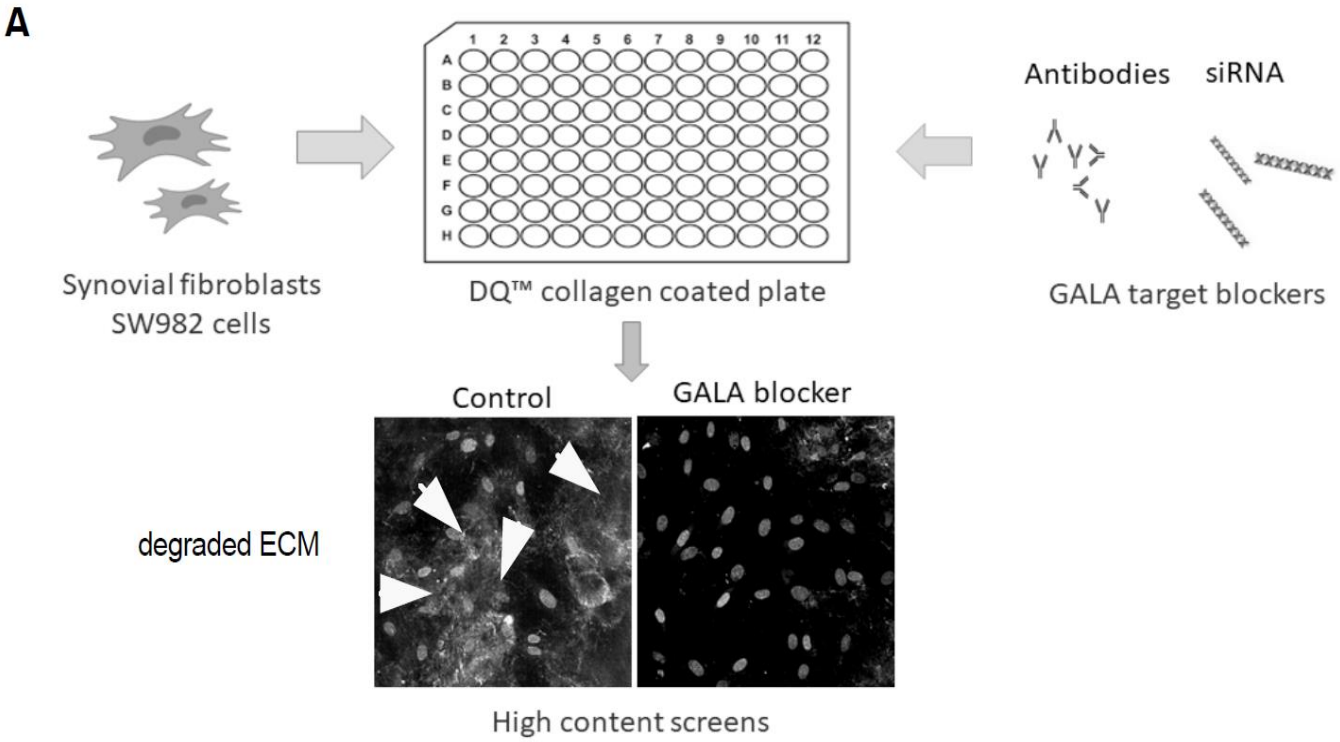
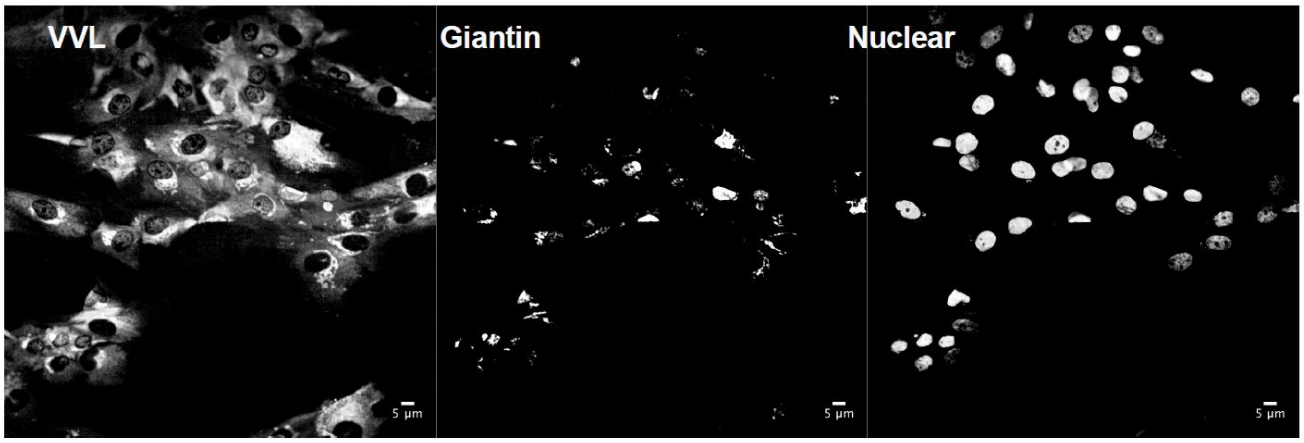

A
Synovial fibroblasts
SW982 cells
DQ™ collagen coated plate
Antibodies
siRNA
GALA target blockers
Control
GALA blocker
degraded ECM
High content screens

FIG. 21 continued

B



C

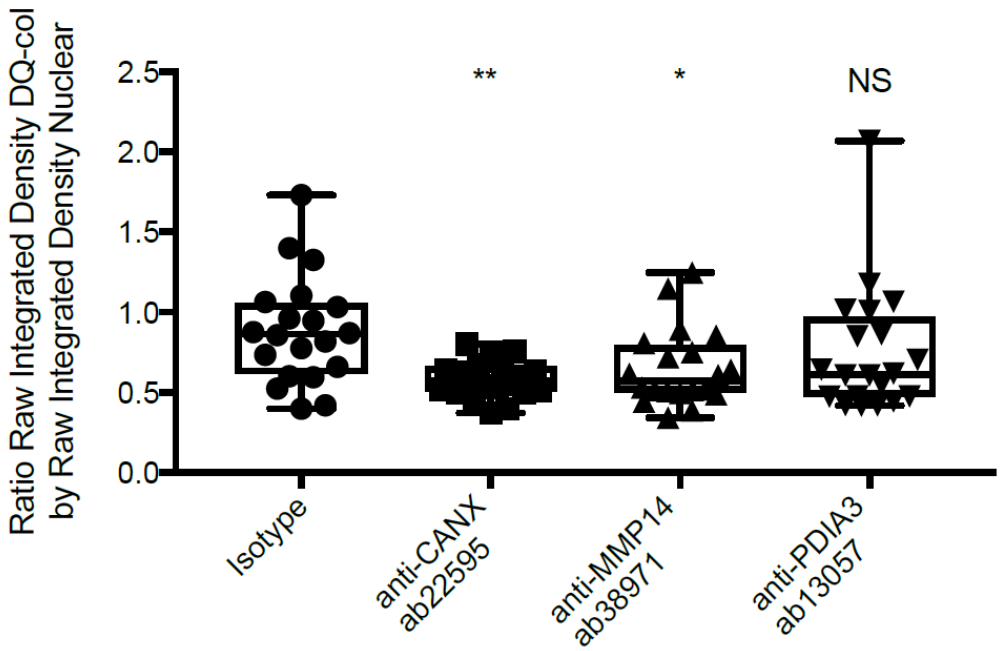
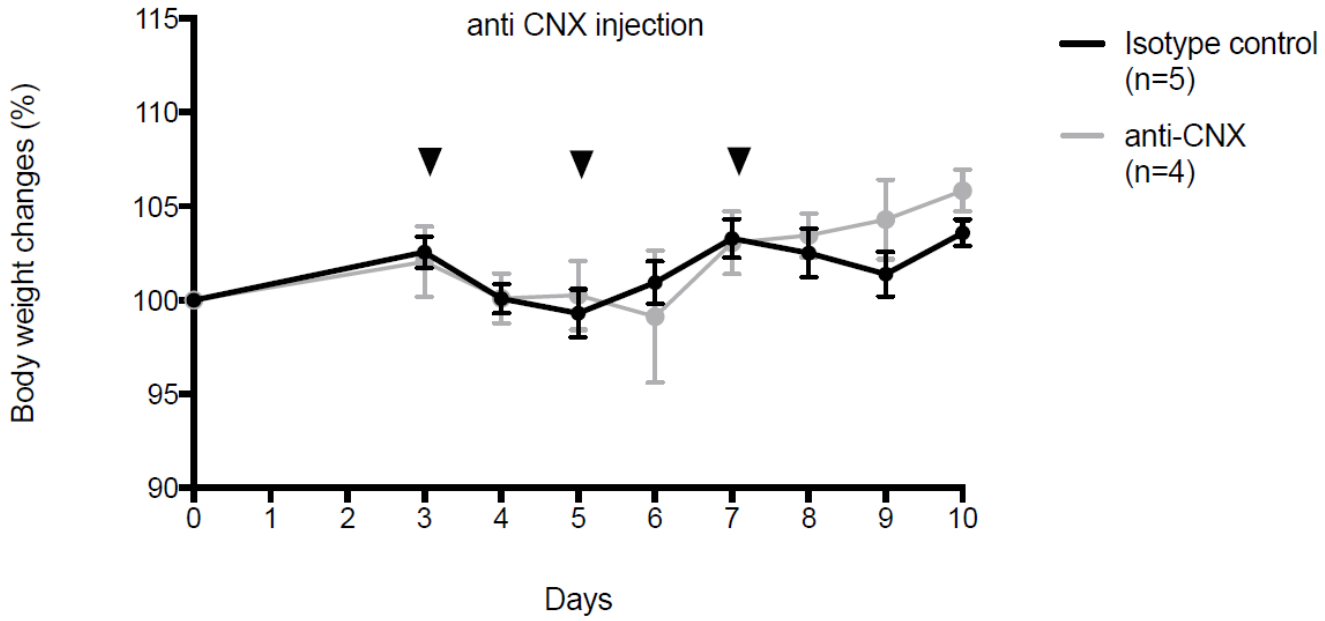


FIG. 22


anti CNX injection
Body weight changes (%)
115
110
105
100
95
90
0
1
2
3
4
5
6
7
8
9
10
Days
Isotype control (n=5)
anti-CNX (n=4)