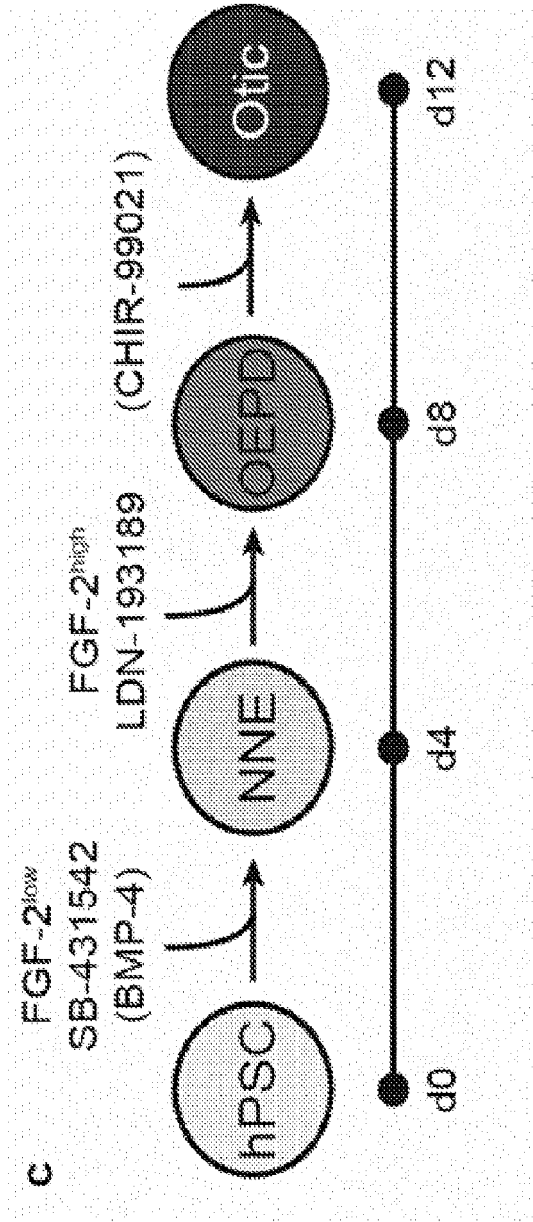
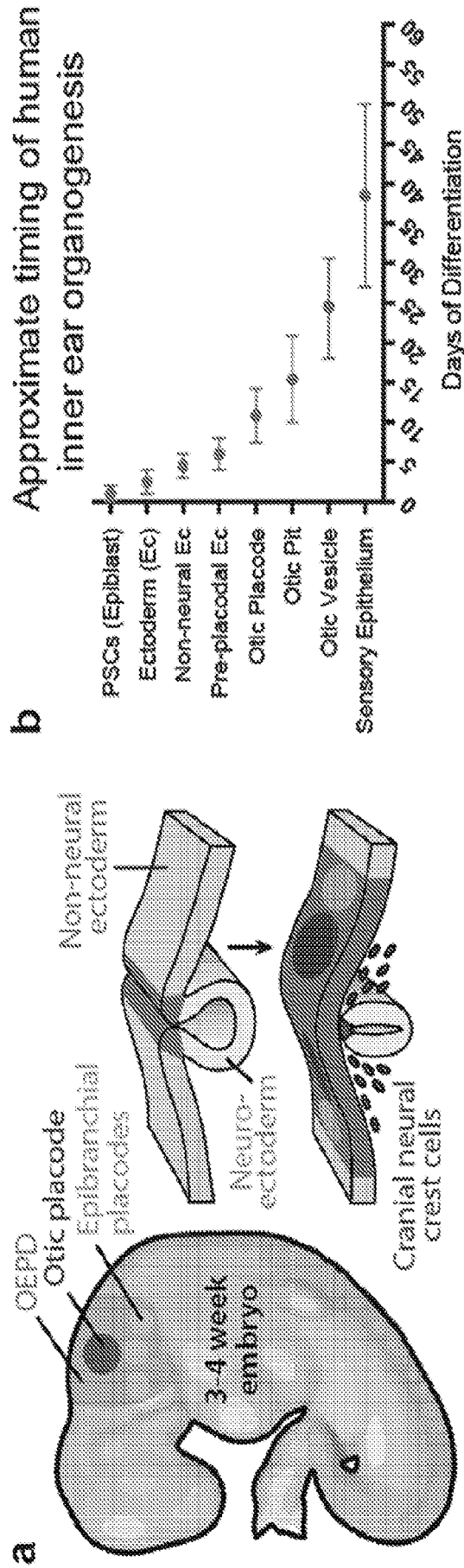
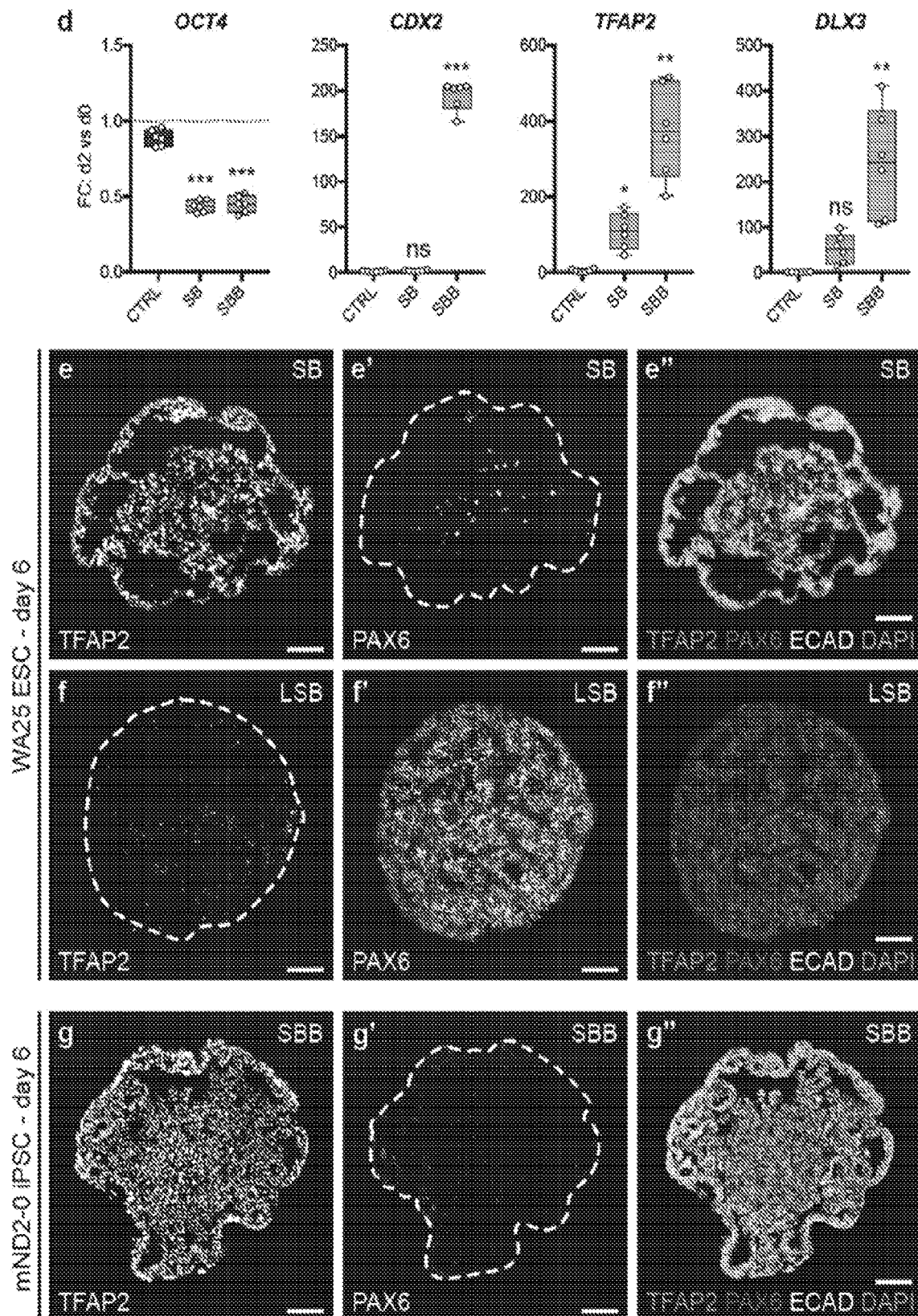


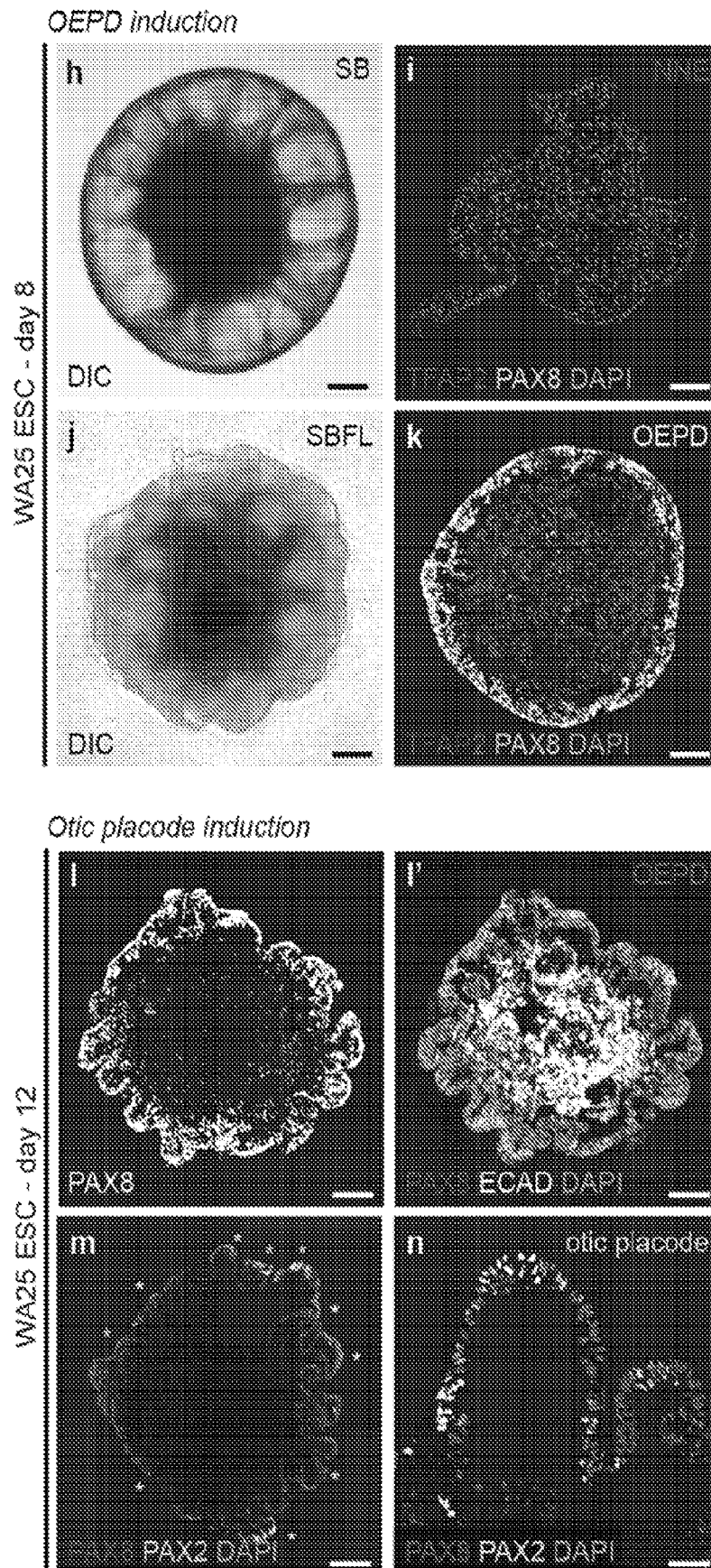
FIGS. 1A-1N



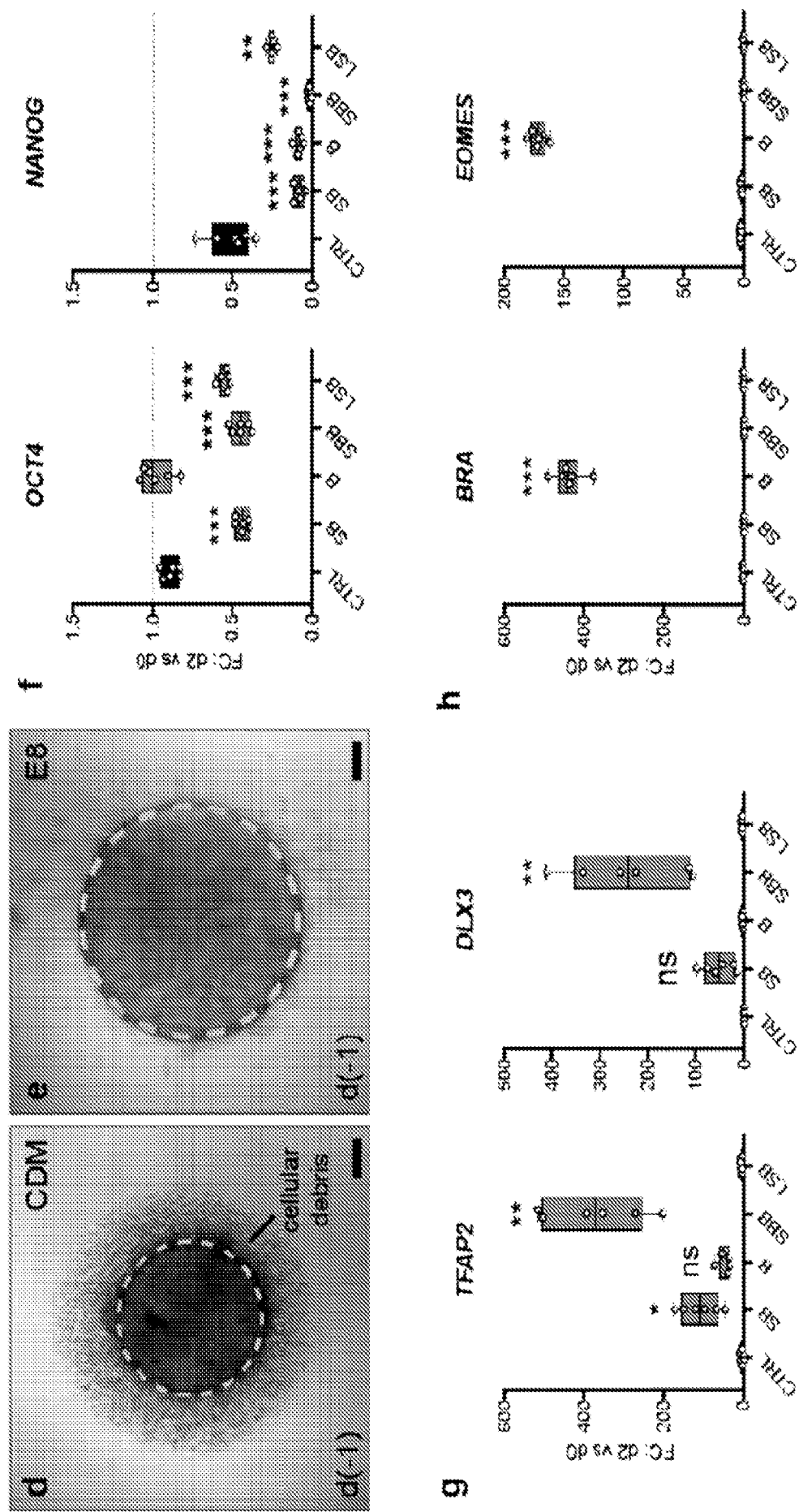
FIGS. 1A-1N, CONTINUED



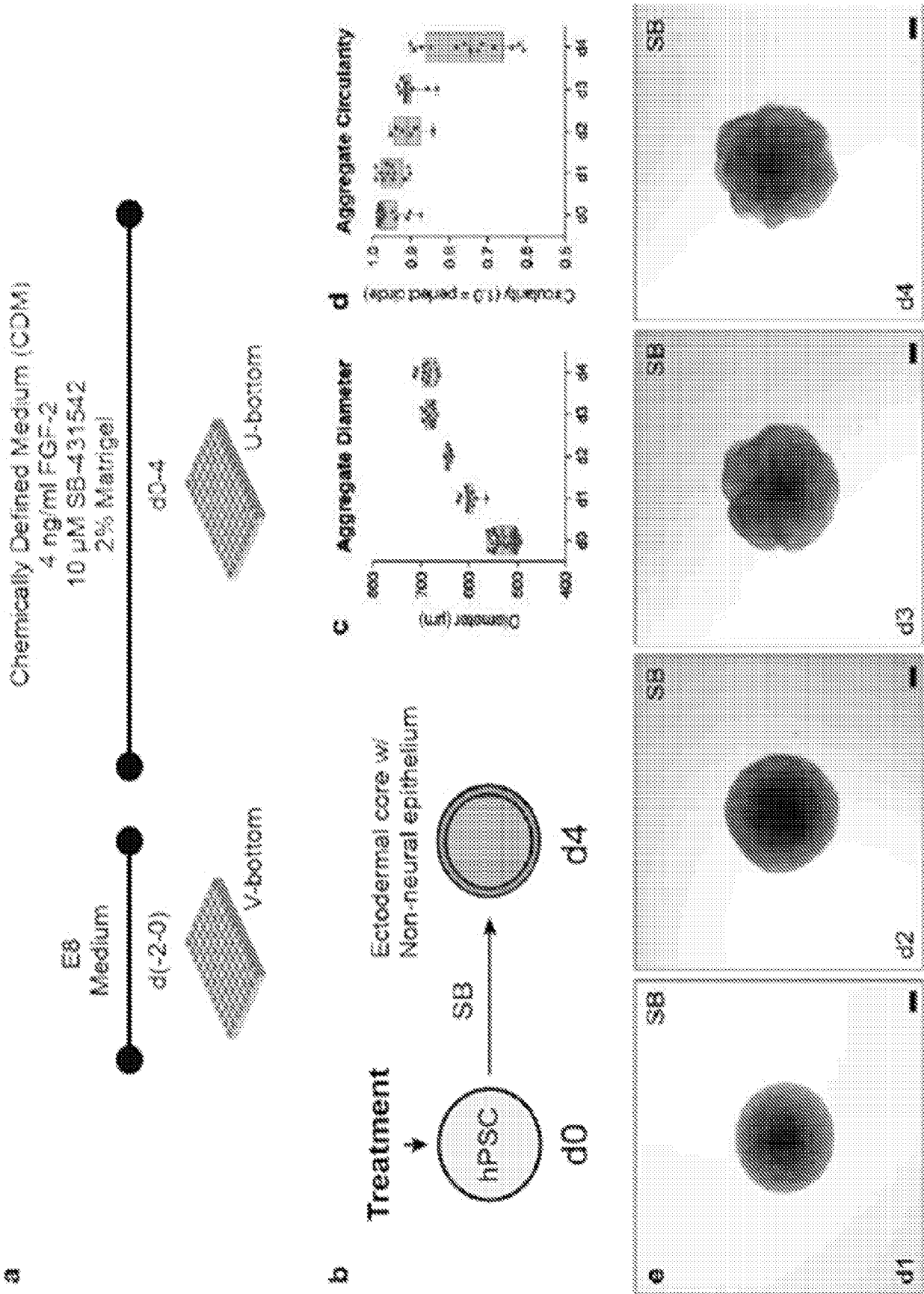
FIGS. 1A-1N, CONTINUED



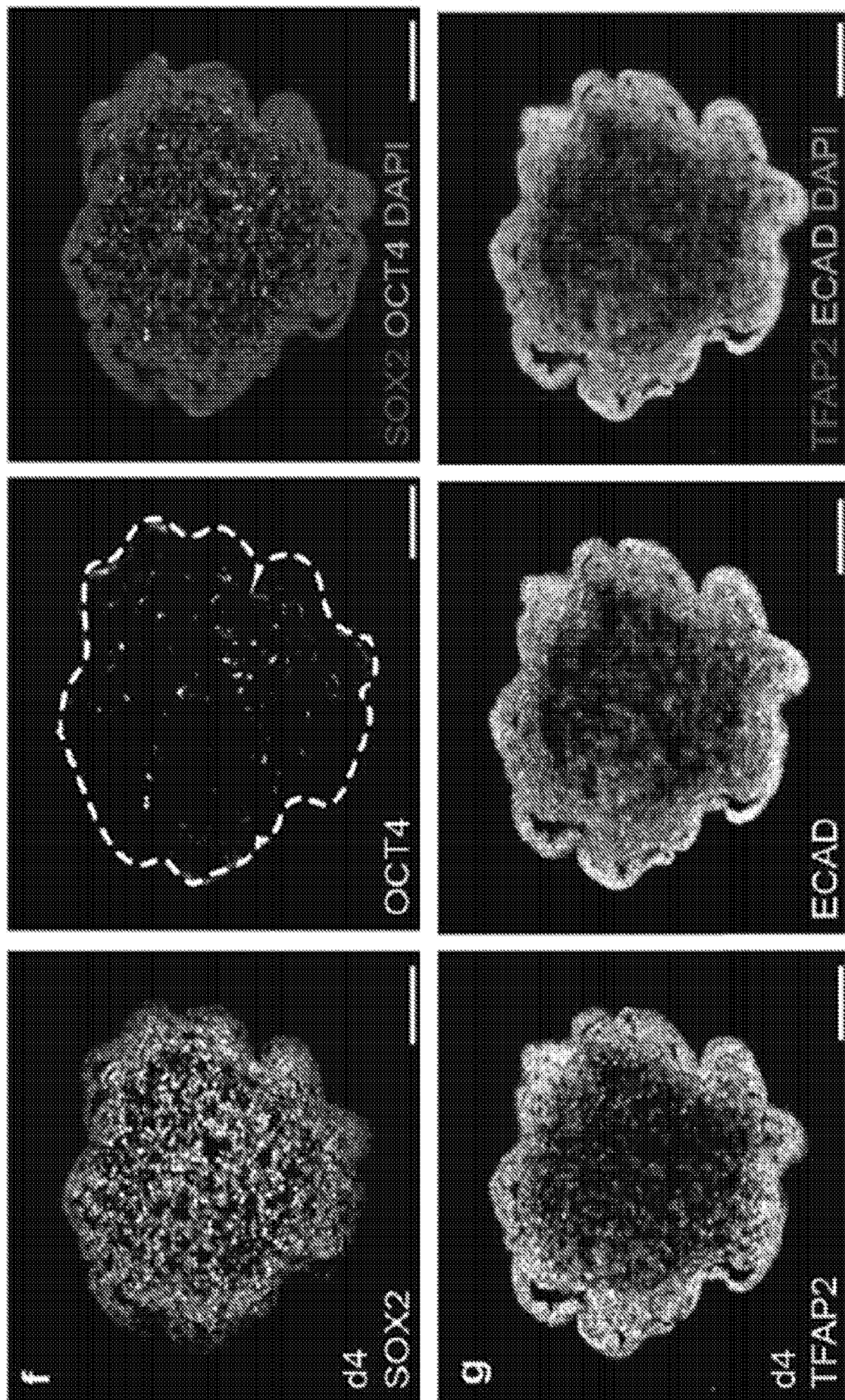
FIGS. 2A-2H, CONTINUED



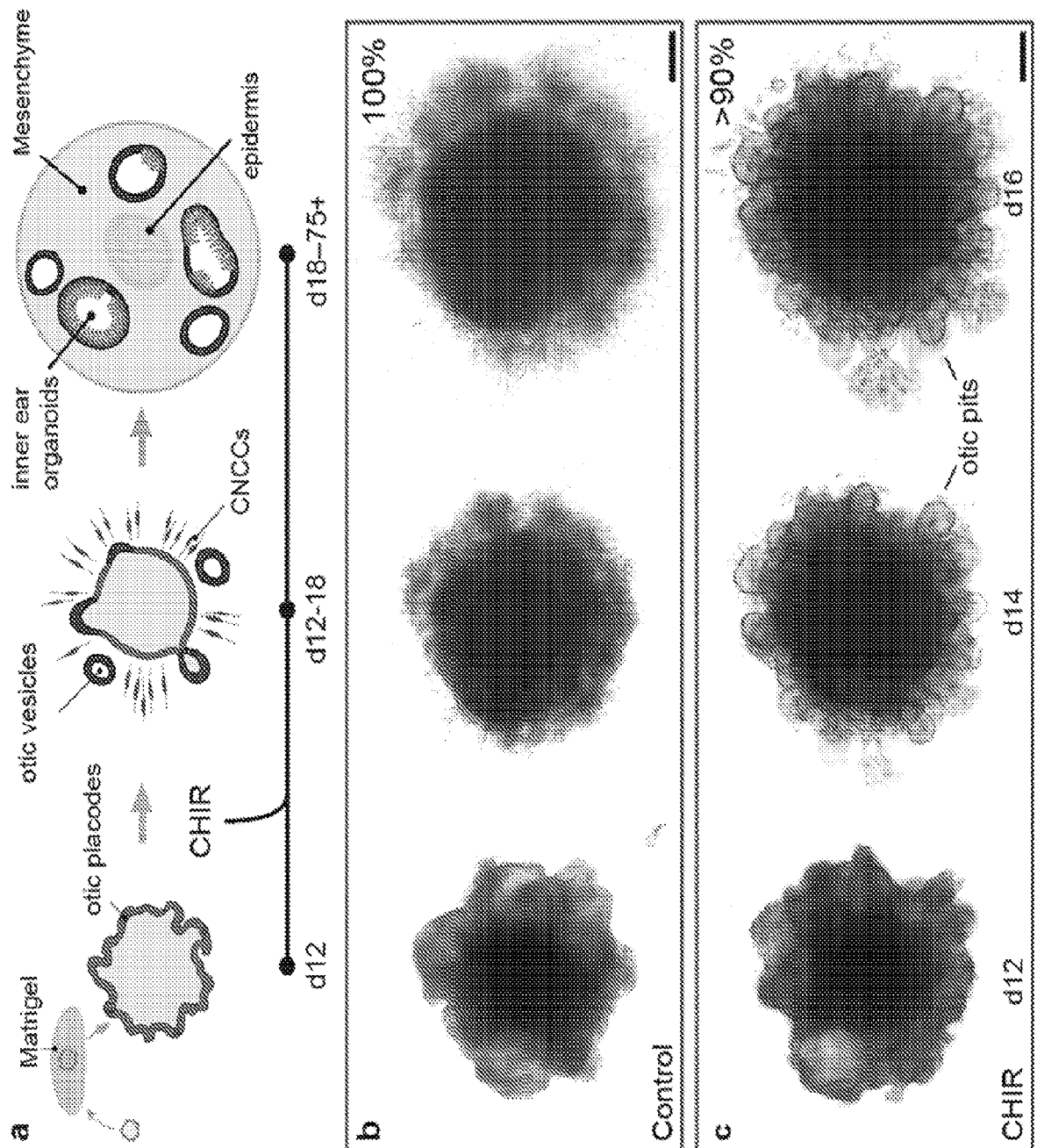
FIGS. 3A-3G



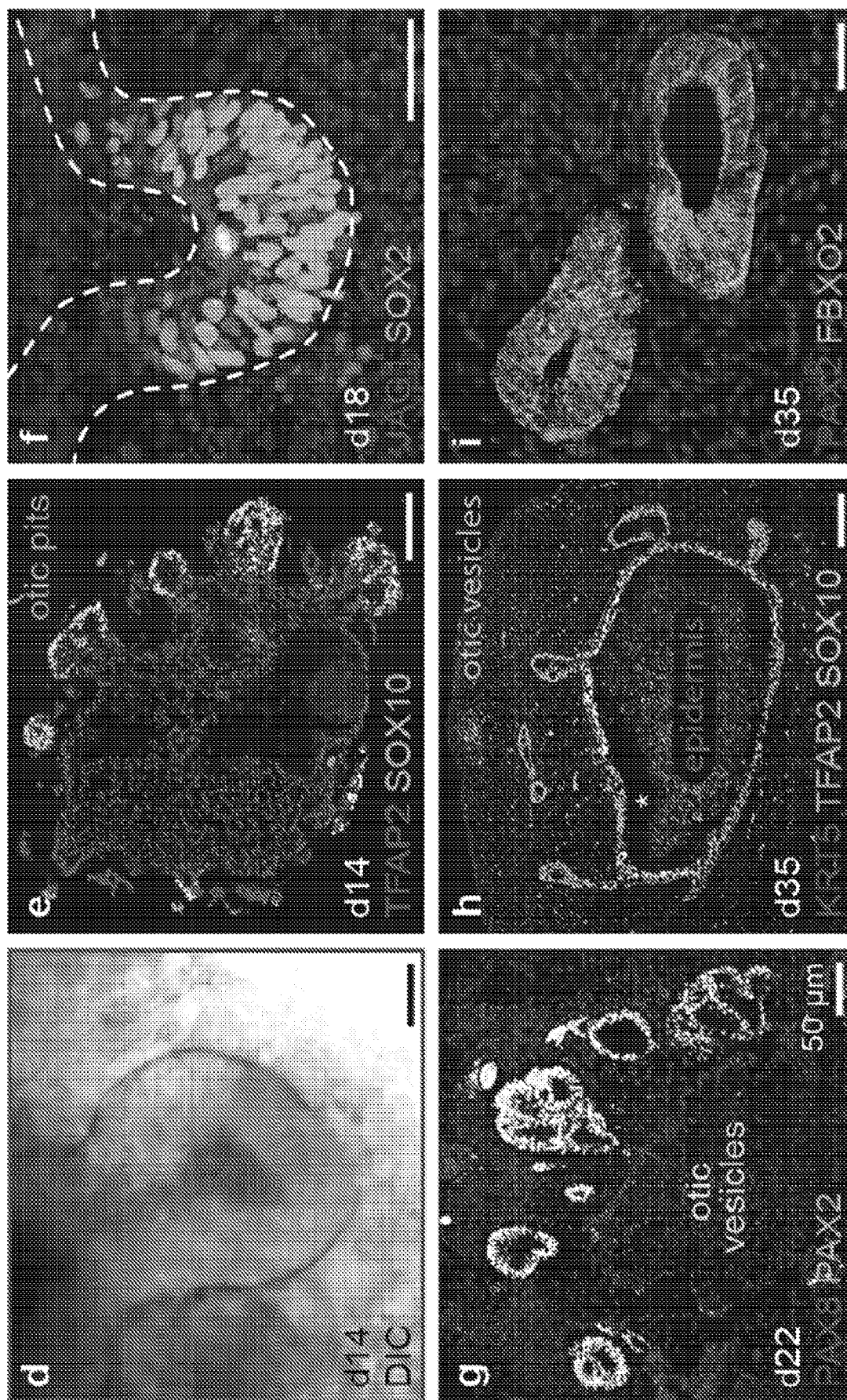
FIGS. 3A-3G, CONTINUED



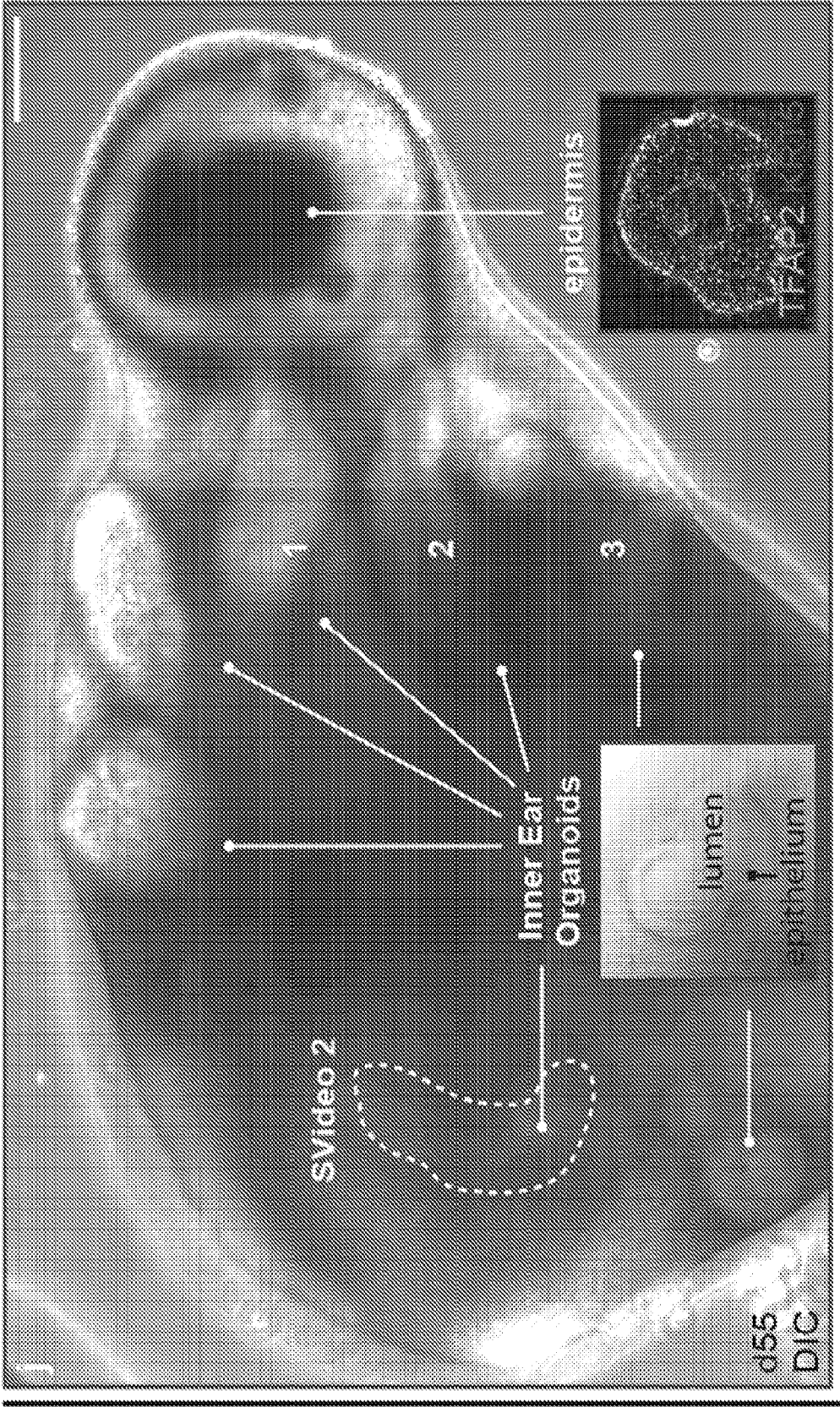
FIGS. 4A-4R



FIGS. 4A-4R, CONTINUED



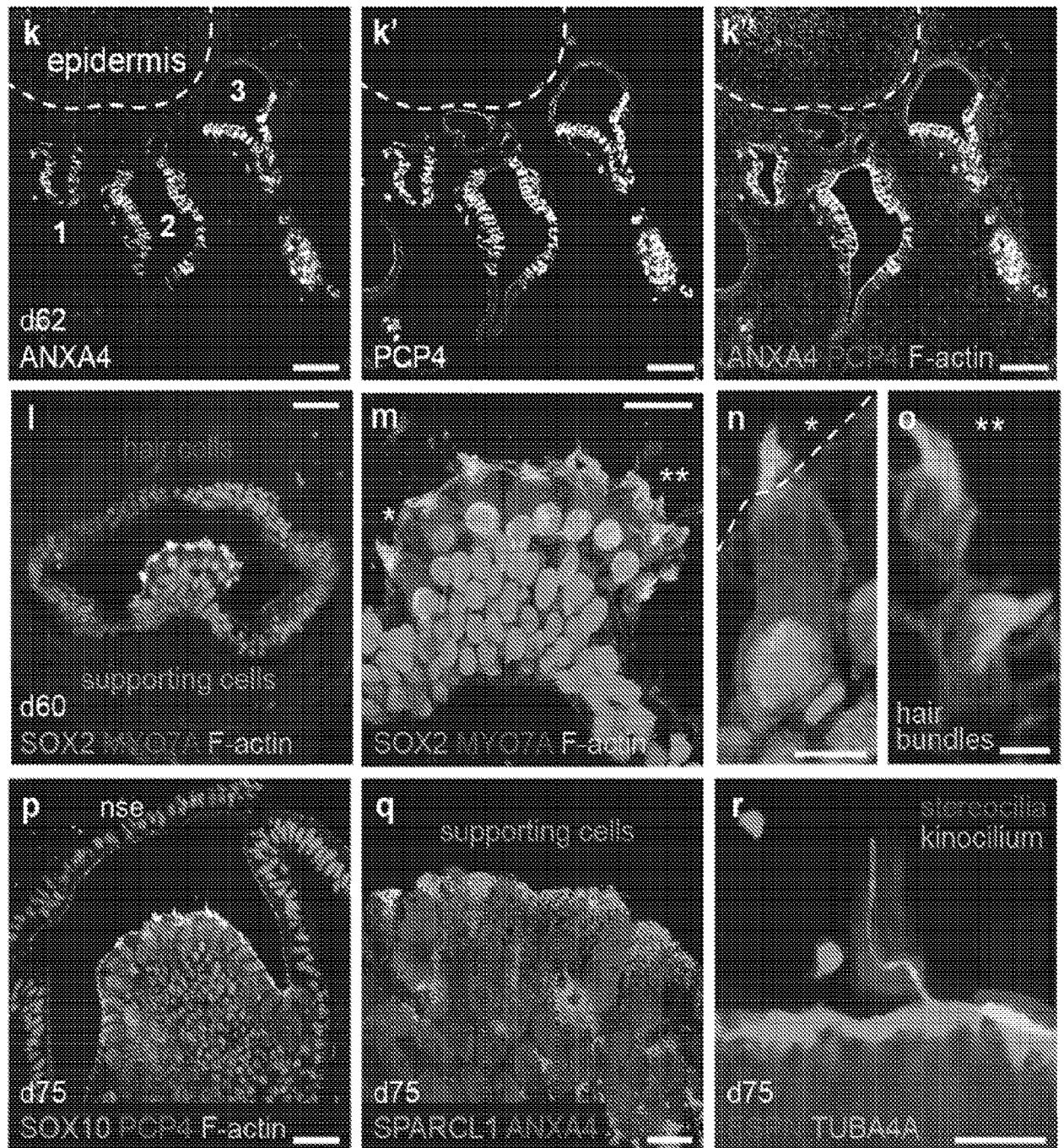
FIGS. 4A-4R, CONTINUED



WA25 ESC-Derived

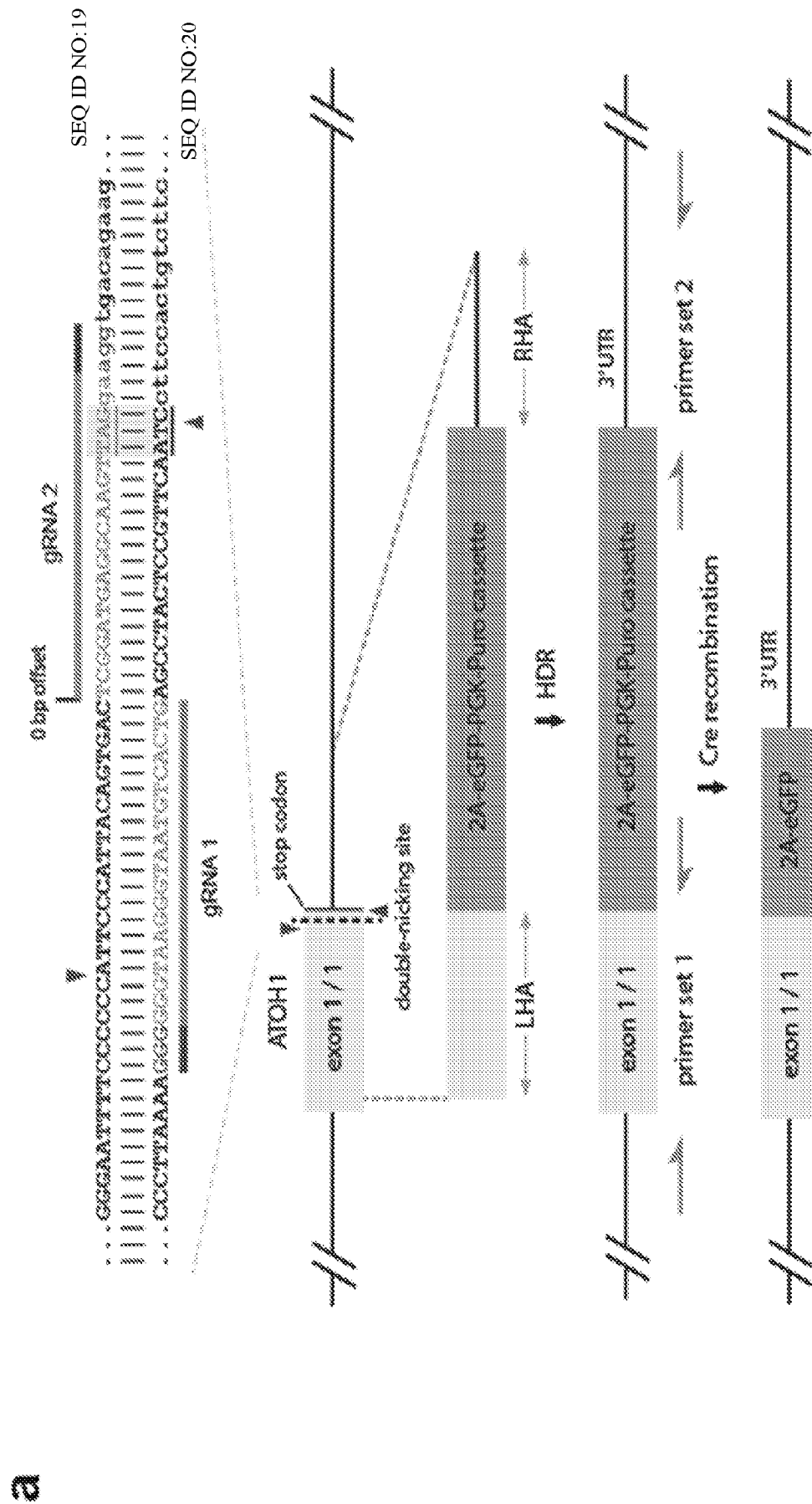
FIGS. 4A-4R, CONTINUED

WA25 ESC-Derived

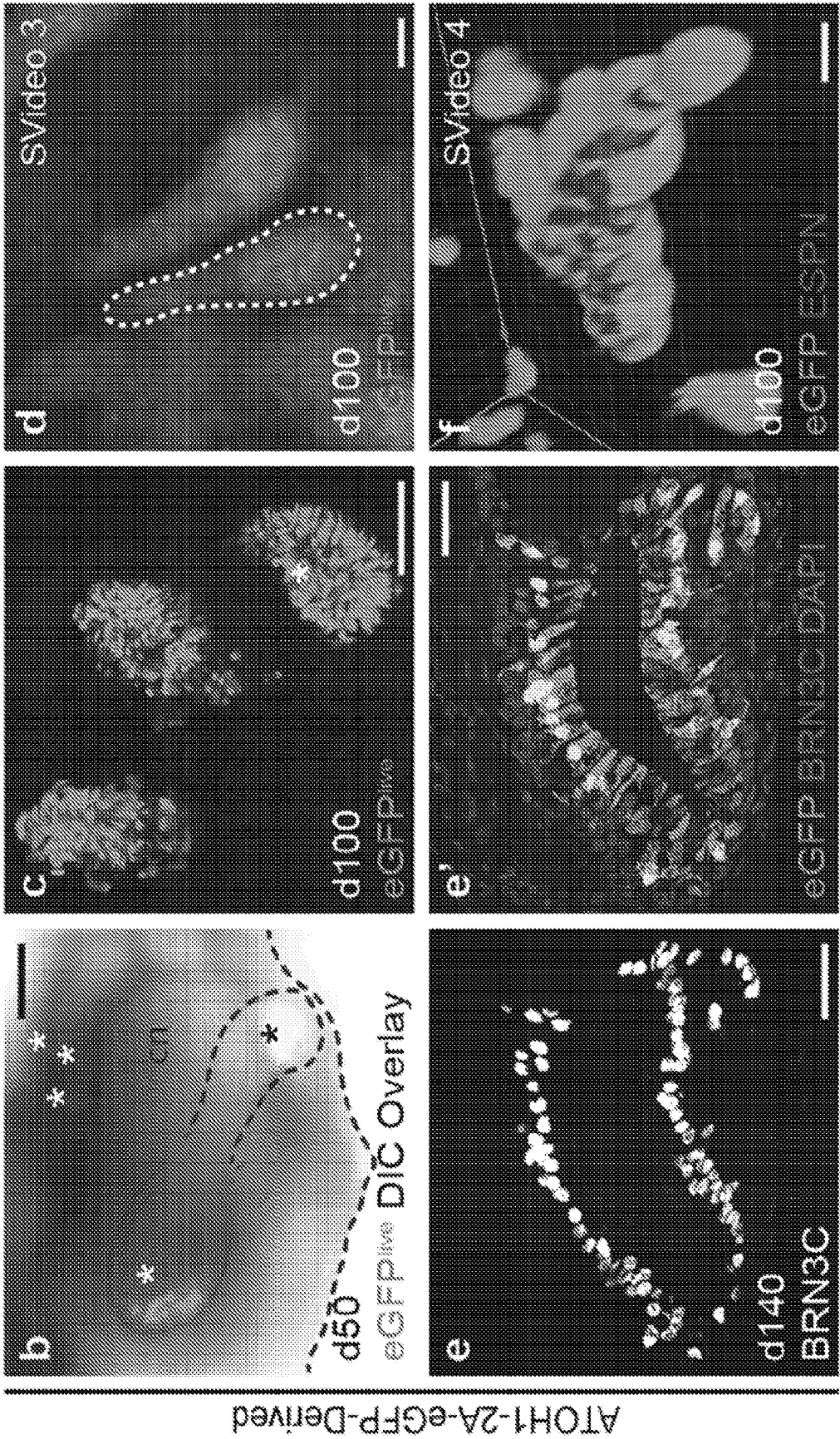


mND2-0 iPSC-Derived

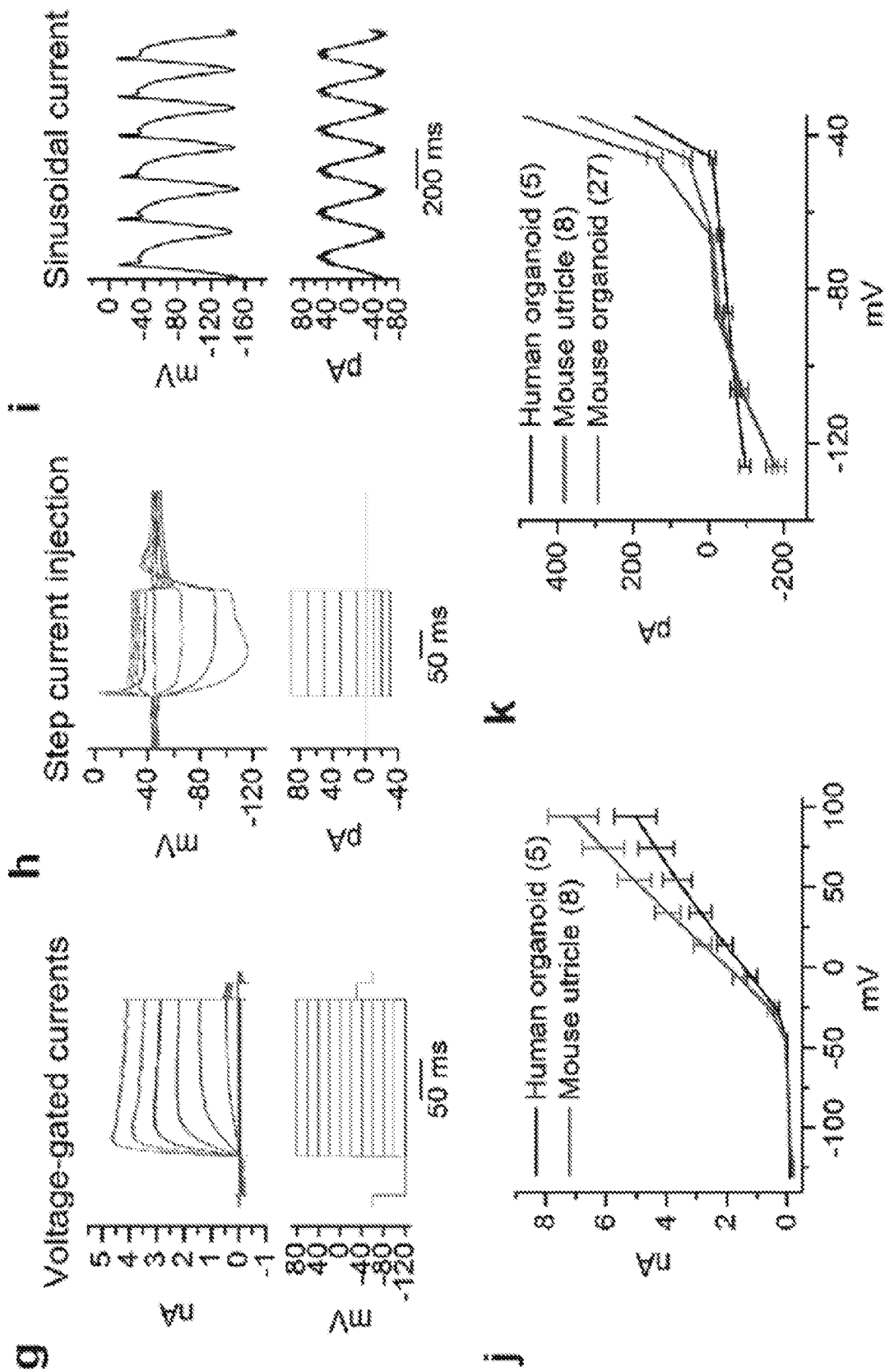
FIGS. 5A-5K



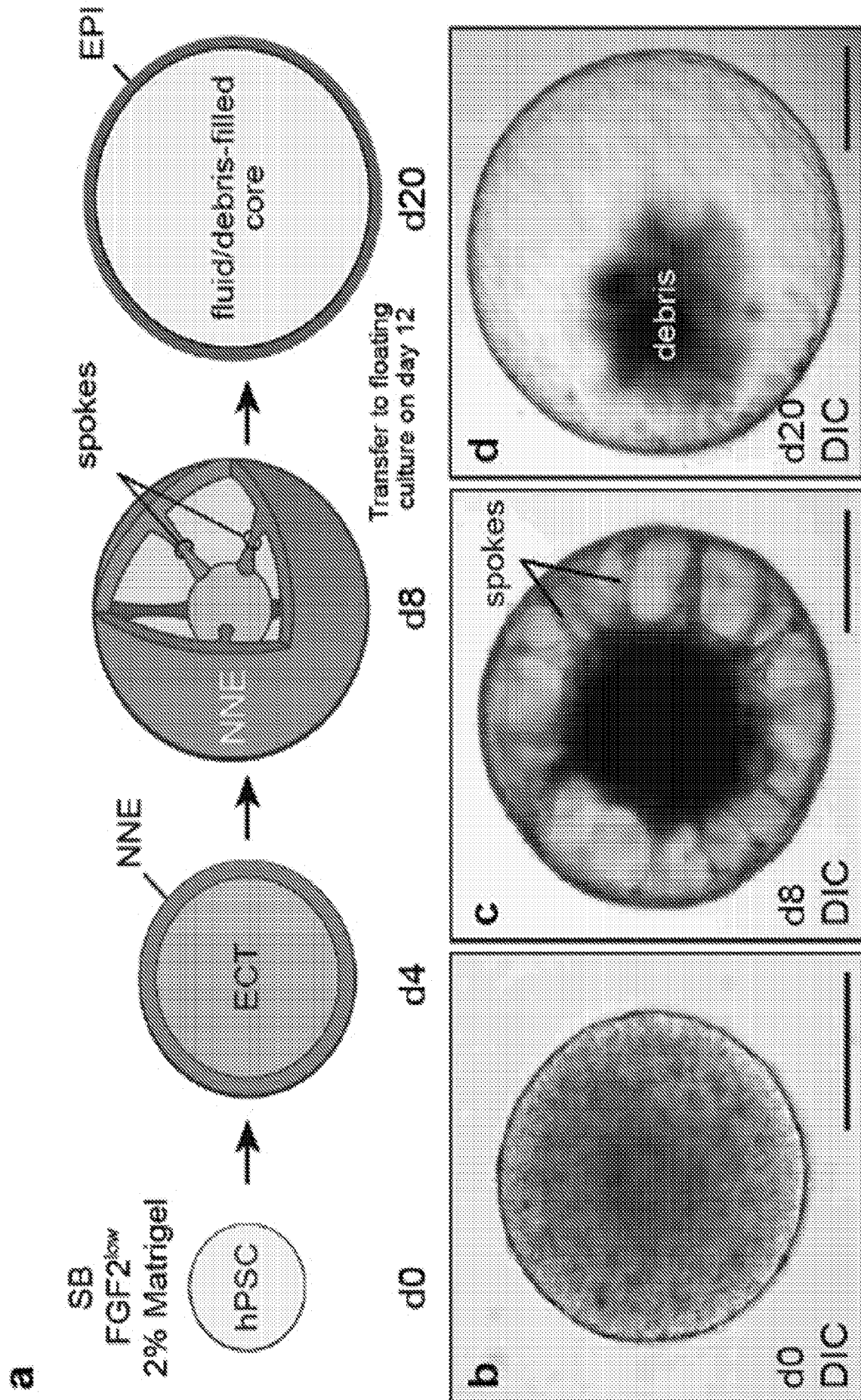
FIGS. 5A-5K, CONTINUED



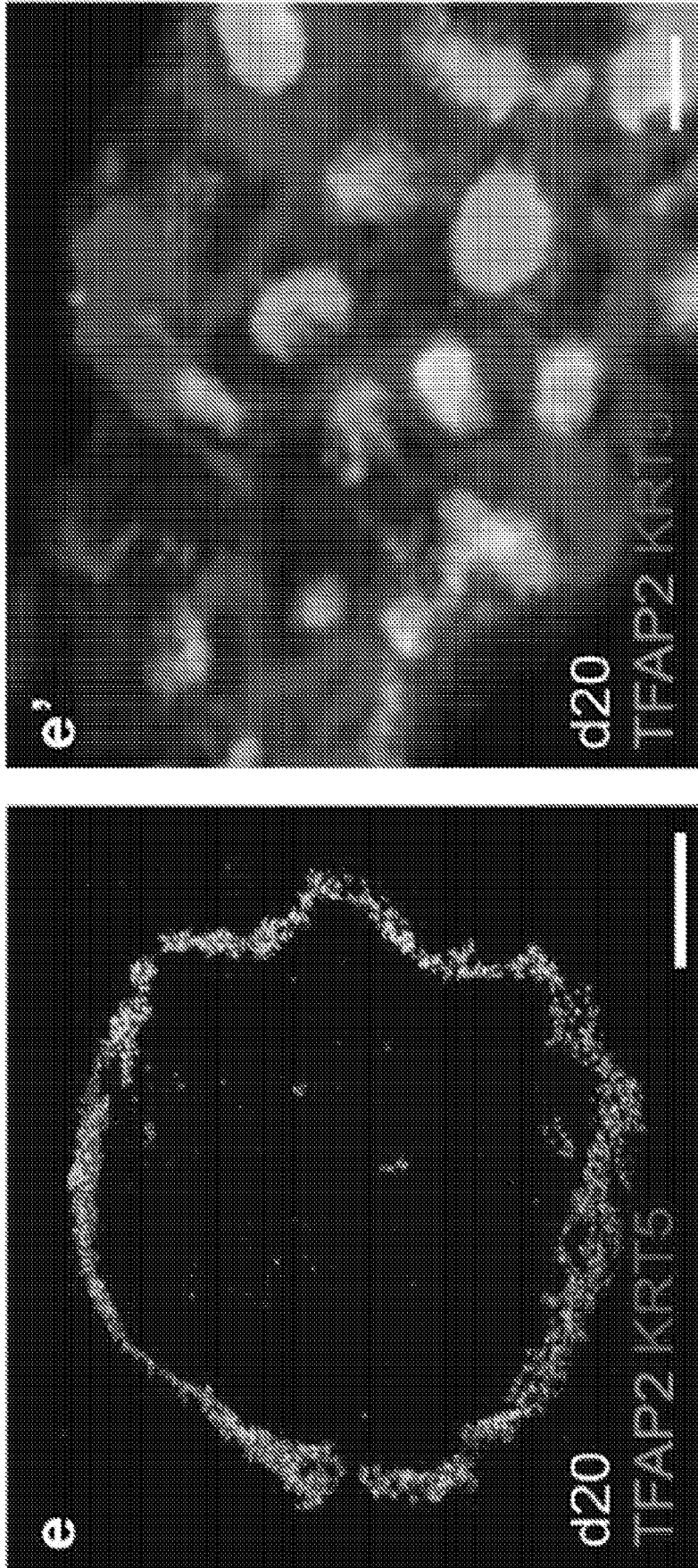
FIGS. 5A-5K, CONTINUED



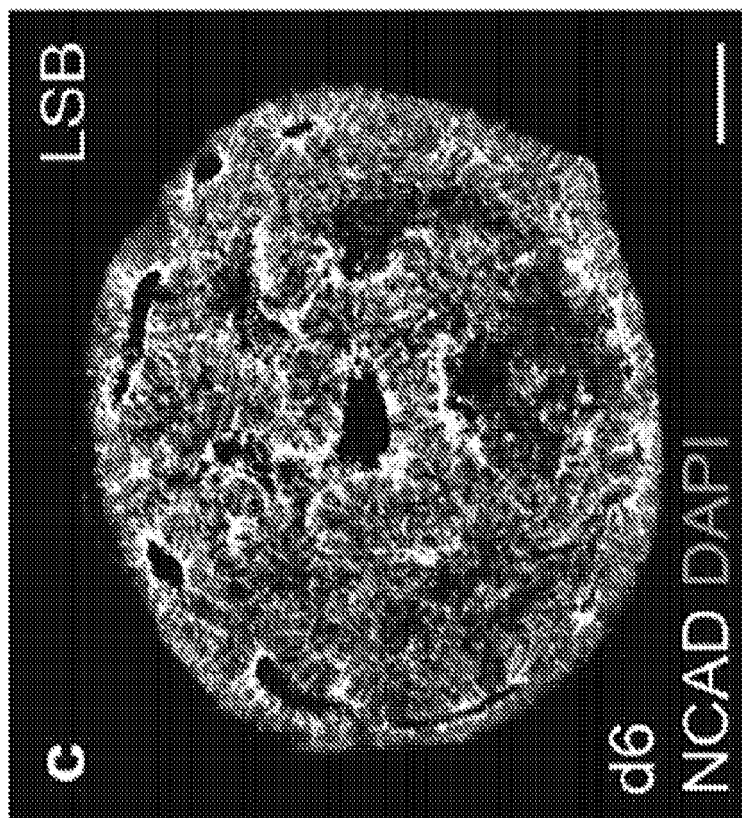
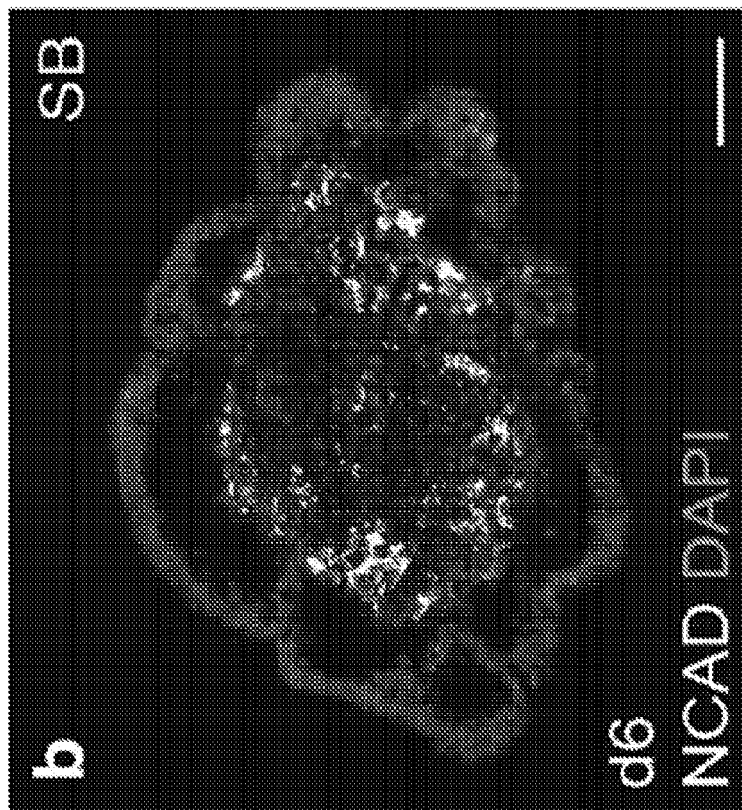
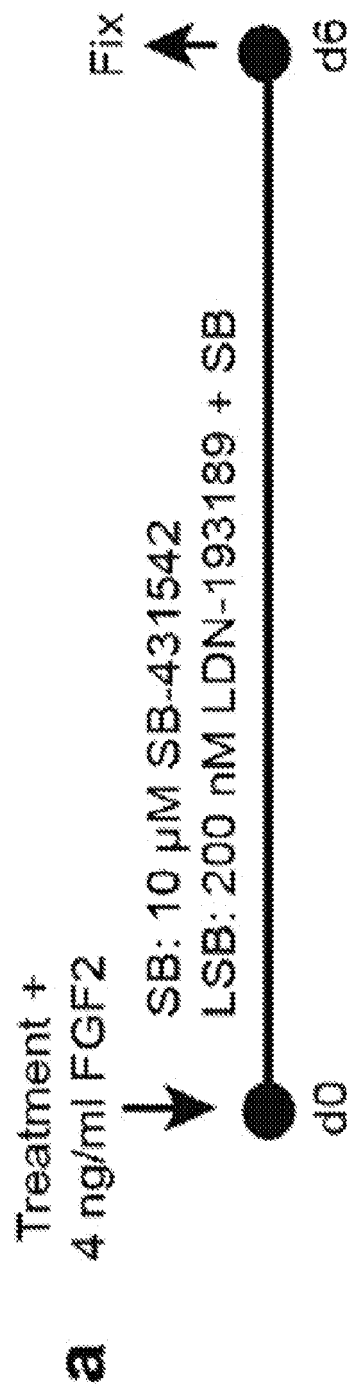
FIGS. 6A-6E



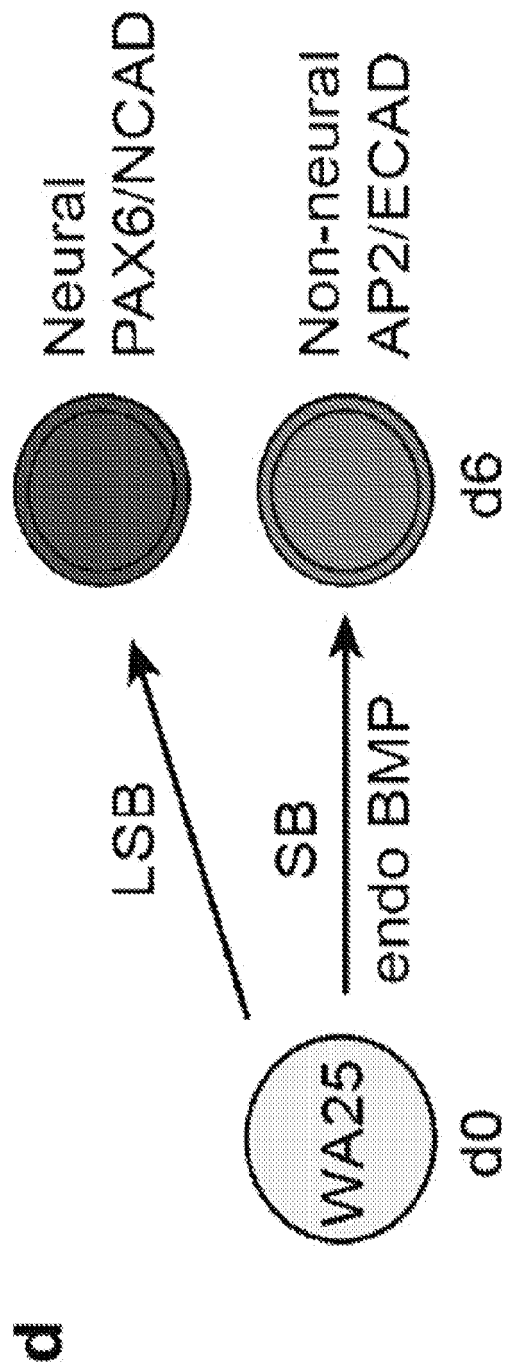
FIGS. 6A-6E, CONTINUED



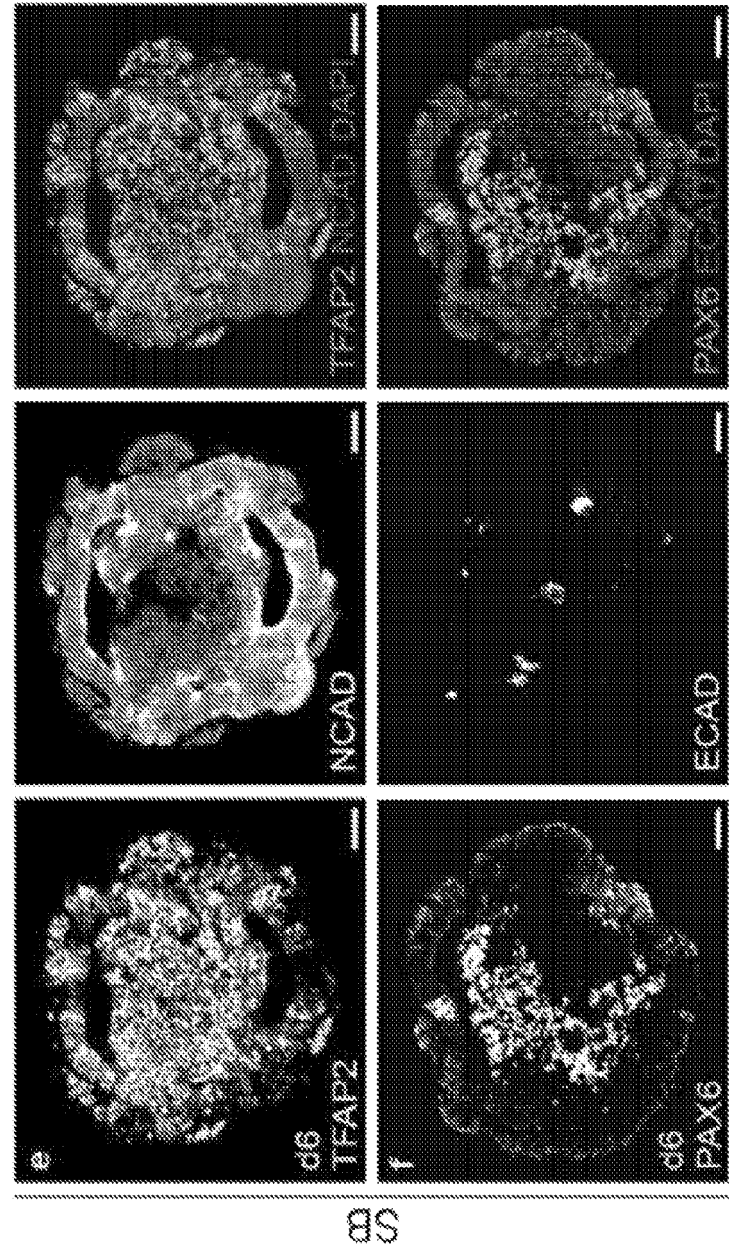
FIGS. 7A-7D



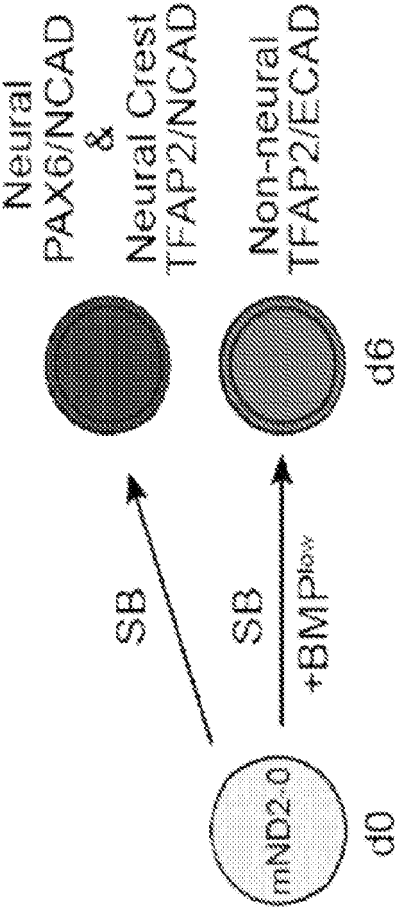
FIGS. 7A-7D, CONTINUED



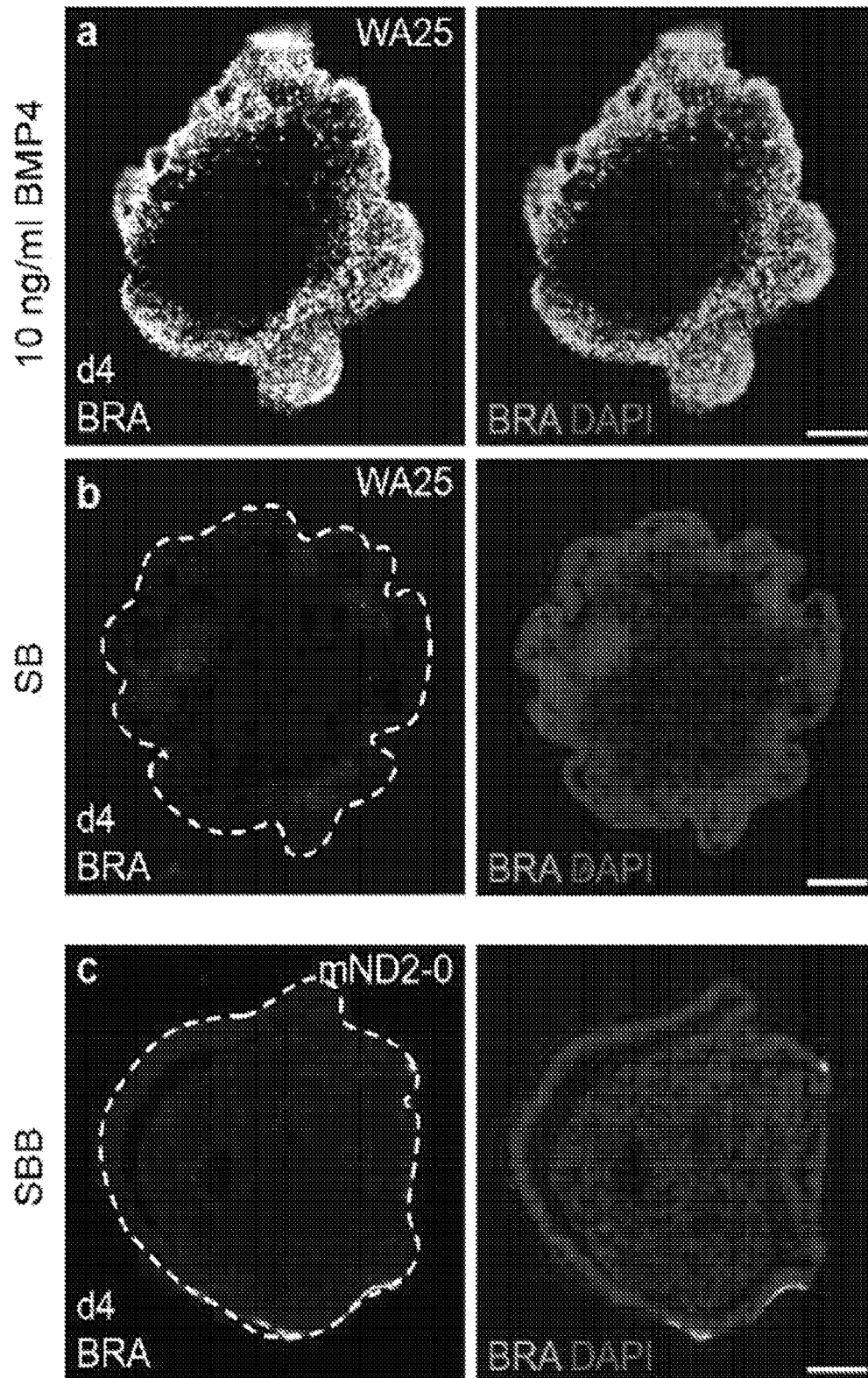
FIGS. 8A-8G



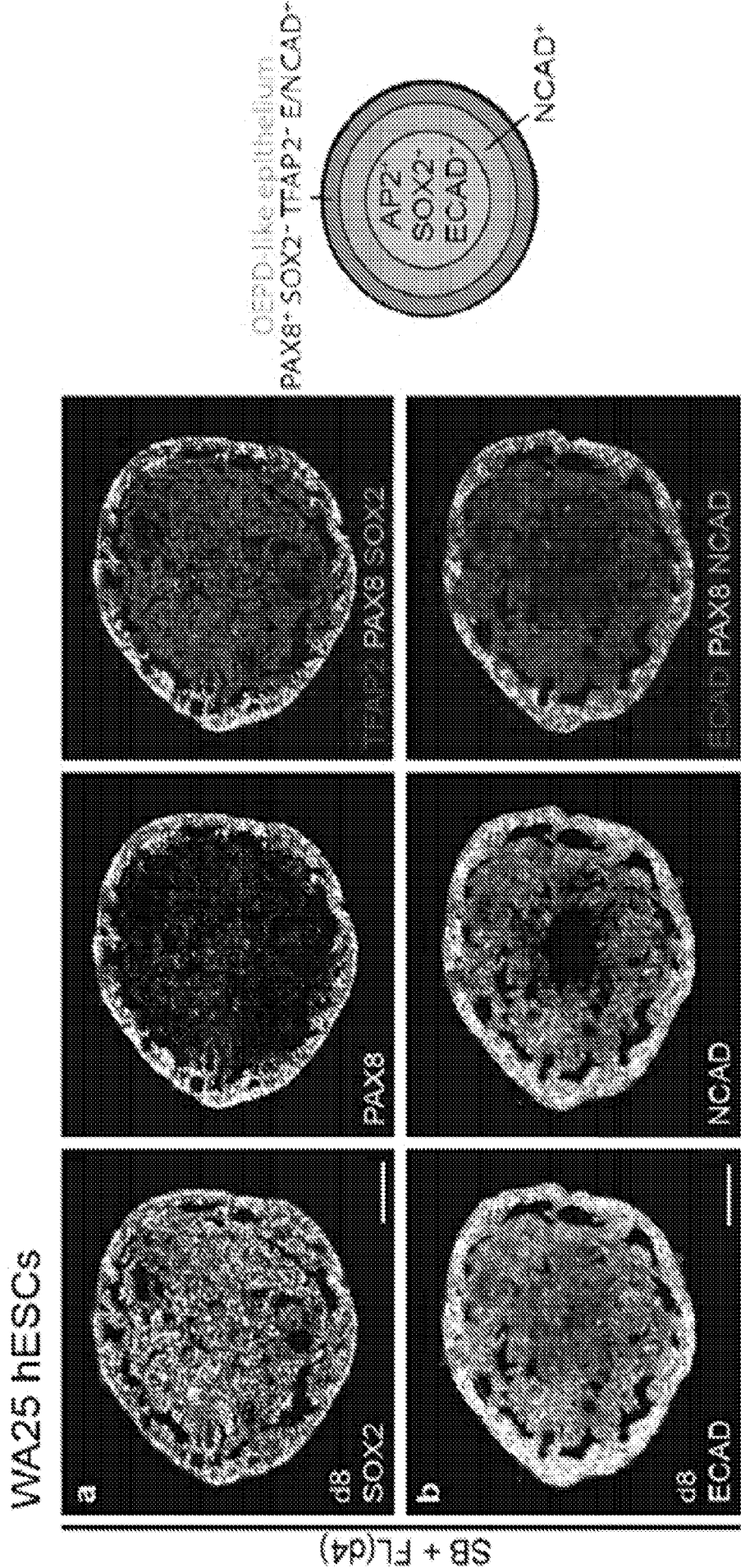
9



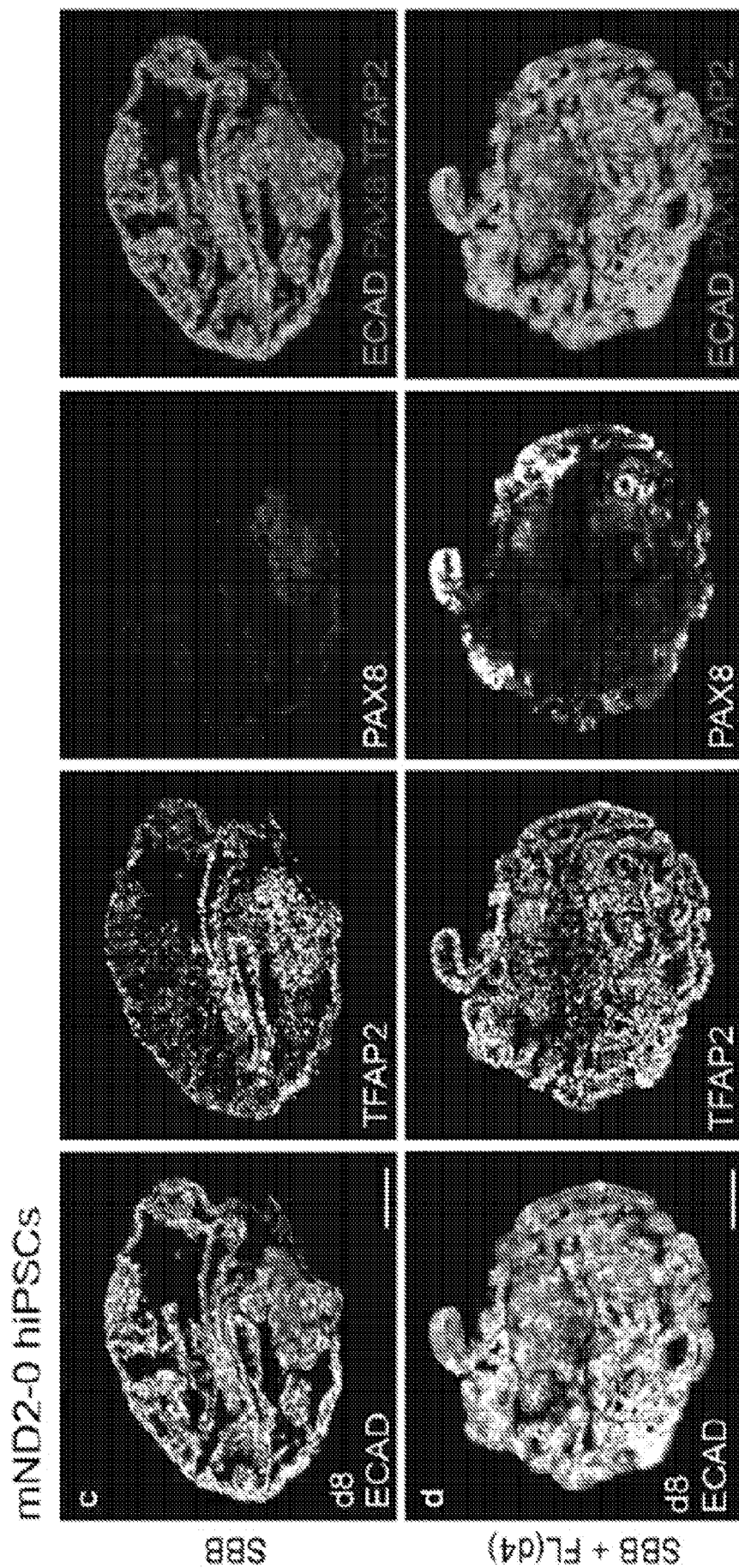
FIGS. 9A-9C



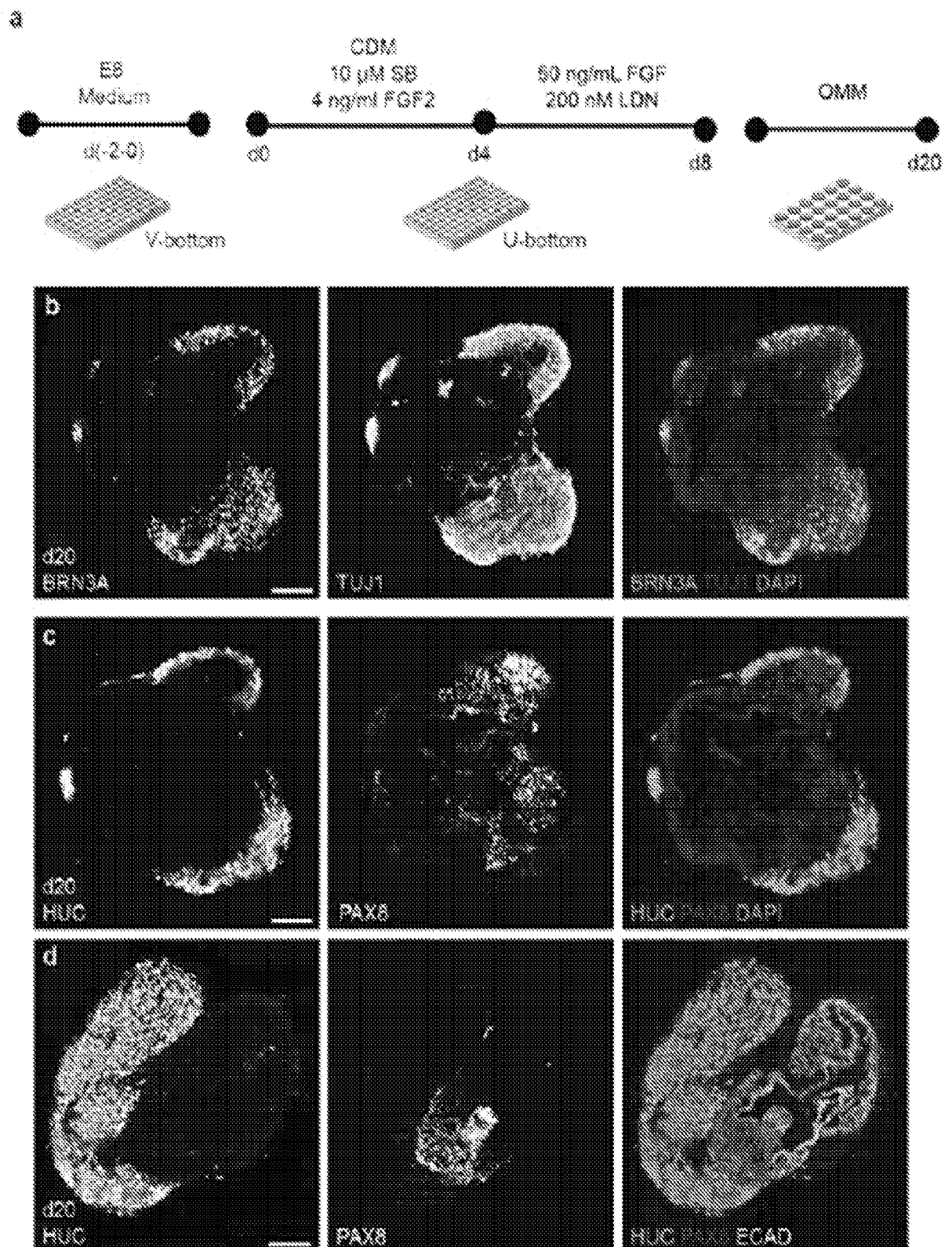
FIGS. 10A-10D



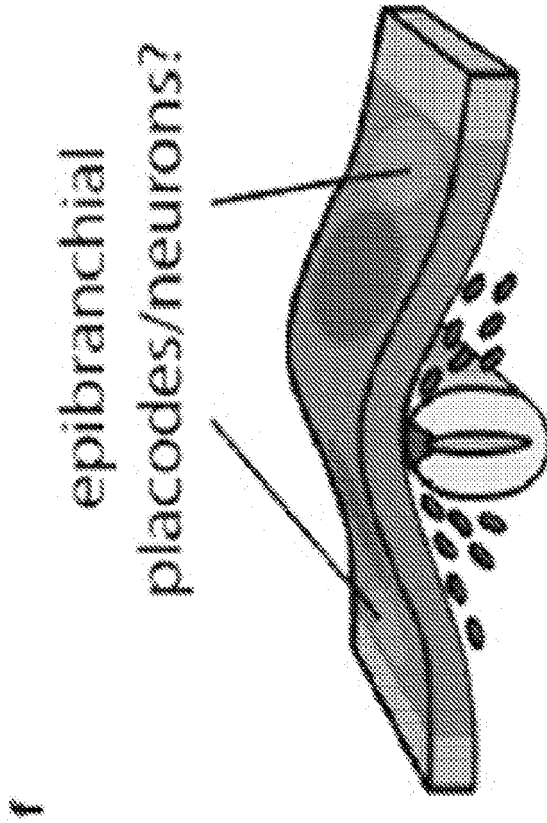
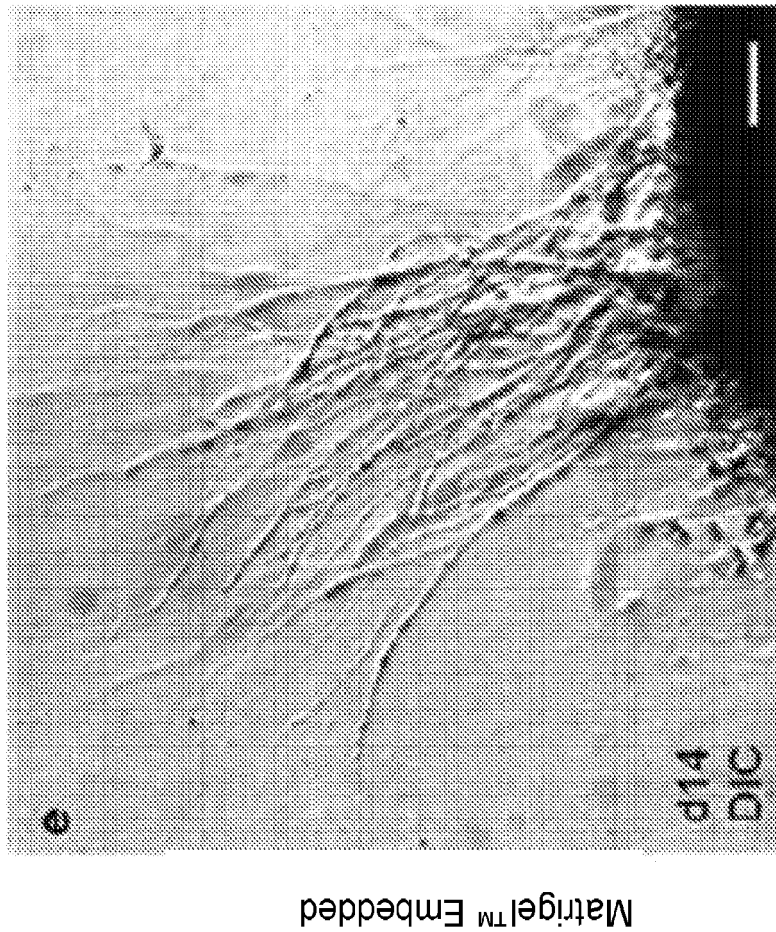
FIGS. 10A-10D, CONTINUED



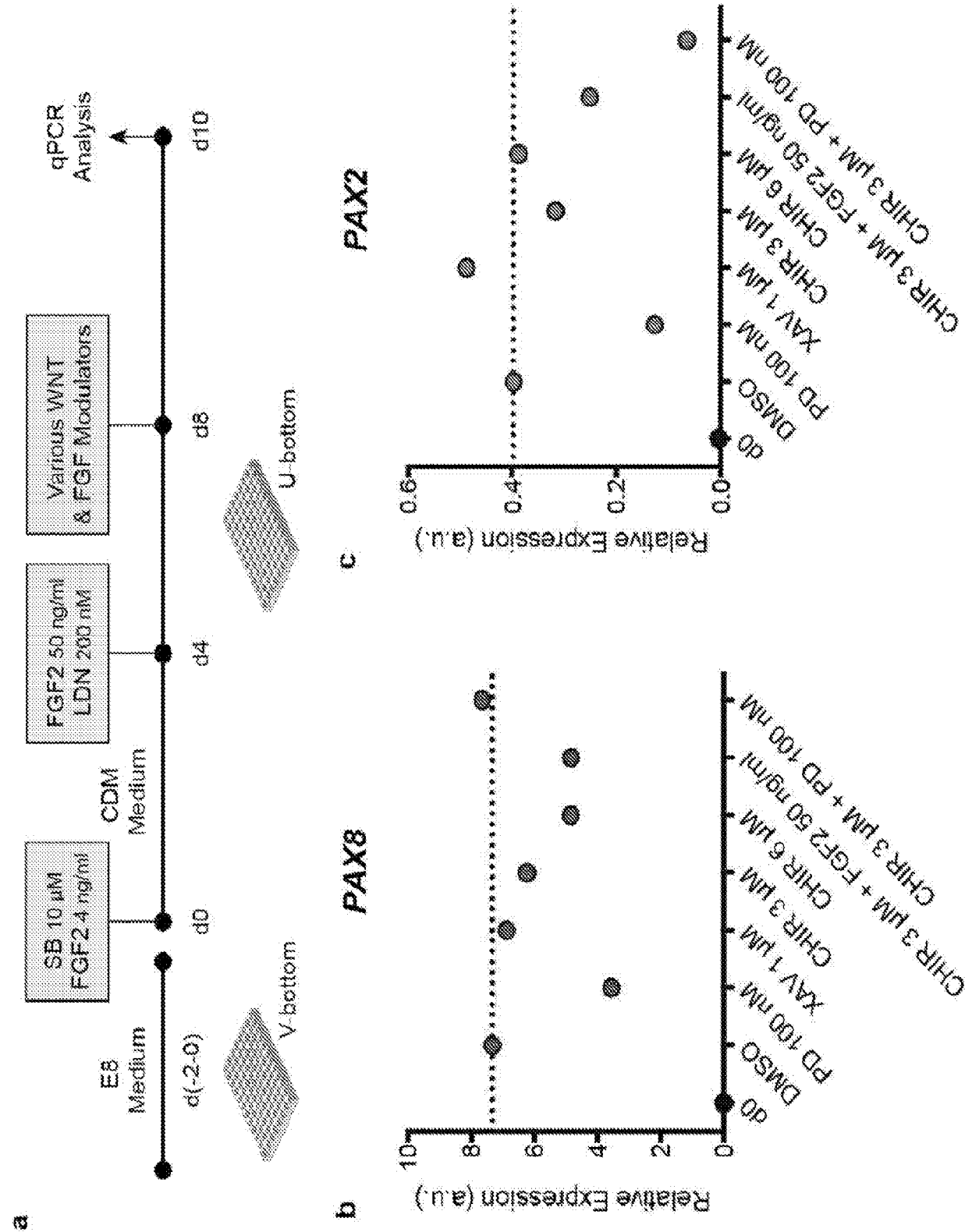
FIGS. 11A-11F



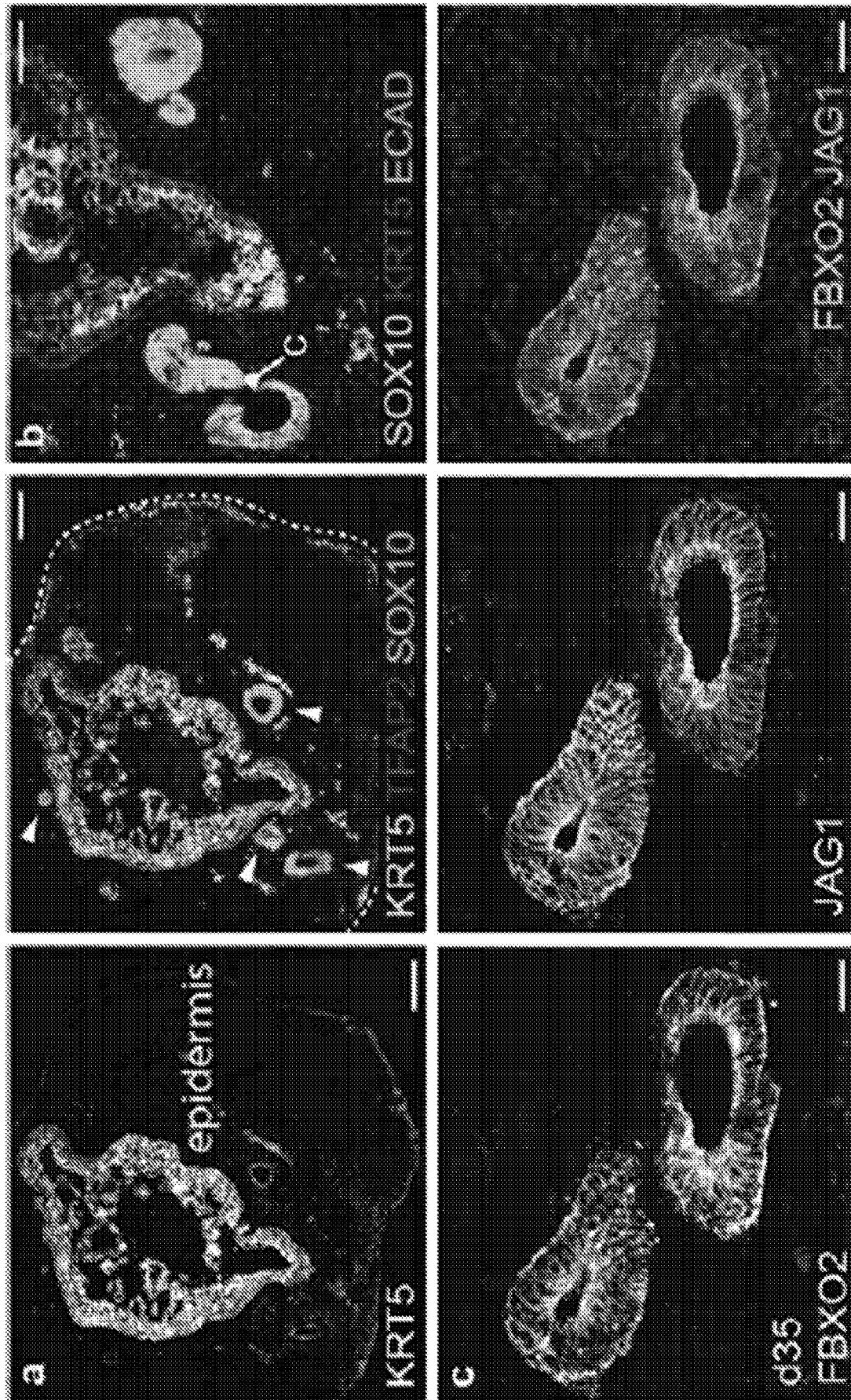
FIGS. 11A-11F, CONTINUED



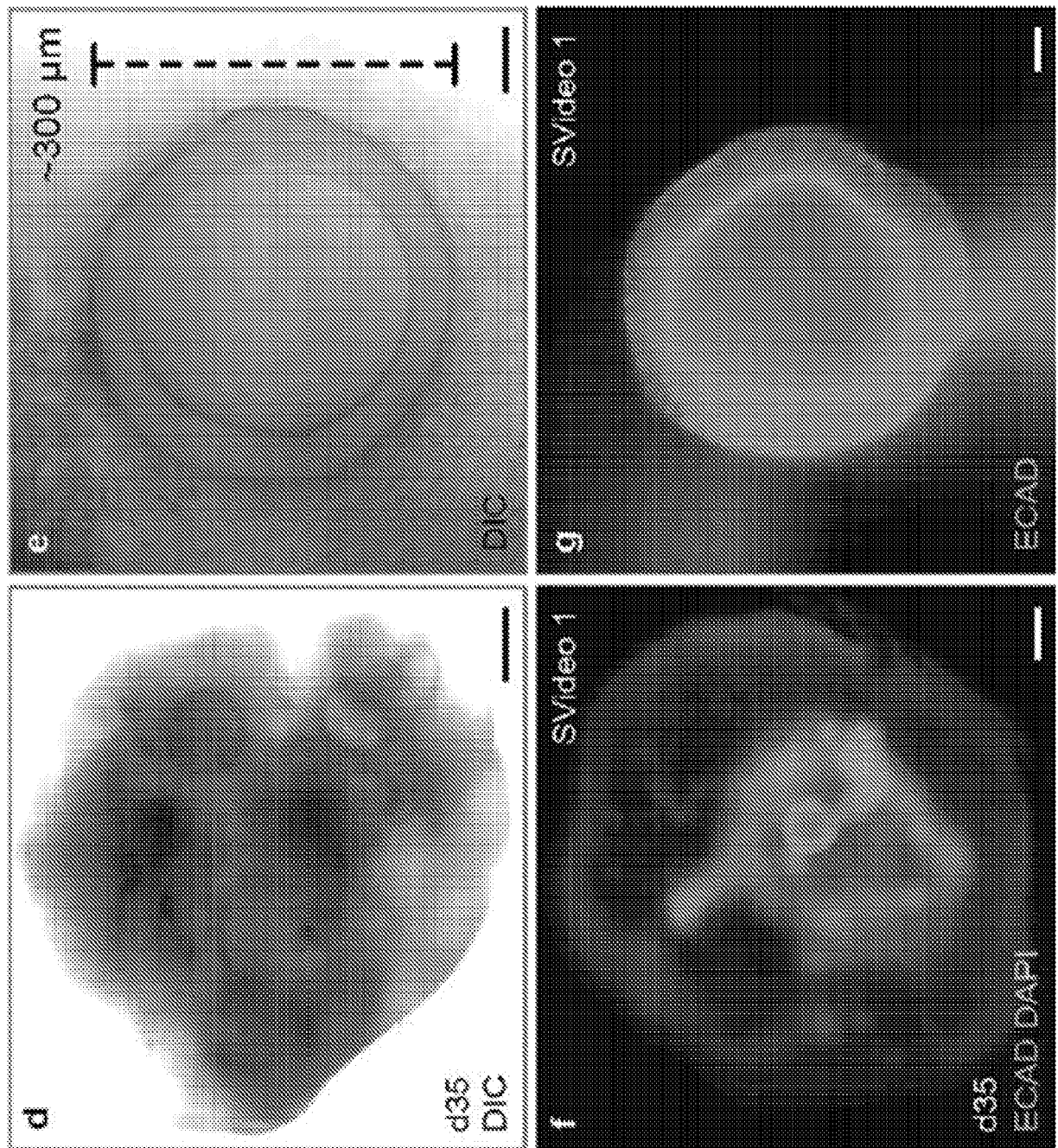
FIGS. 12A-12C



FIGS. 13A-13G



FIGS. 13A-13G, CONTINUED



FIGS. 14A-14E, CONTINUED

Non-Sensory Epithelium

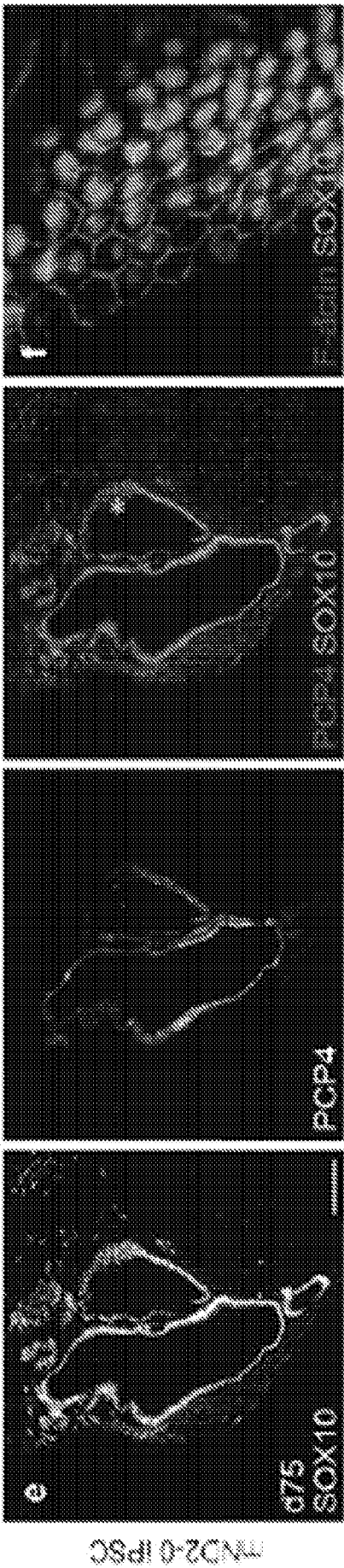
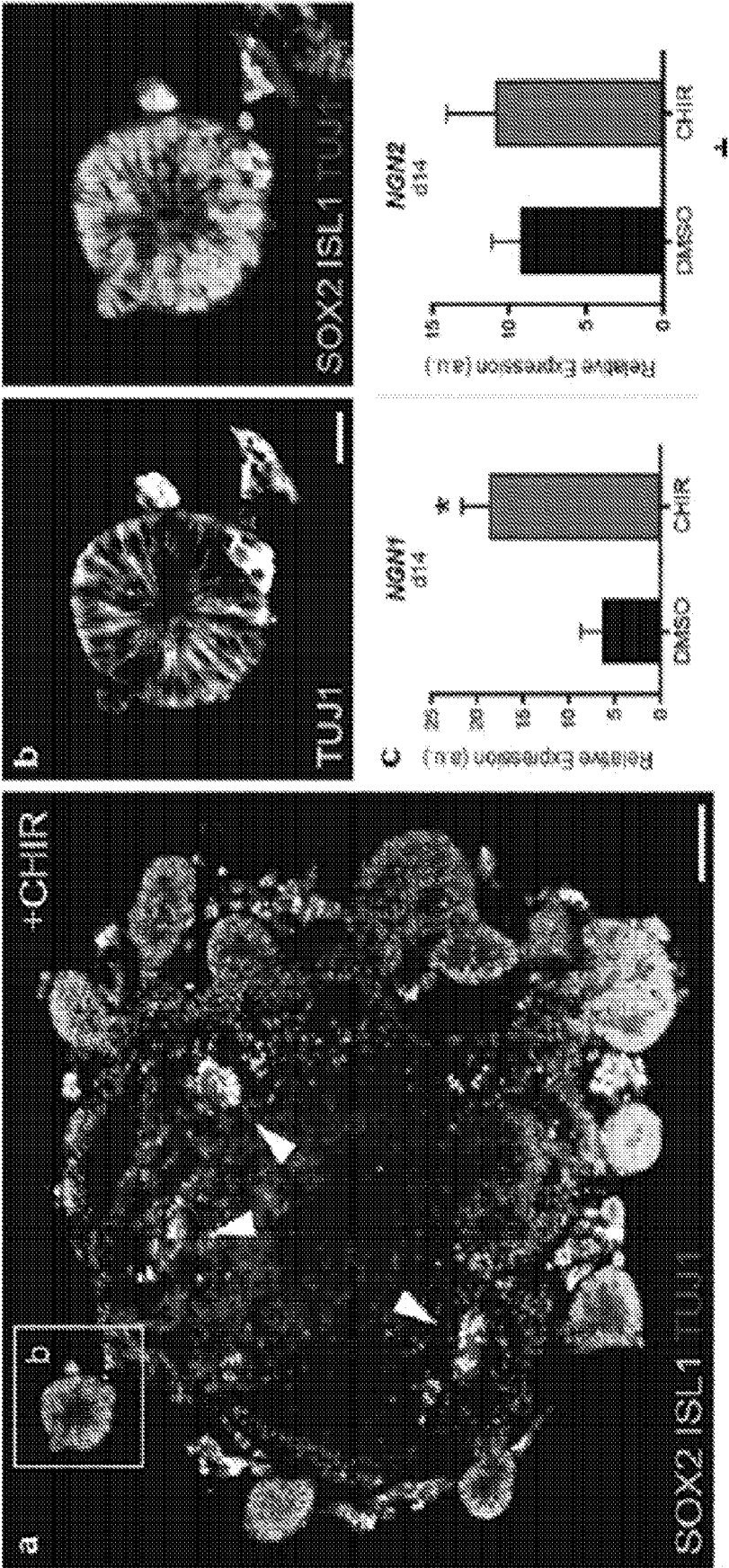


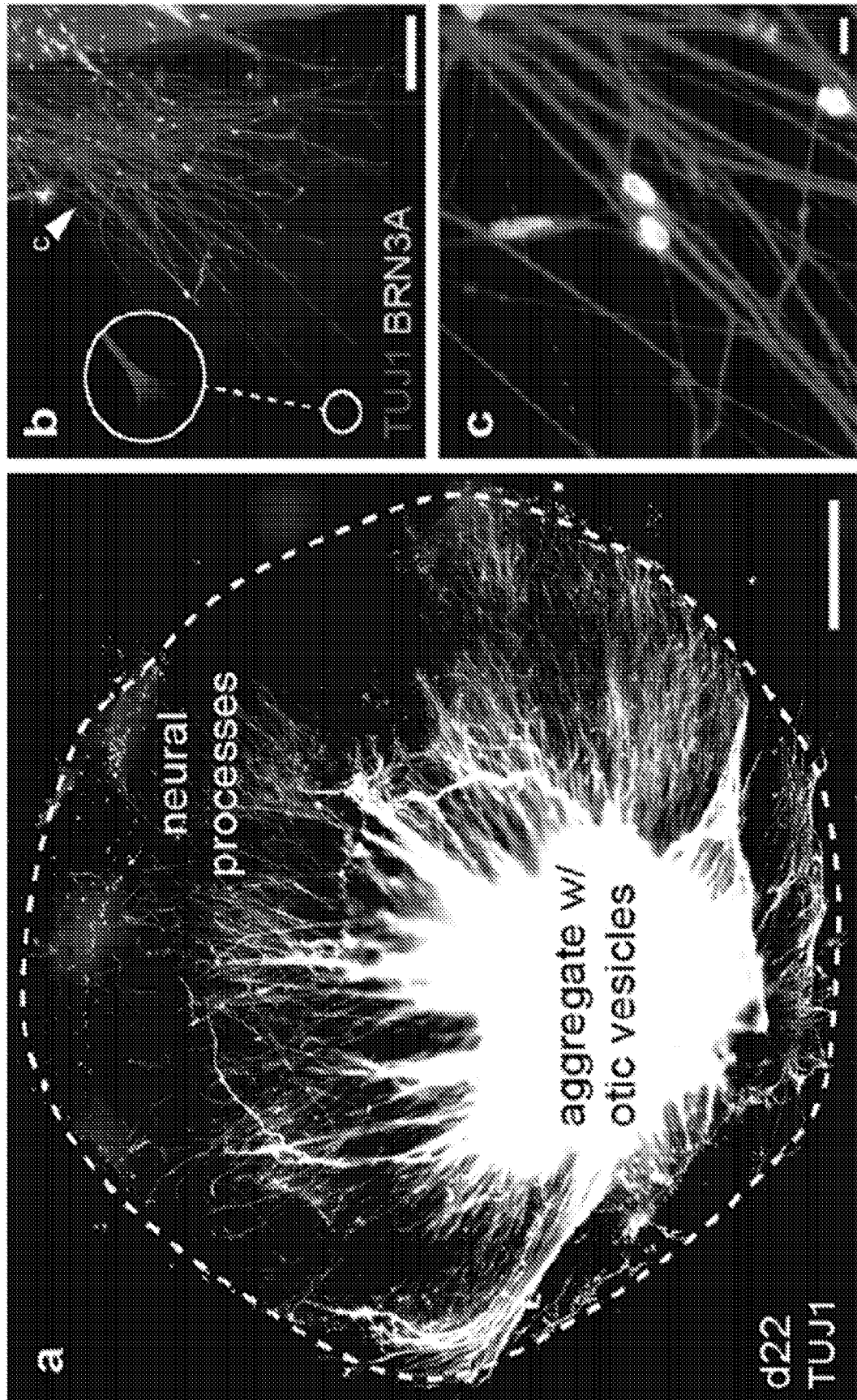
FIG. 15

Study Name	Chen et al. protocol (Nature, 2012) ²	Ronaghi et al. protocol (Stem Cells Dev., 2014) ³	Ealy et al. protocol (PNAS, 2016) ⁸	Koehler et al. protocol (Current)
Culture format	2D	3D to 2D	2D	3D
Demonstration of non-neural induction	(Not shown)	Yes	Yes	Yes
Analysis of "off-target" lineages included (e.g. mesoderm, neuroectoderm, etc.) to confirm proper lineage commitment	(Not shown)	Yes	Yes	Yes
Demonstration of pre-placodal or otic- epibranchial progenitor domain induction	(Not shown)	Yes	Yes	Yes
Expression of hair cell marker genes	Yes	Yes	Yes	Yes
Multiple hair cell marker genes co- expressed in the same cells	Yes	Yes	(Not shown)	Yes
Hair bundle morphology	Disorganized	Mostly disorganized. Organized morphology "in rare instances"	(Not shown)	Organized
Electrophysiological responses	Yes	(Not shown)	(Not shown)	Yes
Presence of supporting cells	(Not shown)	Yes	(Not shown)	Yes
Correct spatial relationship between supporting cells and hair cells	(Not shown)	No	(Not shown)	Yes
Presence of sensory neurons	Yes	(Not shown)	(Not shown)	Yes
Hair cell or hair cell-like cell generation efficiency	"A small subset" of cells differentiated from the OEP's population	1.79% – 5.89%	(Not shown)	Hair cells present in ~17% of aggregates

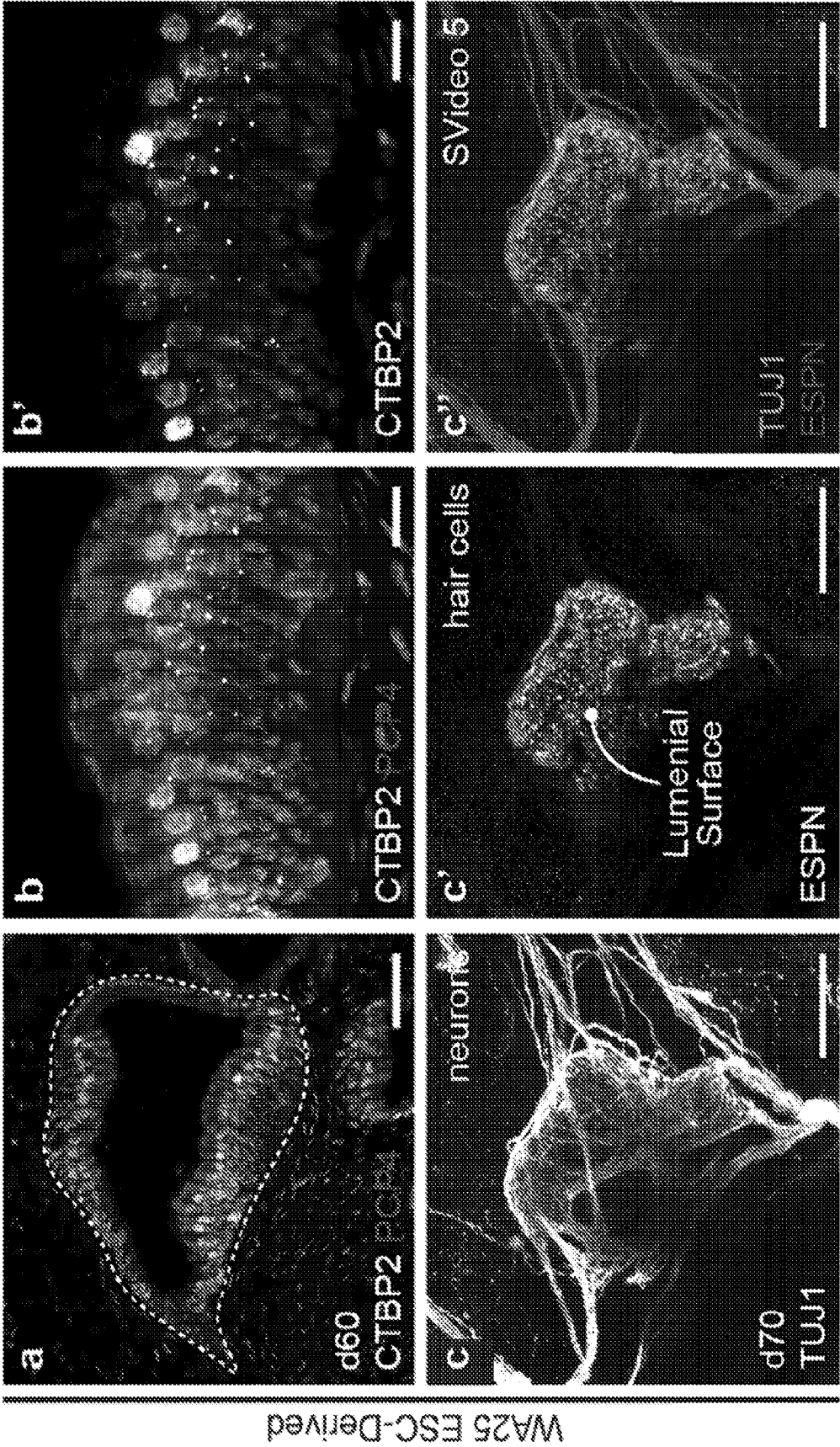
FIGS. 16A-16C



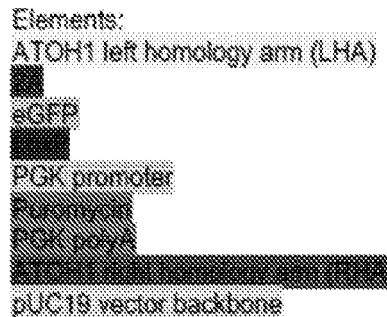
FIGS. 17A-17C



FIGS. 18A-18C



ATOH1-2A-eGFP-PGK-Puro donor plasmid (SEQ ID NO:21)

[illegible]

[illegible]

FIG. 20

**Genomic sequence of the homozygous/bi-allelic
ATOH1-2A-eGFP cell line at the ATOH1 locus (SEQ ID NO:22)**

Elements:

ATOH1 exon 1/1 without the stop codon



CTTTGATTGGCTGCTCGCACGCGCCTGCCCGCGCCCTCCATTGGCTGAGAAGACACGCGACCCGGCGCG
 AGGAGGGGGTTGGGAGAGGAGCGGGGGGAGACTGAGTGGCGCGTGCCGCTTTTTAAAGGGGCGCAGC
 GCCTTCAGCAACCGGAGAAAGCATAGTTGCACGCGACCTGGTGTGTGATCTCCGAGTGGGTGGGGGAGG
 GTCGAGGAGGGAAAAAATAAGACGTTGCAGAAGAGACCCGGAAAGGGCCTTTTTTTTGGTTGAGCTG
 GTGTCCAGTGCTGCCTCCGATCCTGAGCCTCCGAGCCTTTGCAGTGCAATGTCCCGCCTGCTGCATGC
 AGAAGAGTGGGCTGAAGTGAAGGAGTTGGGAGACCACCATCGCCAGCCCCAGCCGCATCATCTCCCGCA
 ACCGCCGCCGCCGCCGACCCACCTGCAACTTTGCAGGCGAGAGAGCATCCCGTCTACCCGCCTGAGC
 TGTCCCTCCTGGACAGCACCGACCCACGCGCCTGGCTGGCTCCCACTTTGCAGGGCATCTGCACGGCAC
 GCGCCGCCAGTATTTGCTACATTCCCGGAGCTGGGTGCCTCAGAGGGCCGCTGCGCCCCGGGACGAG
 GTGGACGGCCGGGGGGAGCTGGTAAGGAGGAGCAGCGCGGTGCCAGCAGCAGCAAGAGCCCCGGG
 CGGTGAAAGTGGGGAACAGCTGTGCAAGCTGAAAGCGGGGTGGTGGTAGACGAGCTGGGCTGCAGC
 CGCCAACGGGCCCTTCCAGCAAACAGGTGAATGGGGTGCAGAAGCAGAGACGGCTAGCAGCCAACGC
 CAGGGAGCGCGCAGGATGCATGGGCTGAACACGCCCTTCGACACAGCTGCACAATGTTATCCCGTCGTT
 CAACAACGACAAGAAGCTGTCCAAATATGAGACCCCTGCAGATGGCCCAAATCTACATCAACGCCTTGTC
 GAGCTGCTACAAACGCCAGCGAGGGGAACAGCCACCGCCGCTCCAGCCTCCTGCAAAAGCGACCA
 CCACCACCTTCGCACCGCGGGCTCCTATGAAGGGGGCGCGGGCAACGCGACCCGAGCTGGGGCTCAGC
 AGGCTTCCGGAGGGAGCCAGCGGCCGACCCGCCGGGAGTTGCCGGACTCGCTTCTCAGCCCCAGCT
 TCTGCGGGAGGGTACTCGGTGCAGCTGGACGCTCTGCACTTCTCGACTTTCCAGGACAGCGCCCTGACA
 GCGATGATGGCGCAAAAGAATTTGTCTCCTTCTCTCCCGGGAGCATCTTGCAGCCAGTGCAGGAGGAAA
 ACAGCAAACTTCGCCTCGGTCCACAGAAGCGACGGGAATTTCCCCCATTCCATTACAGTGACTC
 GGATGAGGCAAGTGCTAGC

ATOH1 exon 1/1 without the stop codon

eGFP

GAATTC

GGGCGCGCCGAAGGTGACAGAAGCCTGAAAACCTGAGACAGAAACAAACTGCCCTTTCAGTGGCGG
 GGAAGCCCCGGGTTAAAGATCCCGCACCCCTTAATTTTGTCTGCGATGGTGGTTGTTAGCAACGA
 CTTGGCTTCAGATGGCAGCTACATTTGATGGTTTGCAAATGCCGCCGCTGTTCCAAACTTCCTACGGTCCA
 TATTGTTTGATGAAAACCTTCTGTTAAATTTGTGTCTTTCCGCCACCTTCTGCTCCCCCTTTAGATAGAT
 ACGGTATAATTGTAGGTACCCGTATATGGCATCATTATTCTAGTTCCCTGCTGCCAATACGCTGCTAAAAC
 GTCGCATCTTCTCTGTCACTGGTTTGGGTTAATTTATTTTACGCCCTGGGCATCCATCCTTGTGTGTTGC
 GCACTCAAGTGTGGGAGATTTAGTCTTCCGAAGTTGTTTTCCAAATGCACAATGAAACGCAAAATTAGTG
 CTTCCAAAGTGGATAACTTTTACTATGGAATTGTTAGAAAACAAGAACTTTAAGGTTTATATATTGTATAA
 ACATACCCAGTATGTGCATCCGATCGCGAGAAGGTTGGCGTCTTTTAGGAAACTCCGCGCACGCACTTTA
 TCAGCCGCTGCTGCGGTGGTGGCTCCAGGAGAACTCAACTGCCAATTGCAGACCAGTTTTTTTTTTTTTA
 AACACAGCCACTTATAATTCTTAAGCTCTTGCAAATGTTTGTGTTAAAAAATGAAAAATGAAAAATCTAG
 TAGTGTCAAACGCATTTGGTCAATTTTATTTGCTTGTGTTAATATTAGAAAACCTTATTTATTGTTTGCTAC
 CATTTCTACTTATCTTGATTCATTTTACGTTTCTACTCGAGATCATTTTATTTTAAATTTAGCAAAGCCAAC
 TGCCCTTGTGTTAATGTATTTGTTTGCAAATGATTAAATTAATGTGAAAAGAAGCCTTTTGTCACTTATTC
 CTTGAGTATAACTACTGAAAACAATTTTCAAATGAATGACTTTGAAGAATTGAGTTAAGTCTTCTATTCAATG
 TCATTTATGCGATCTTACAGTTTGAAGAAAAATGTTGTAAACTTGGTGCCTTCAGGTAGTATAAACCC
 TTCAAAGAAAAGCACTCAAGTCAATAATTAAATTTGTGAGATAAACTTCTTCCAAATTTGCAGCACAGTTTT
 GCCTCTTTGATGGCCAGGATCTT