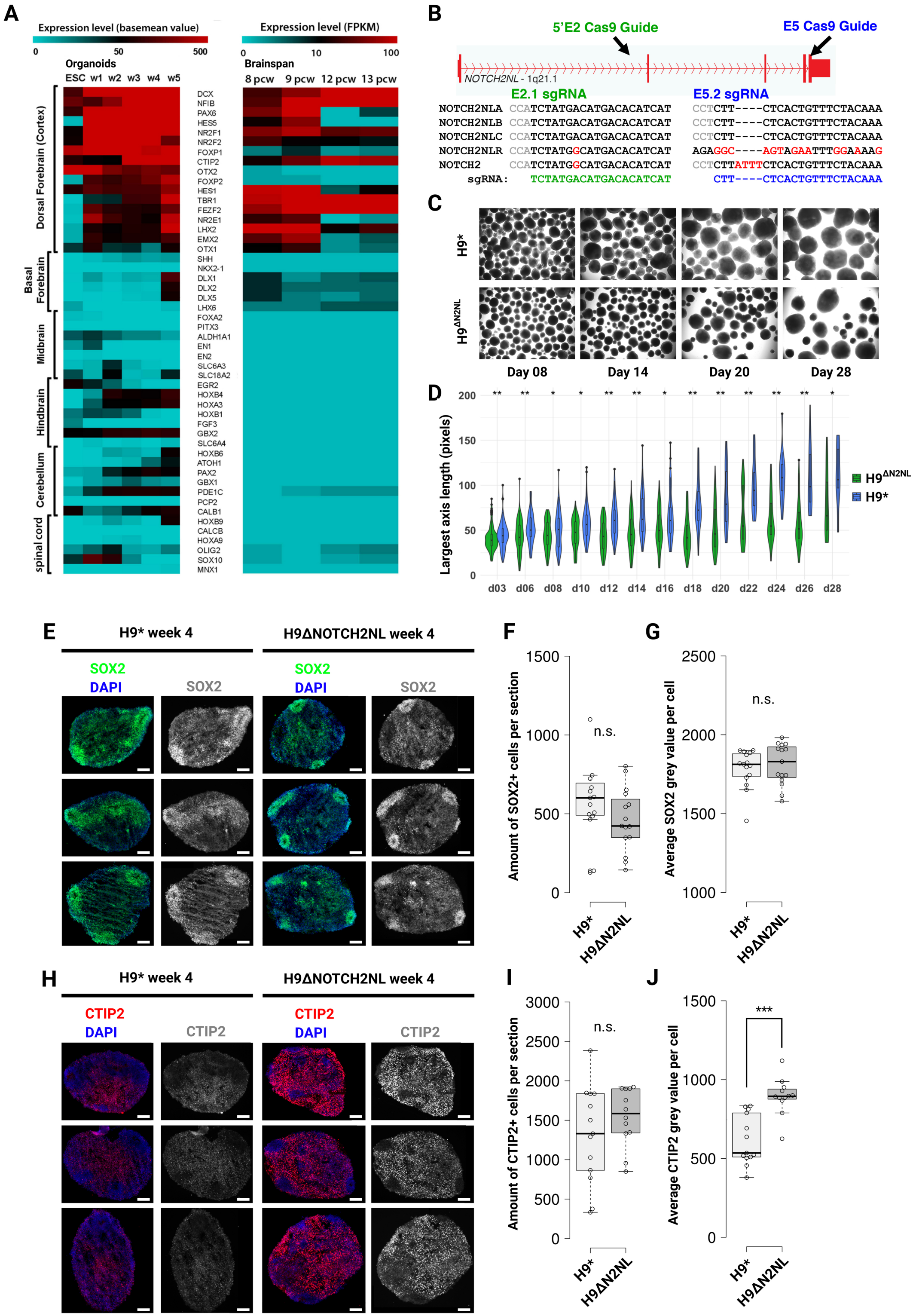
A
Expression level (basemean value)
0
50
500
Organoids
ESC w1 w2 w3 w4 w5
Expression level (FPKM)
0
10
100
Brainspan
8 pcw 9 pcw 12 pcw 13 pcw
Dorsal Forebrain (Cortex)
Basal Forebrain
Midbrain
Hindbrain
Cerebellum
spinal cord
DCX
NFIB
PAX6
HES5
NR2F1
NR2F2
FOXP1
CTIP2
OTX2
FOXP2
HES1
TBR1
FEZF2
NR2E1
LHX2
EMX2
OTX1
SHH
NKX2-1
DLX1
DLX2
DLX5
LHX6
FOXA2
PITX3
ALDH1A1
EN1
EN2
SLC6A3
SLC18A2
EGR2
HOXB4
HOXA3
HOXB1
FGF3
GBX2
SLC6A4
HOXB6
ATOH1
PAX2
GBX1
PDE1C
PCP2
CALB1
HOXB9
CALCB
HOXA9
OLIG2
SOX10
MNX1
B
5'E2 Cas9 Guide
E5 Cas9 Guide
NOTCH2NL - 1q21.1
E2.1 sgRNA
E5.2 sgRNA
NOTCH2NLA CCATCTATGACATGACACATCAT CCTCTT----CTCACTGTTTCTACAAA
NOTCH2NLB CCATCTATGACATGACACATCAT CCTCTT----CTCACTGTTTCTACAAA
NOTCH2NLC CCATCTATGACATGACACATCAT CCTCTT----CTCACTGTTTCTACAAA
NOTCH2NLR CCATCTATGGCATGACACATCAT AGAGGC----AGTAGAATTTGGAAAAG
NOTCH2 CCATCTATGGCATGACACATCAT CCTCTTATTTCTCACTGTTTCTACAAA
sgRNA: TCTATGACATGACACATCAT CTT----CTCACTGTTTCTACAAA
C
H9*
H9ΔN2NL
Day 08
Day 14
Day 20
Day 28
D
Largest axis length (pixels)
200
150
100
50
0
d03 d06 d08 d10 d12 d14 d16 d18 d20 d22 d24 d26 d28
H9ΔN2NL
H9*
E
H9* week 4
H9ΔNOTCH2NL week 4
SOX2
DAPI
SOX2
F
Amount of SOX2+ cells per section
1500
1000
500
0
n.s.
H9*
H9ΔN2NL
G
Average SOX2 grey value per cell
2500
2000
1500
1000
n.s.
H9*
H9ΔN2NL
H
H9* week 4
H9ΔNOTCH2NL week 4
CTIP2
DAPI
CTIP2
I
Amount of CTIP2+ cells per section
3000
2500
2000
1500
1000
500
0
n.s.
H9*
H9ΔN2NL
J
Average CTIP2 grey value per cell
1500
1000
500
0
***
H9*
H9ΔN2NL