

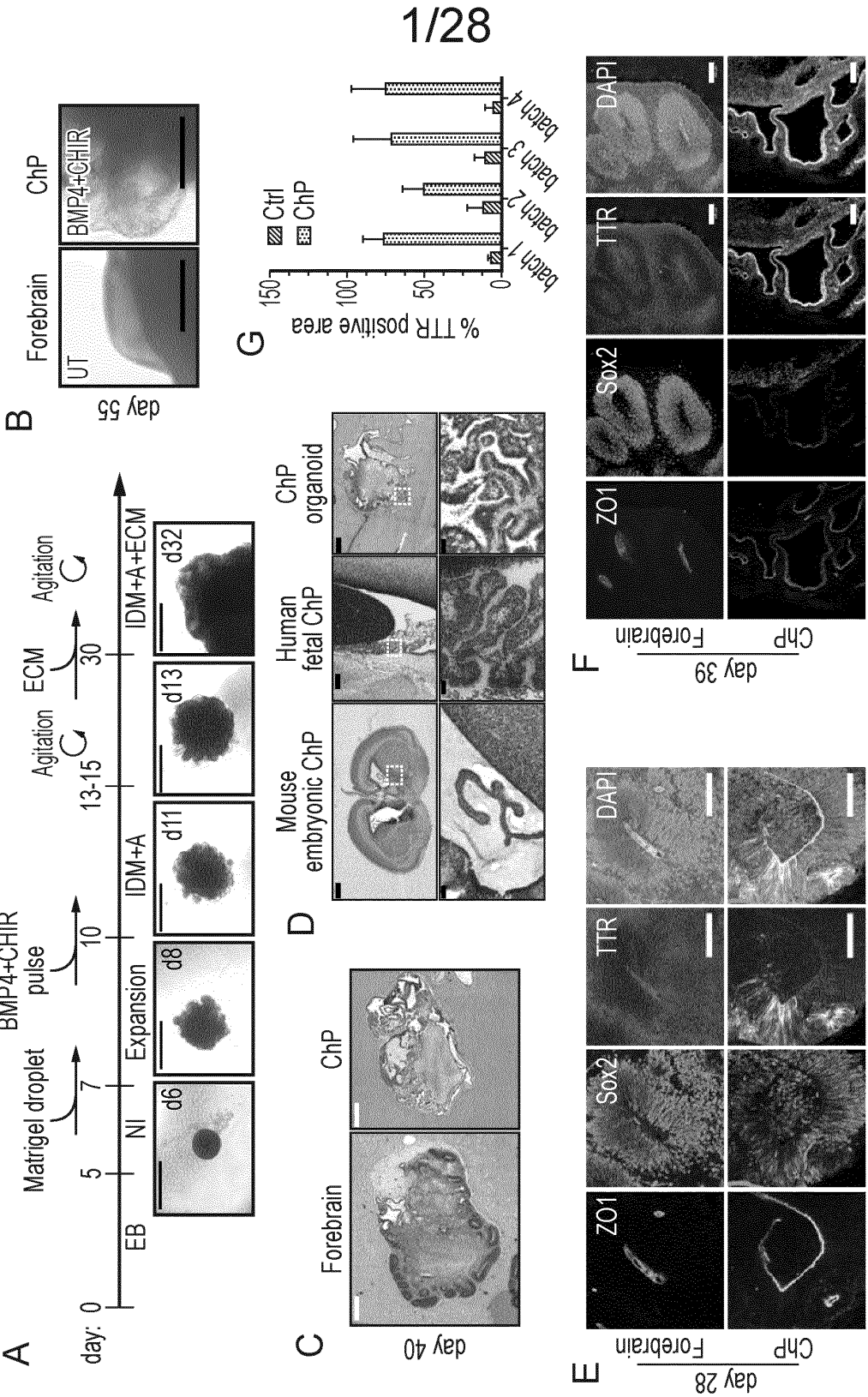


FIG. 1

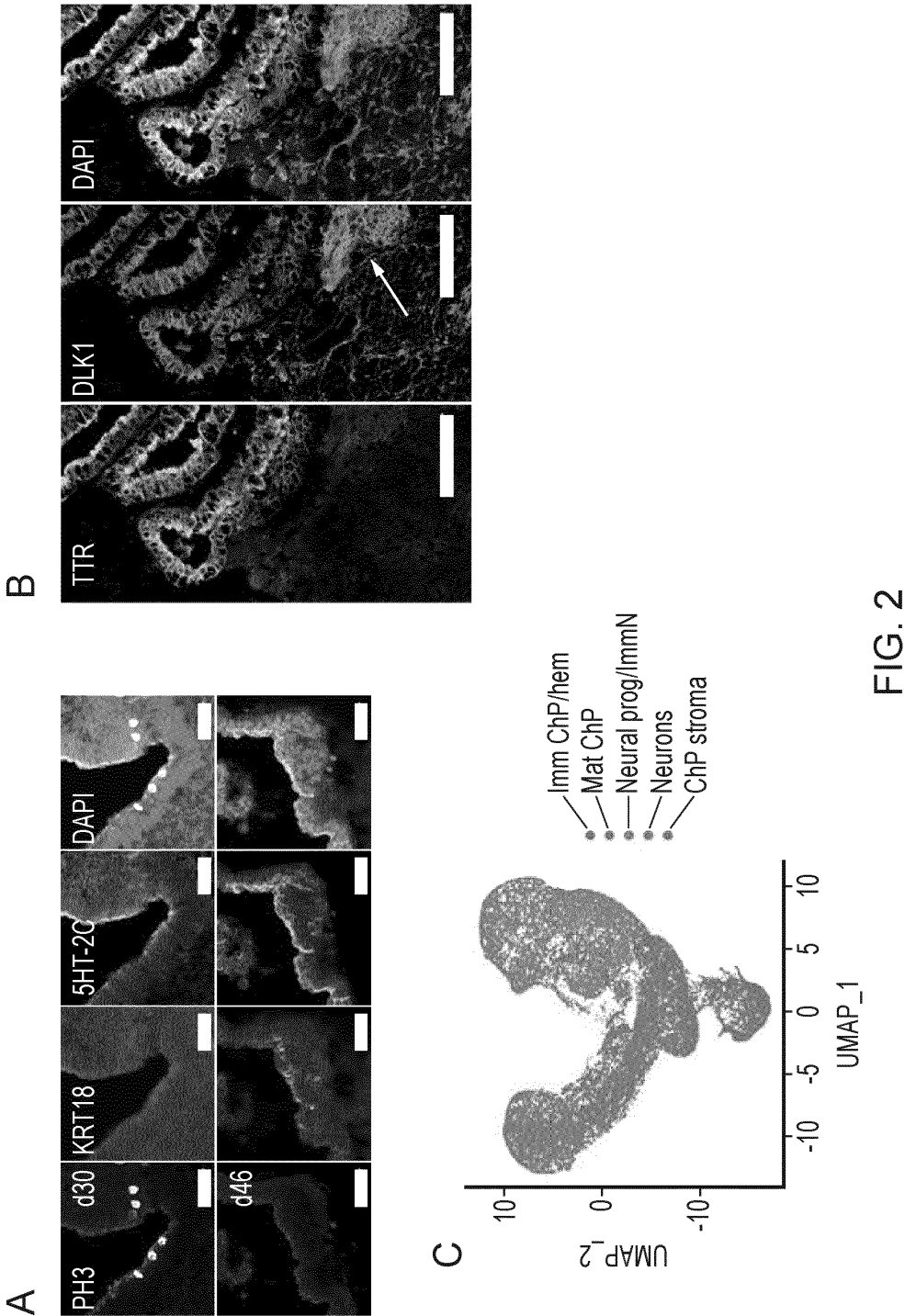


FIG. 2

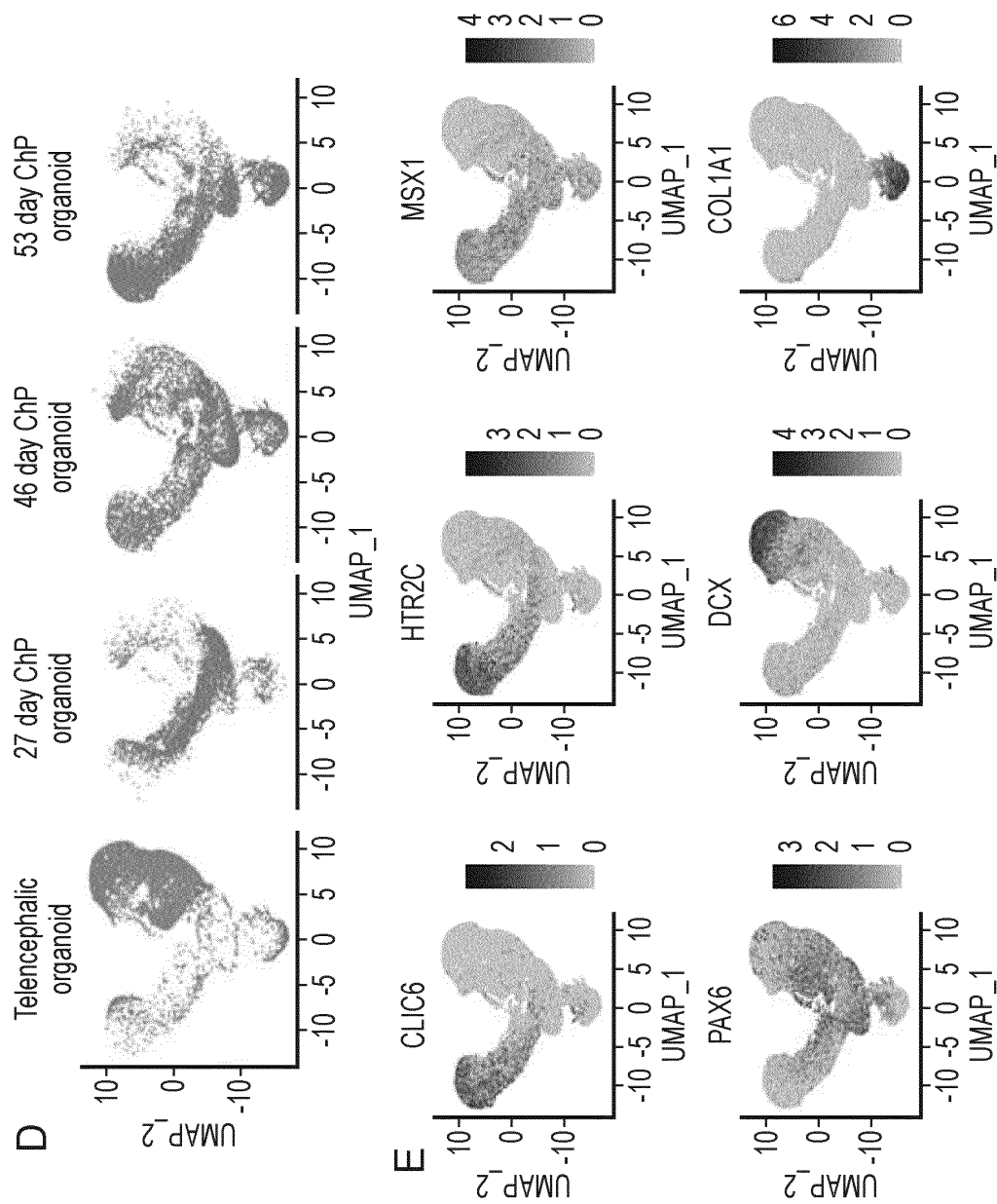


FIG. 2 (Continued)

4/28

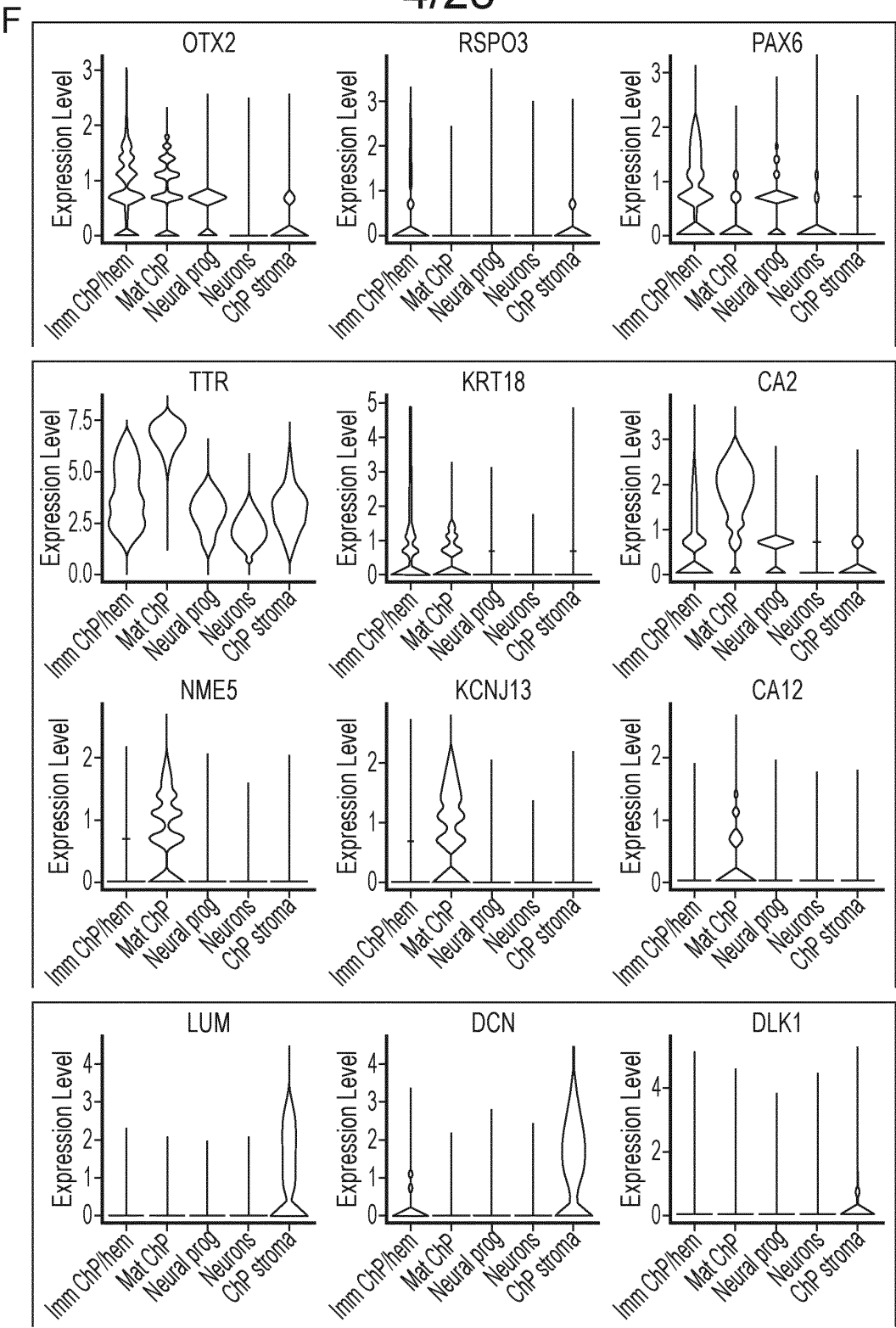


FIG. 2 (Continued)

5/28

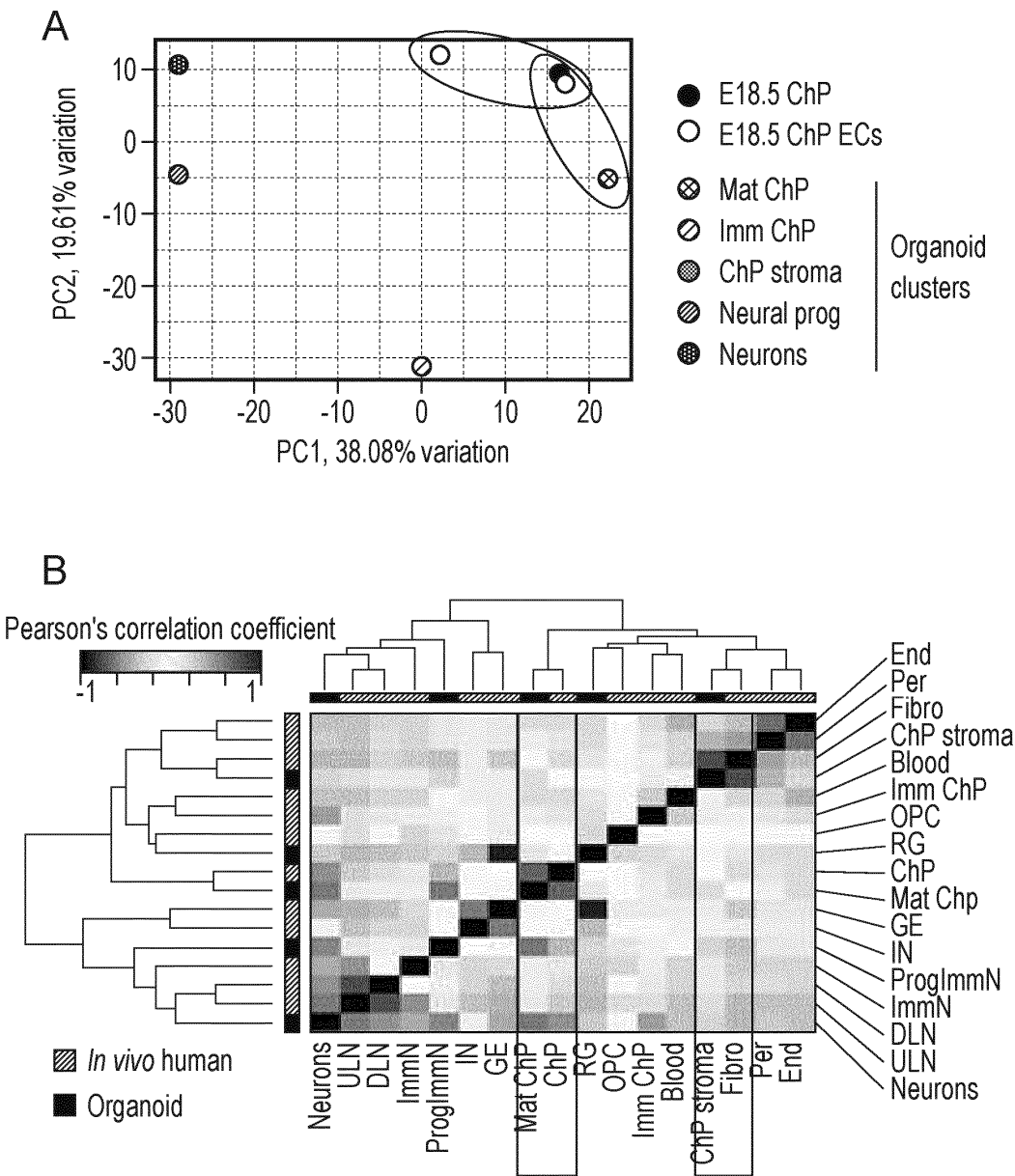


FIG. 3

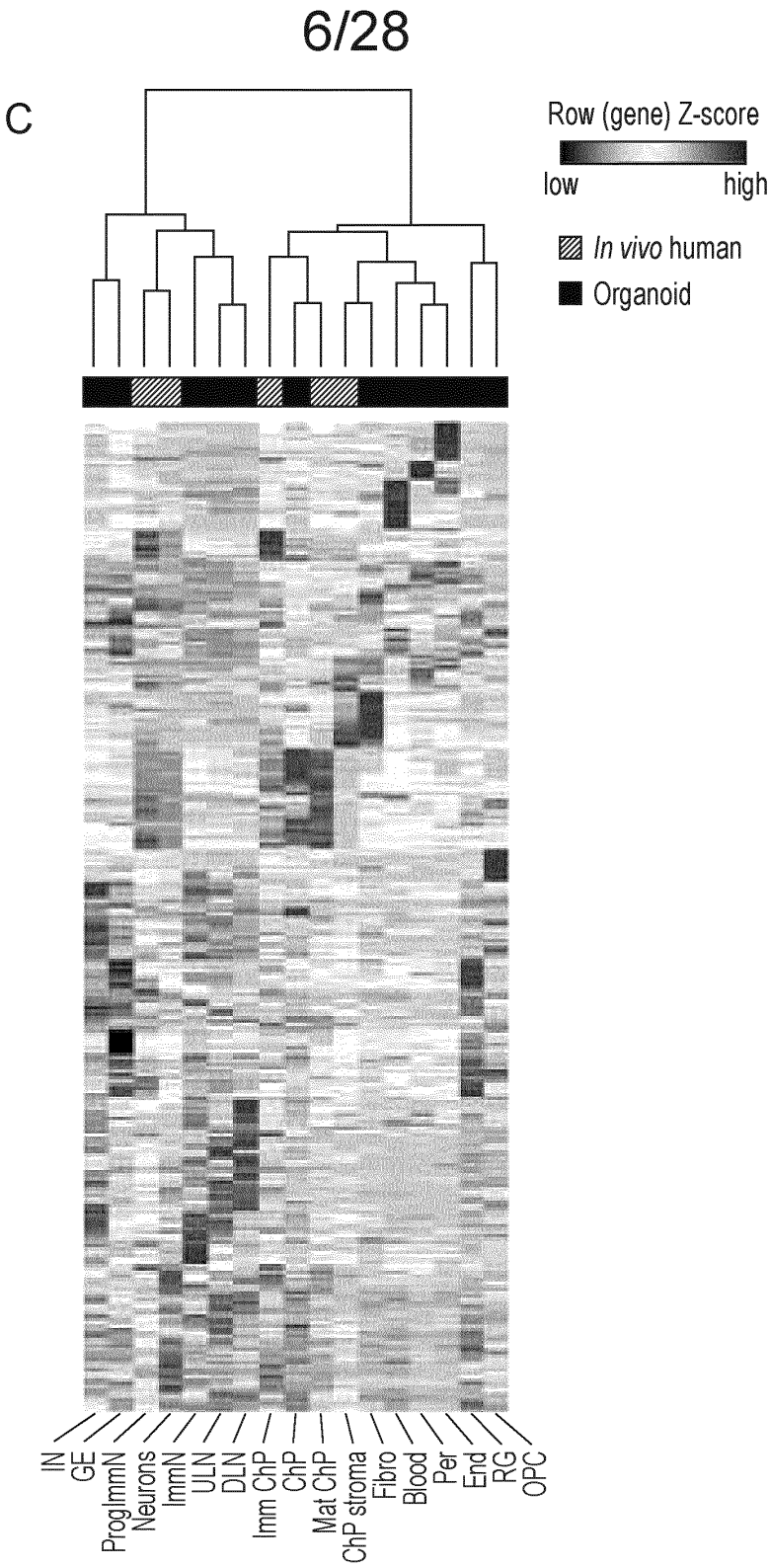


FIG. 3 (Continued)

7/28

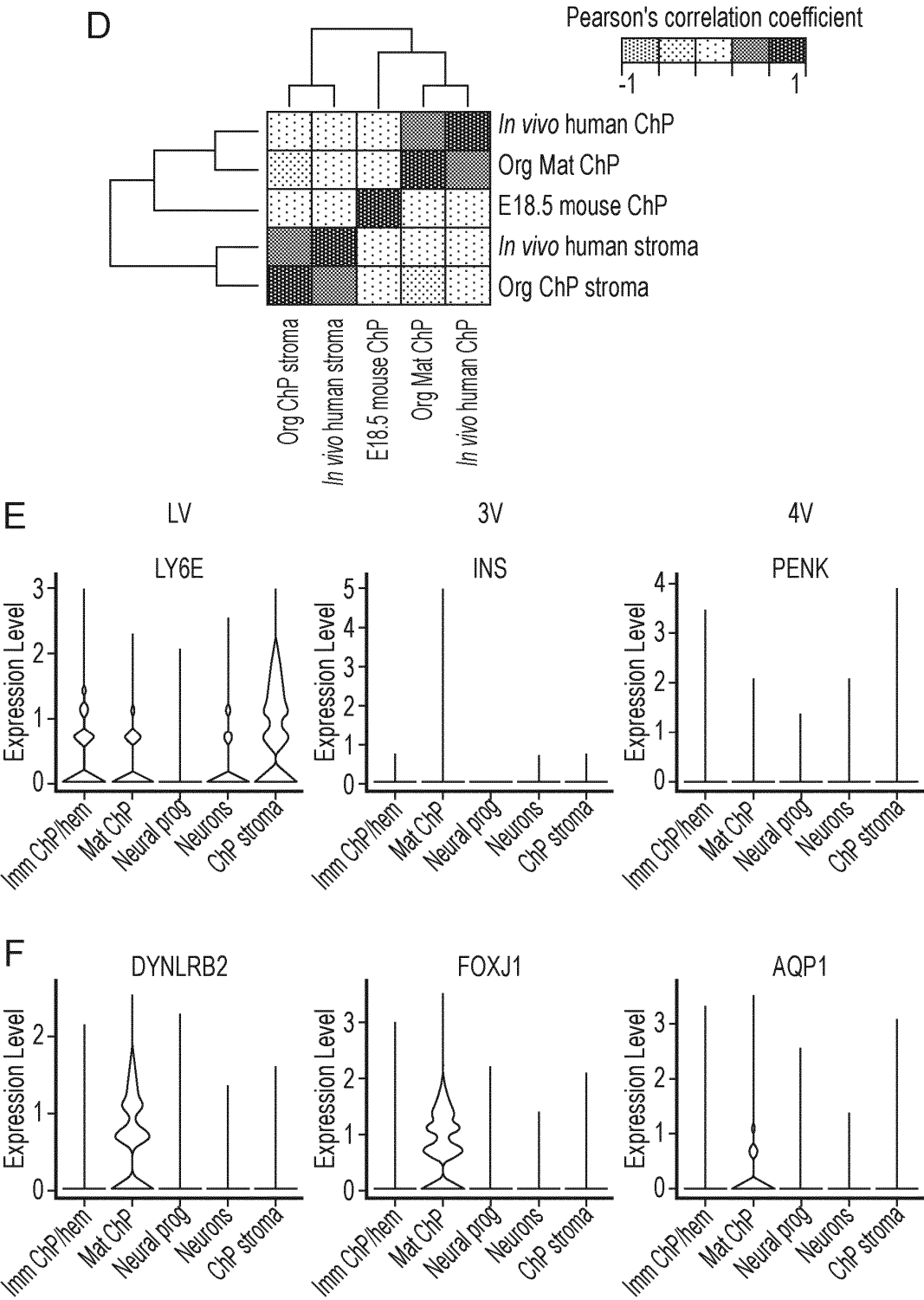


FIG. 3 (Continued)

8/28

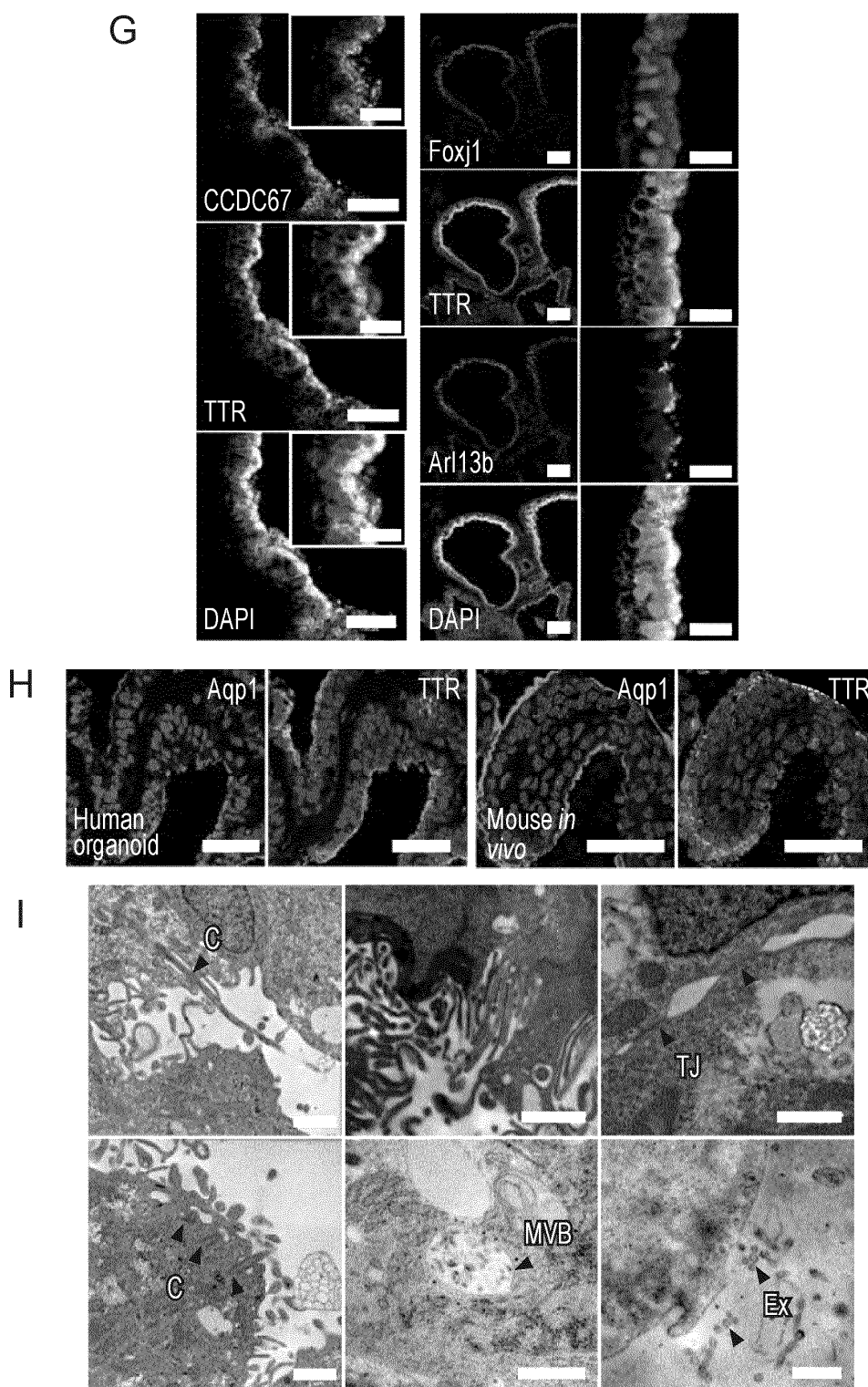


FIG. 3 (Continued)

9/28

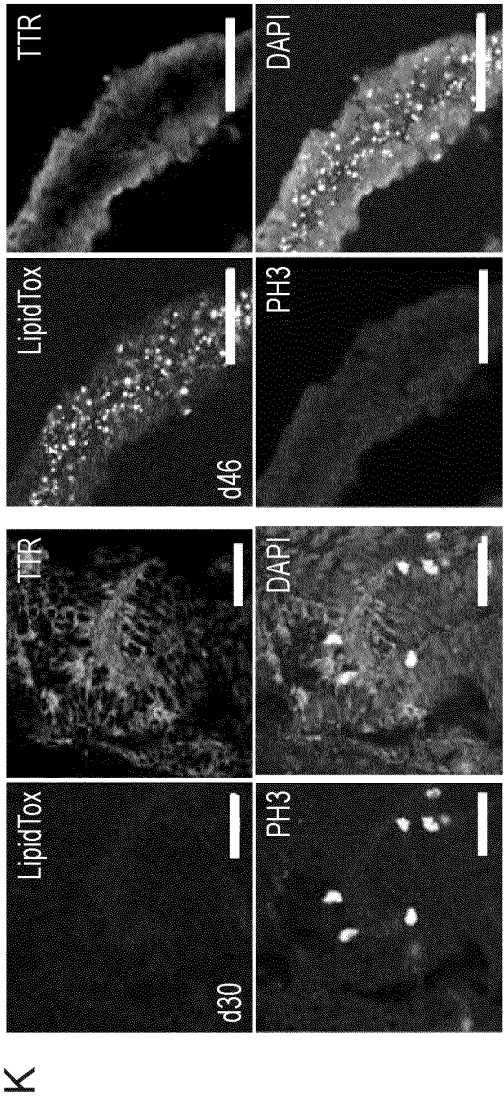
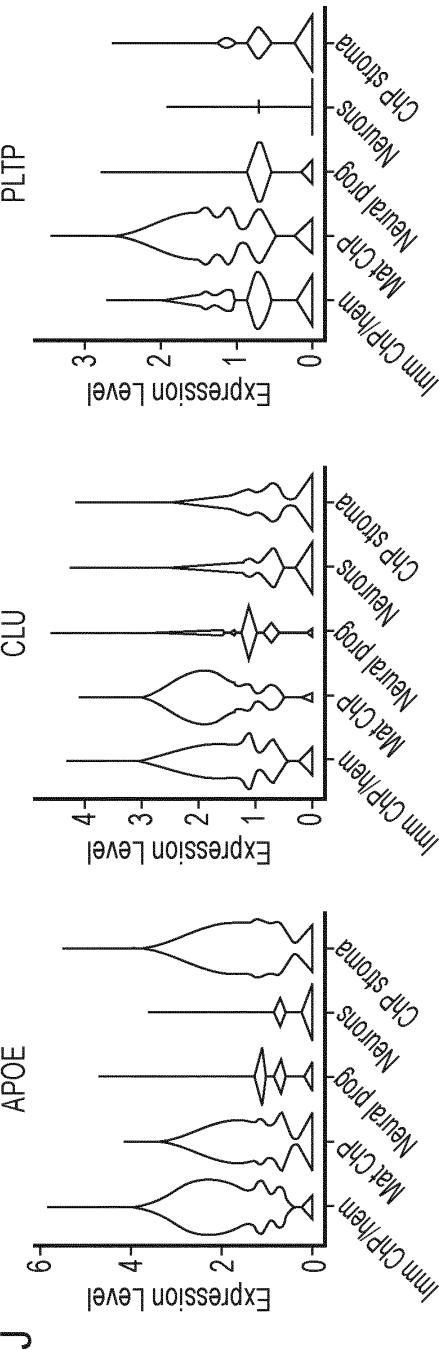


FIG. 3 (Continued)

10/28

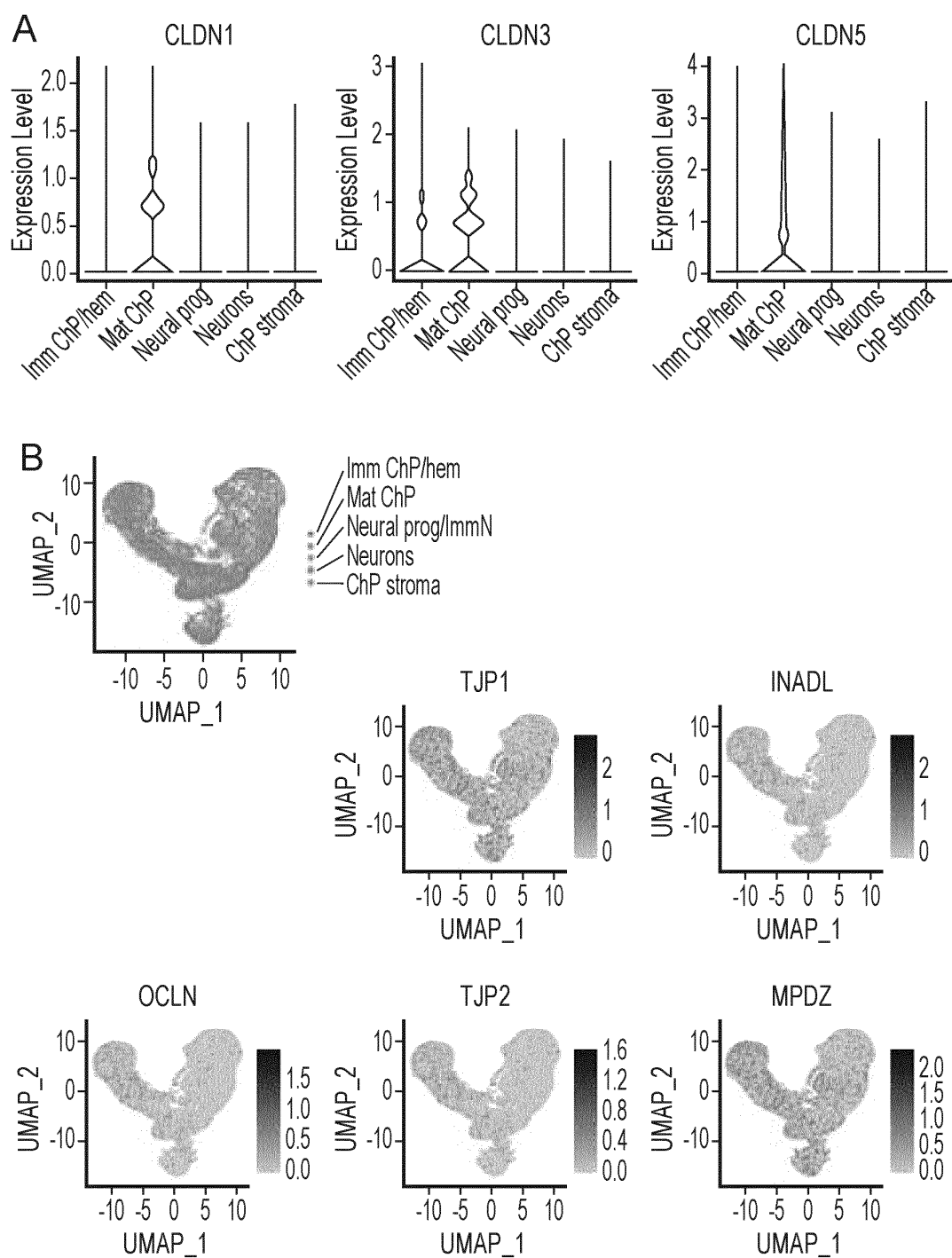


FIG. 4

11/28

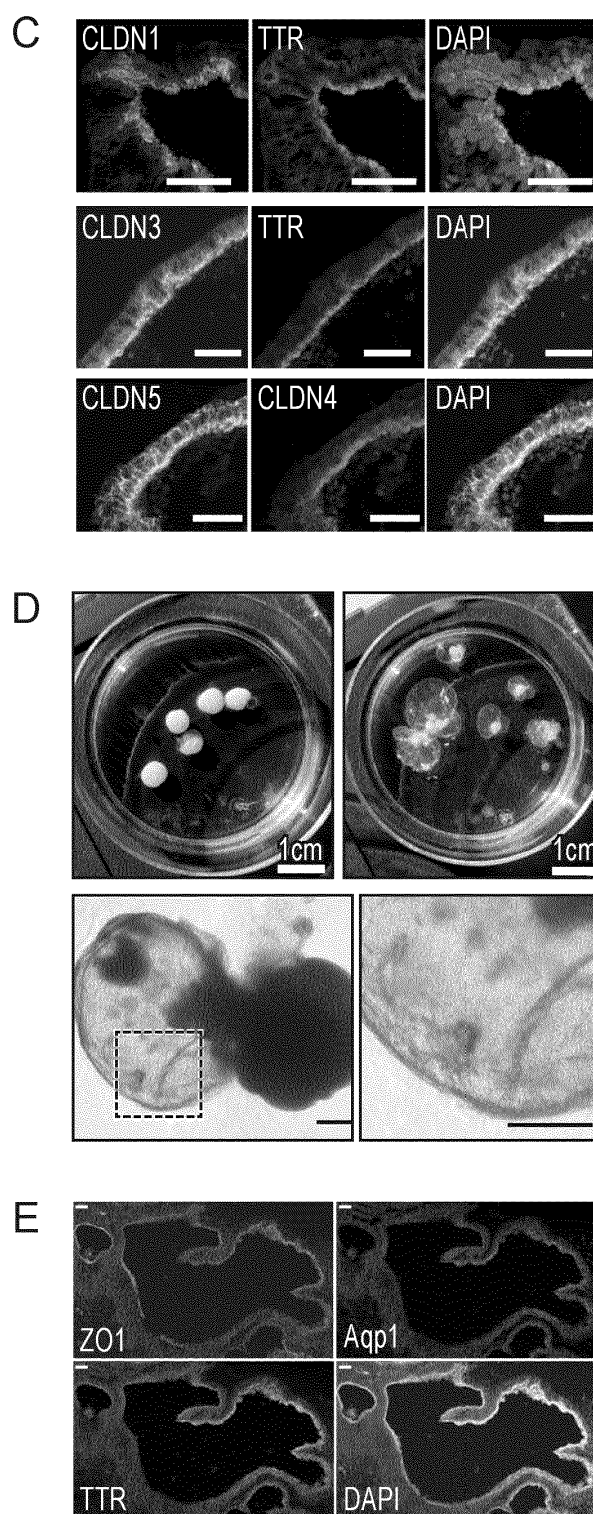


FIG. 4 (Continued)

12/28

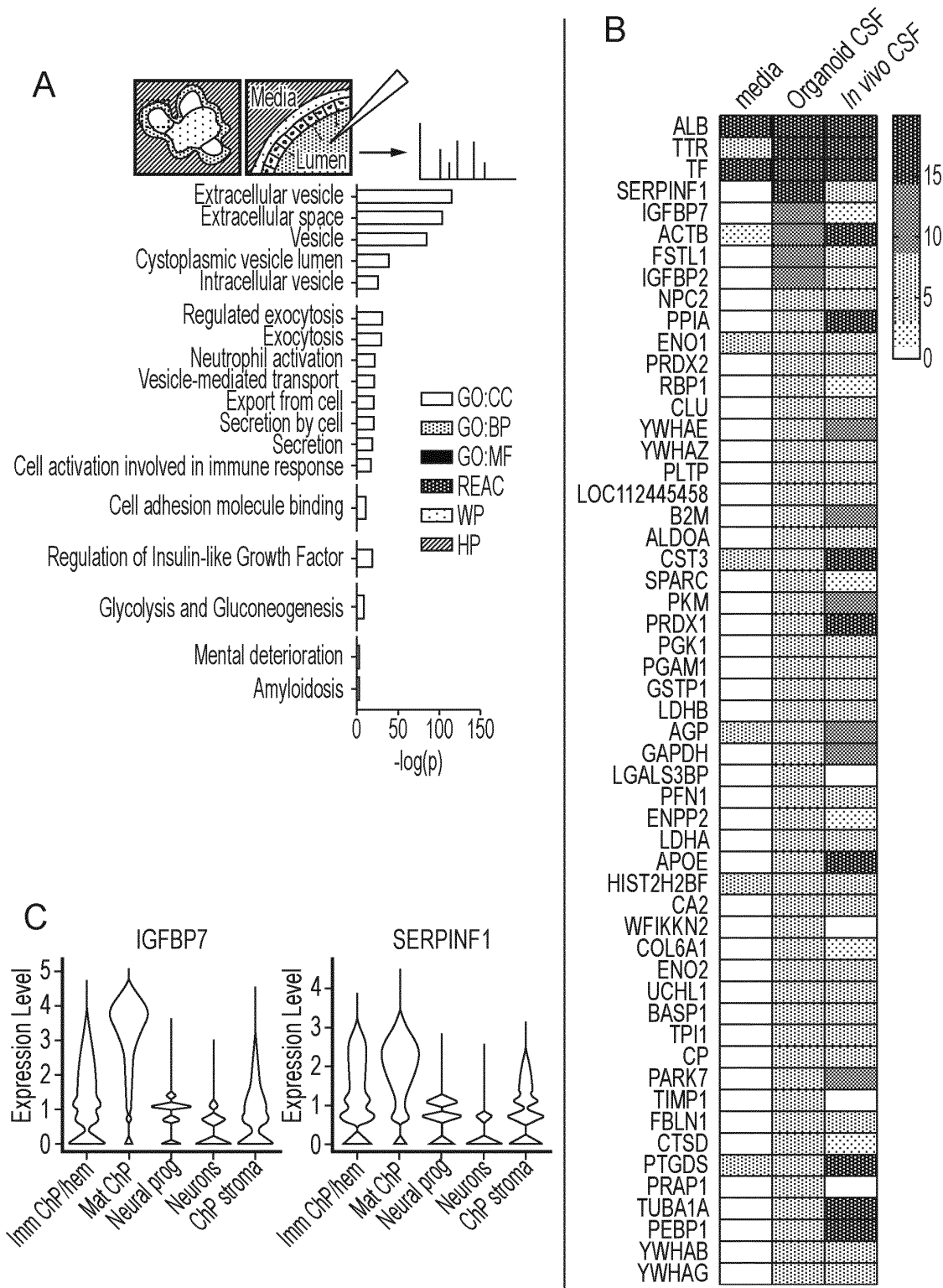
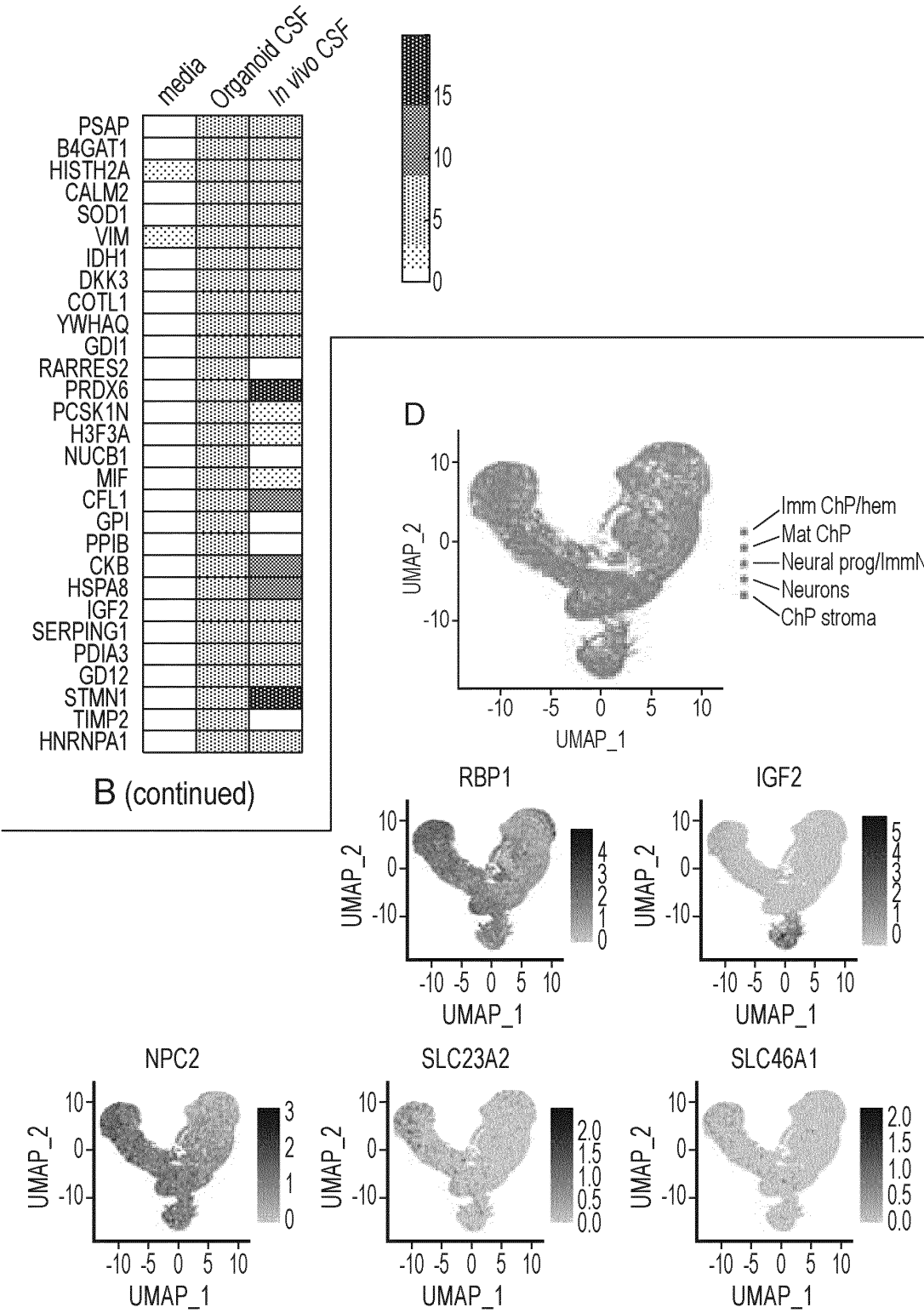


FIG. 5

13/28



14/28

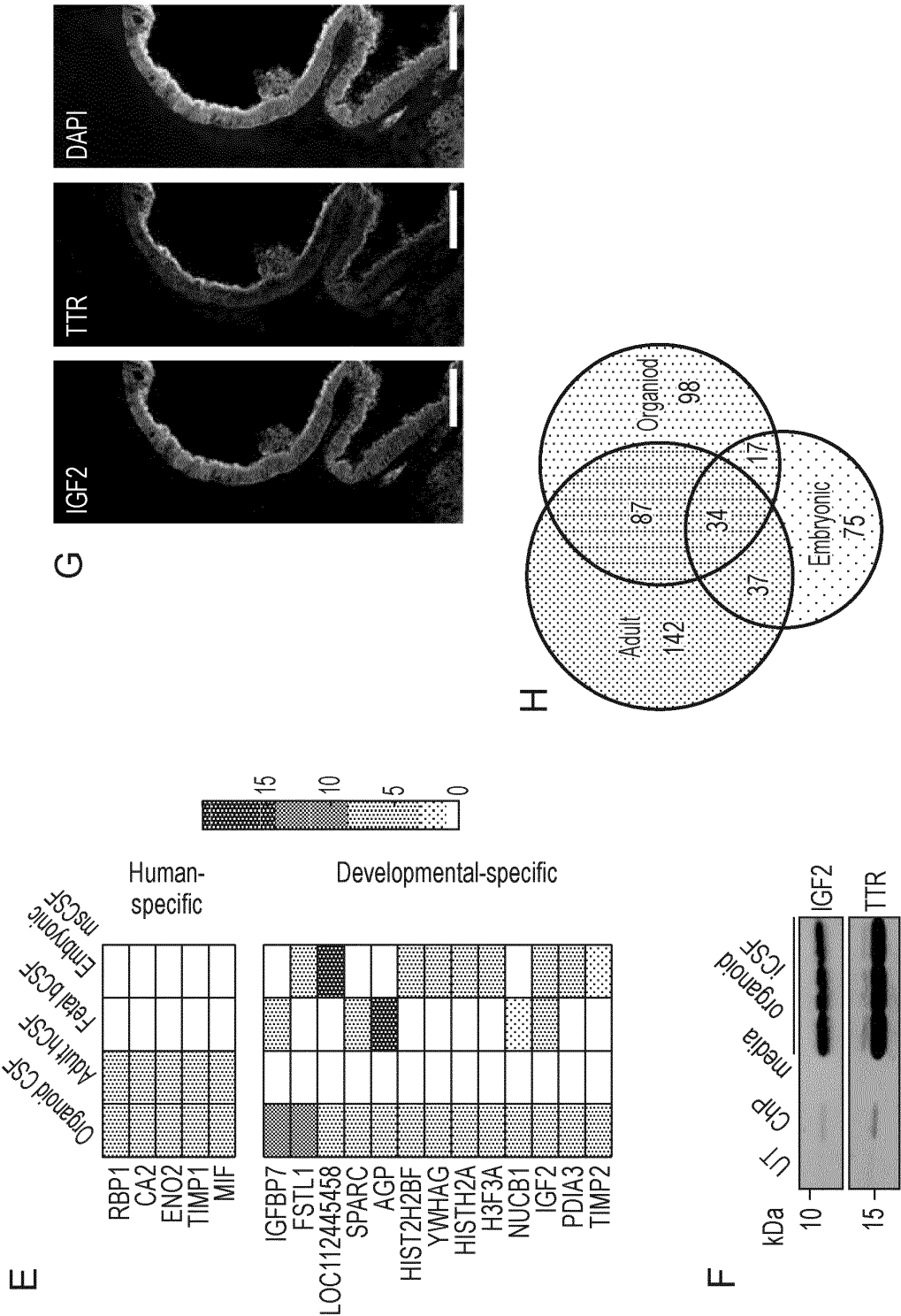


FIG. 5 (Continued)

15/28

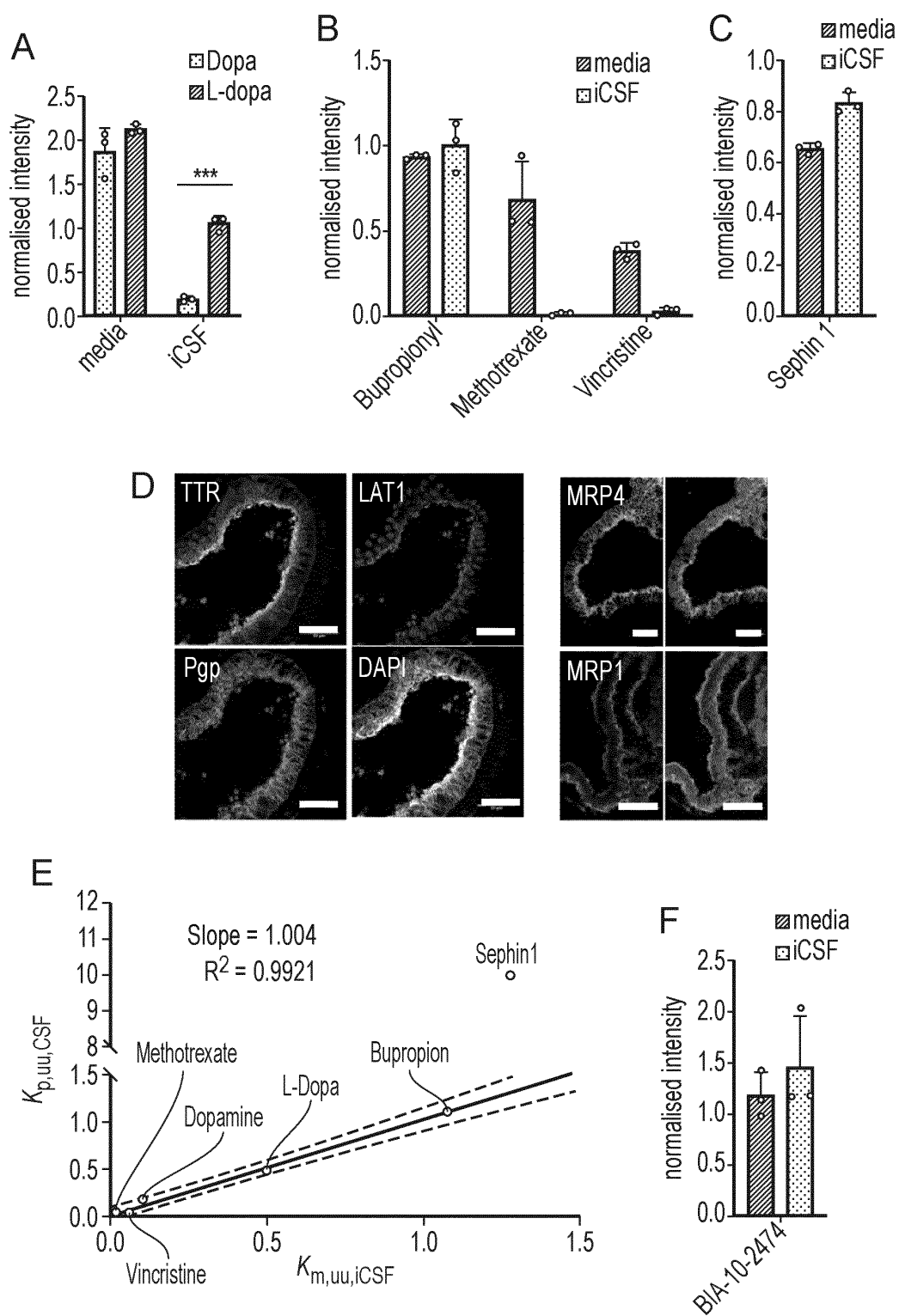


FIG. 6

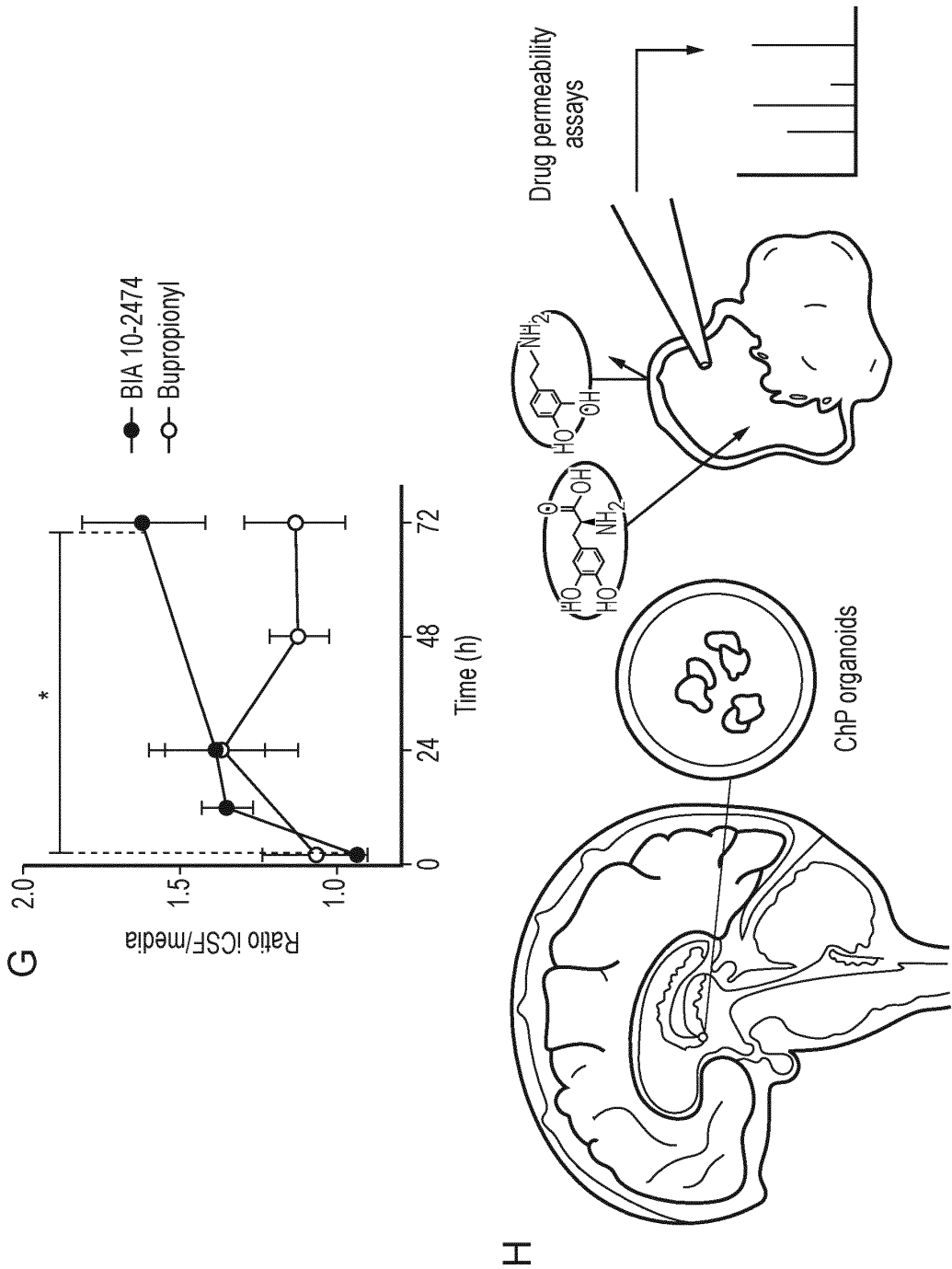


FIG. 6 (Continued)

17/28

A

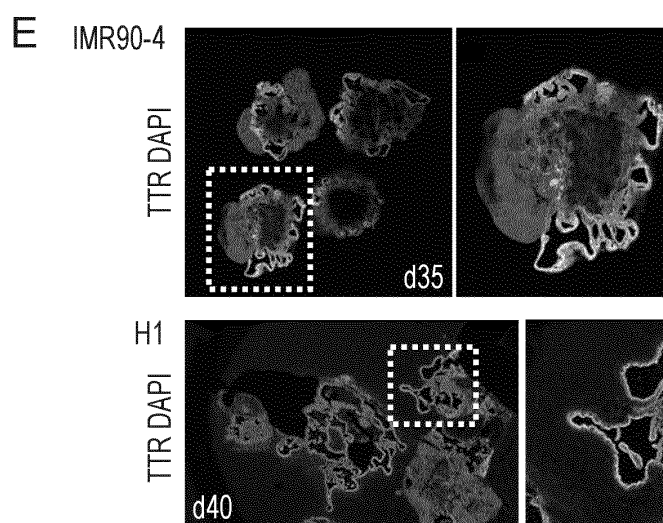
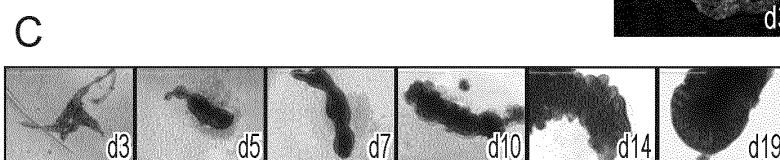
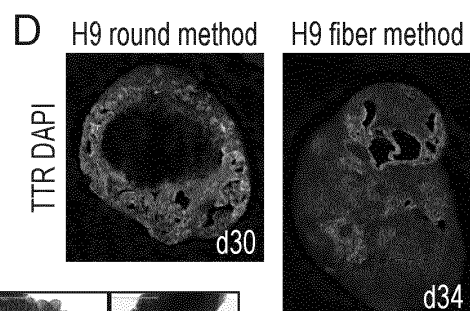
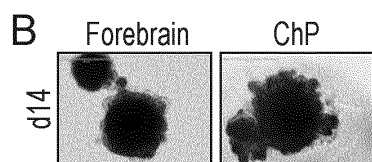
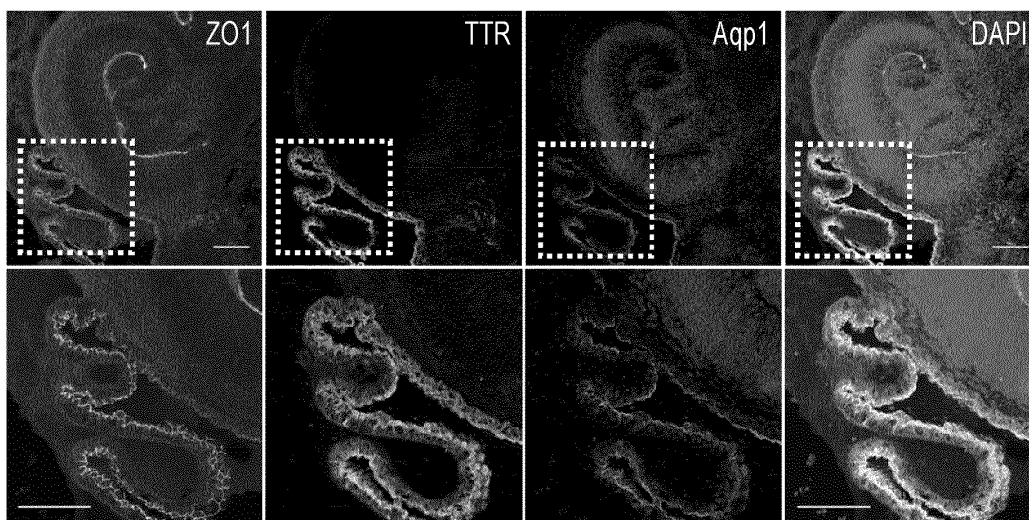


FIG. 7

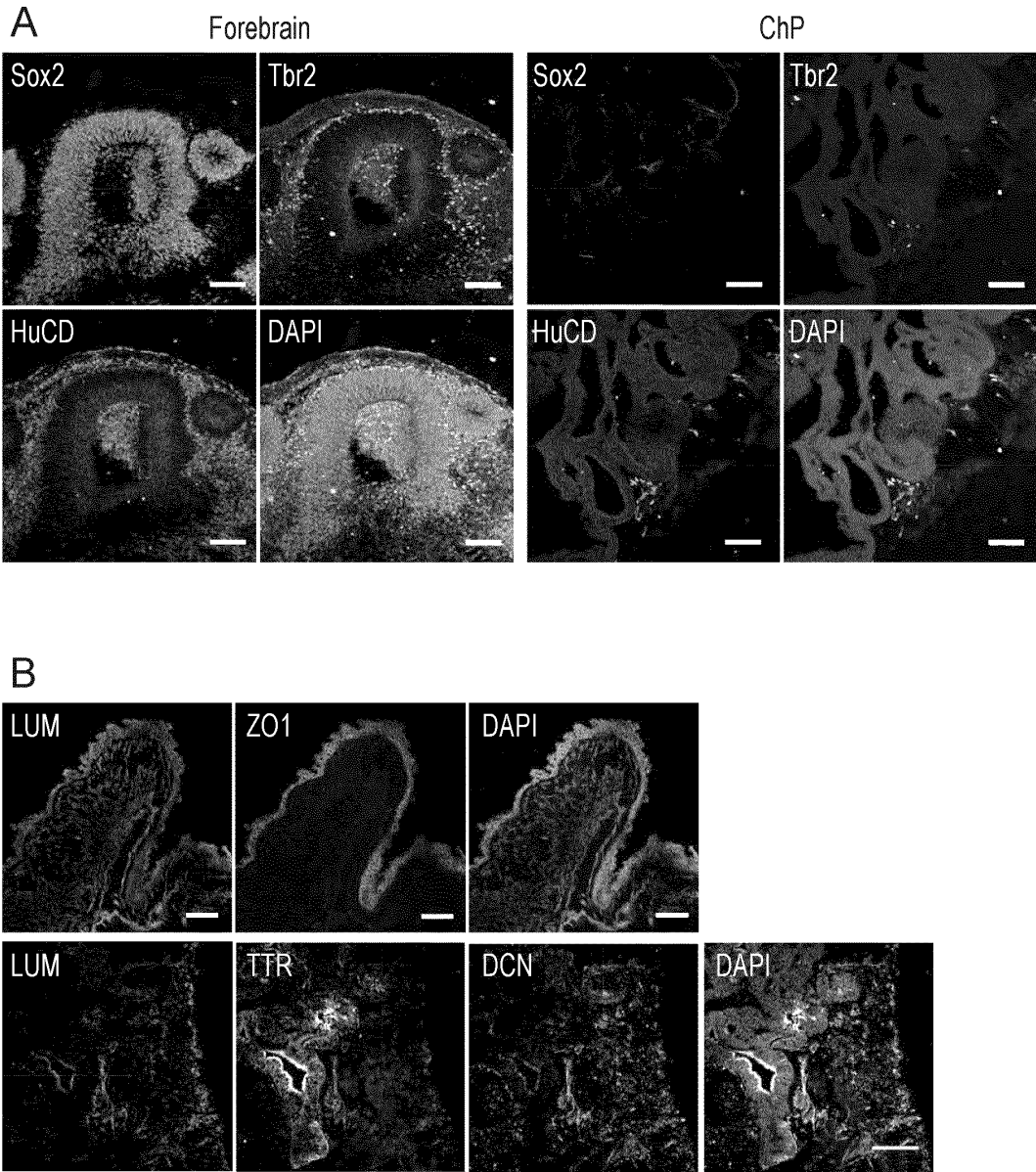


FIG. 8

19/28

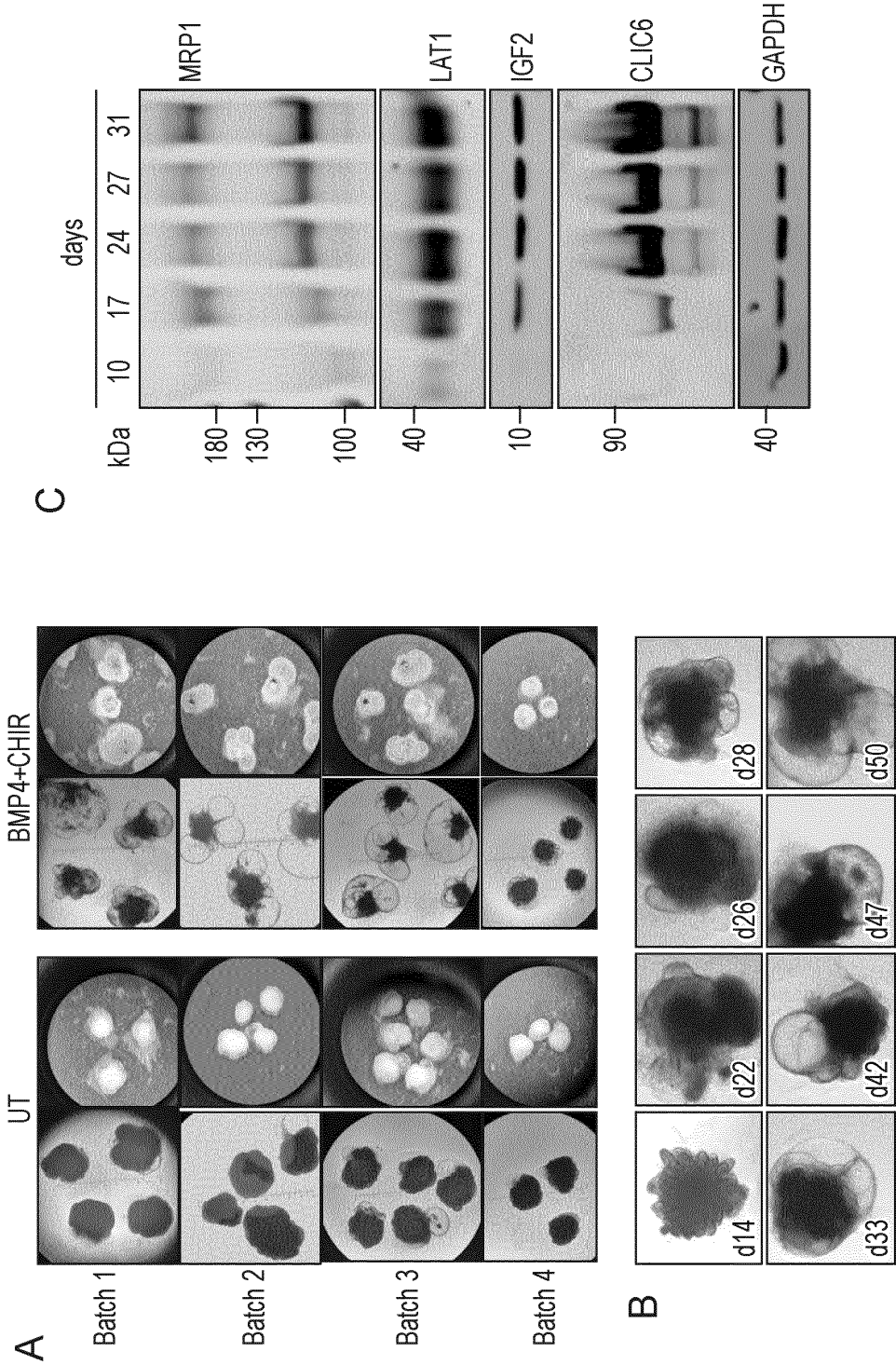
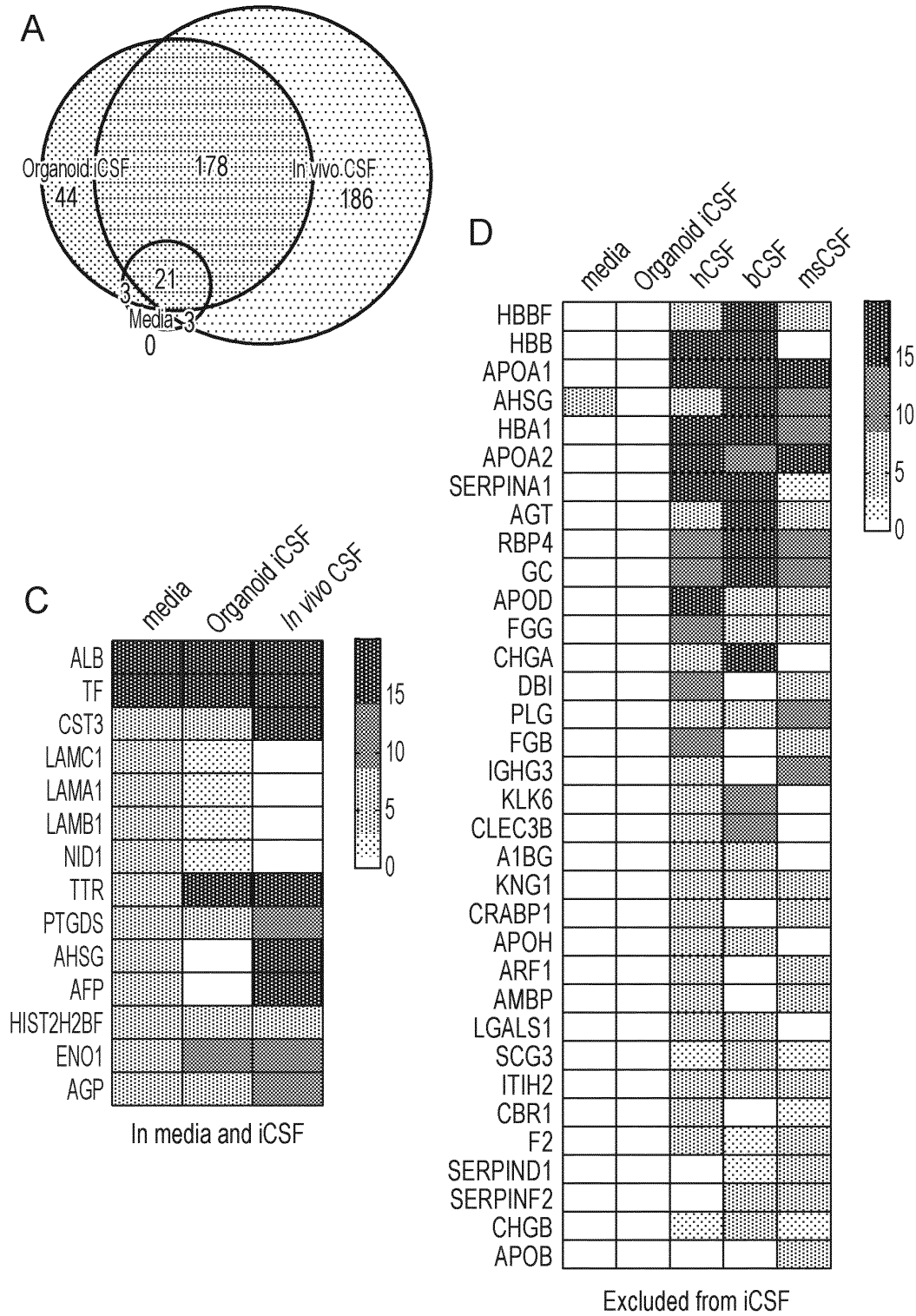


FIG. 9

20/28



21/28

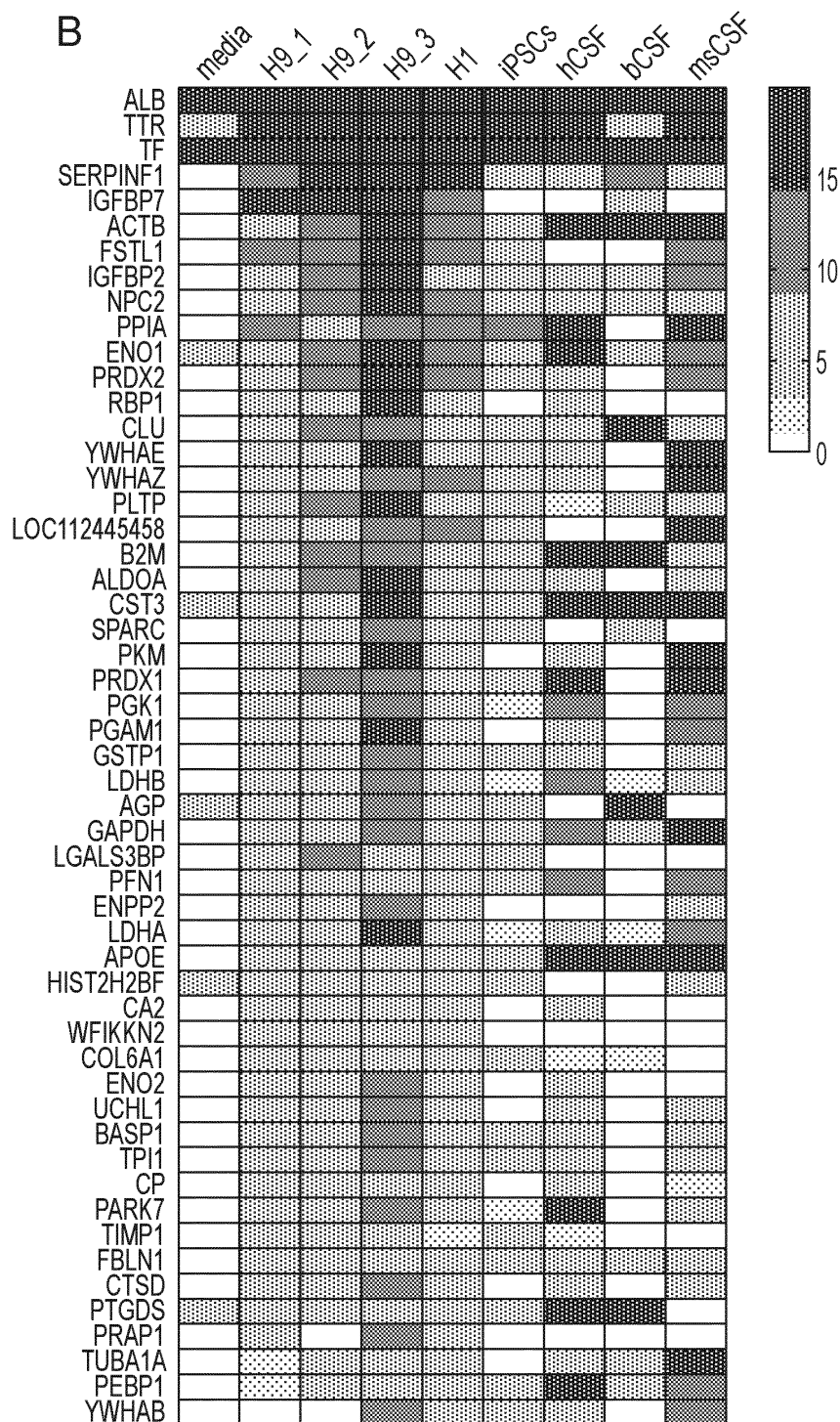


FIG. 10 (Continued)

22/28

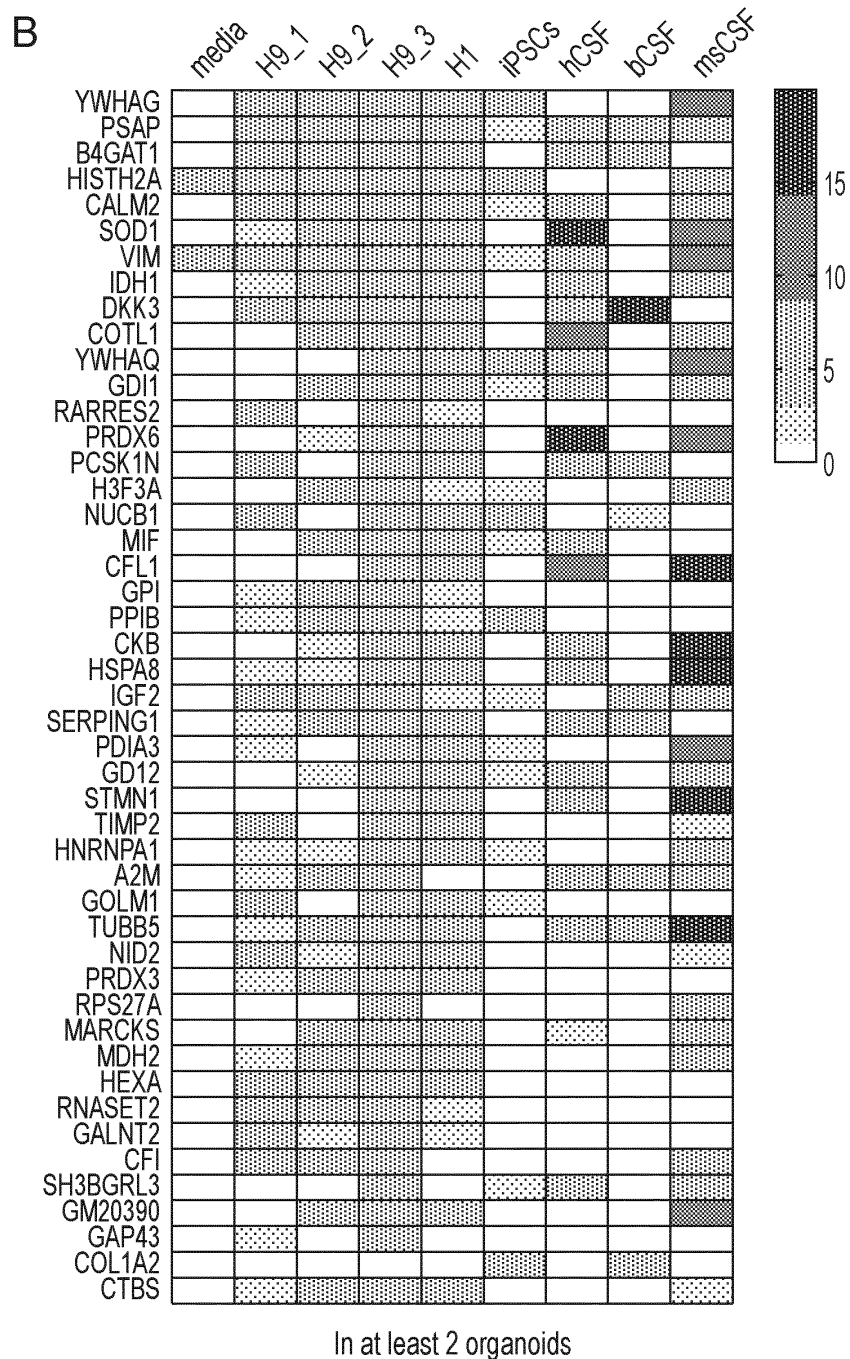


FIG. 10 (Continued)

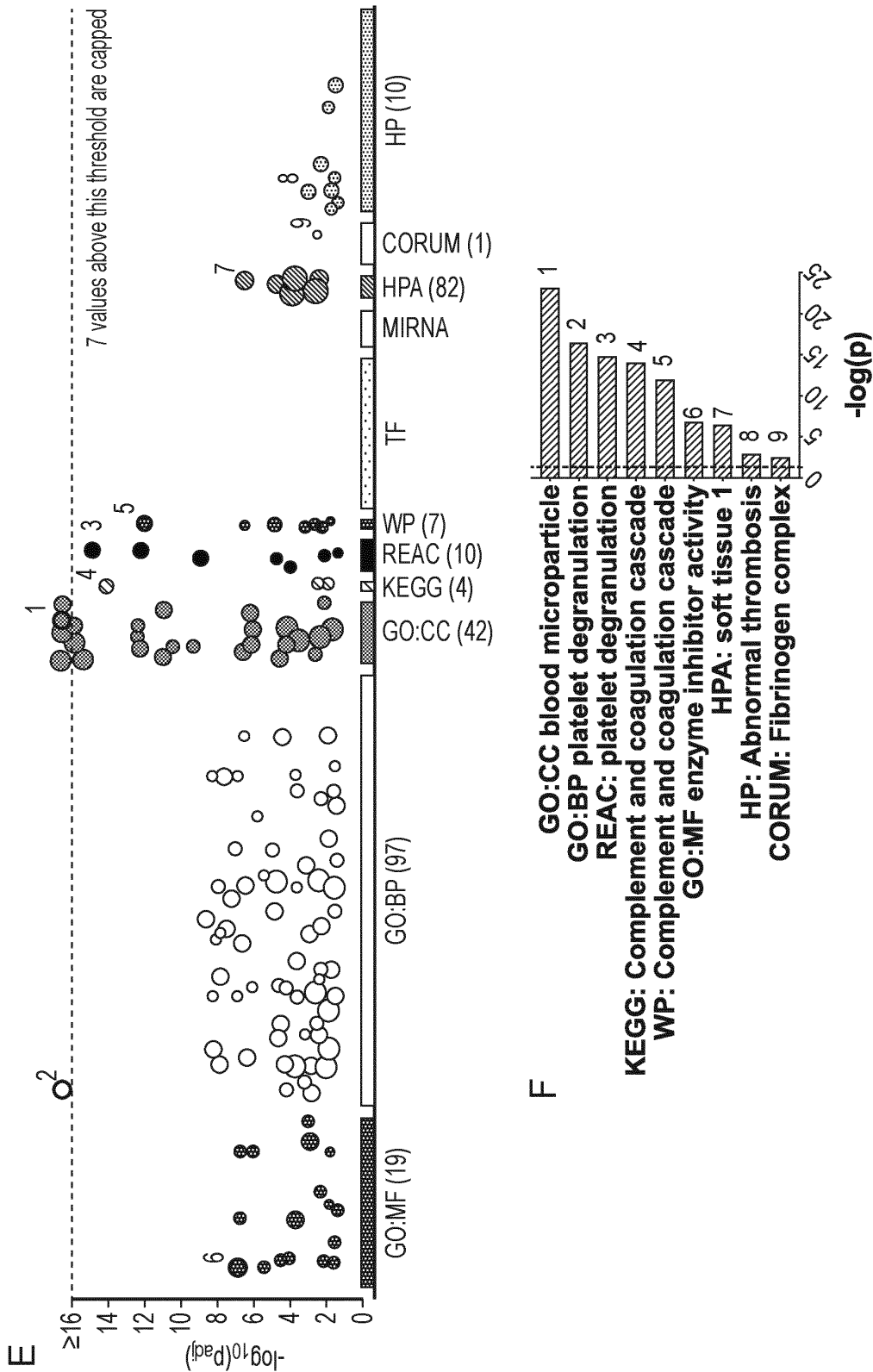


FIG. 10 (Continued)

24/28

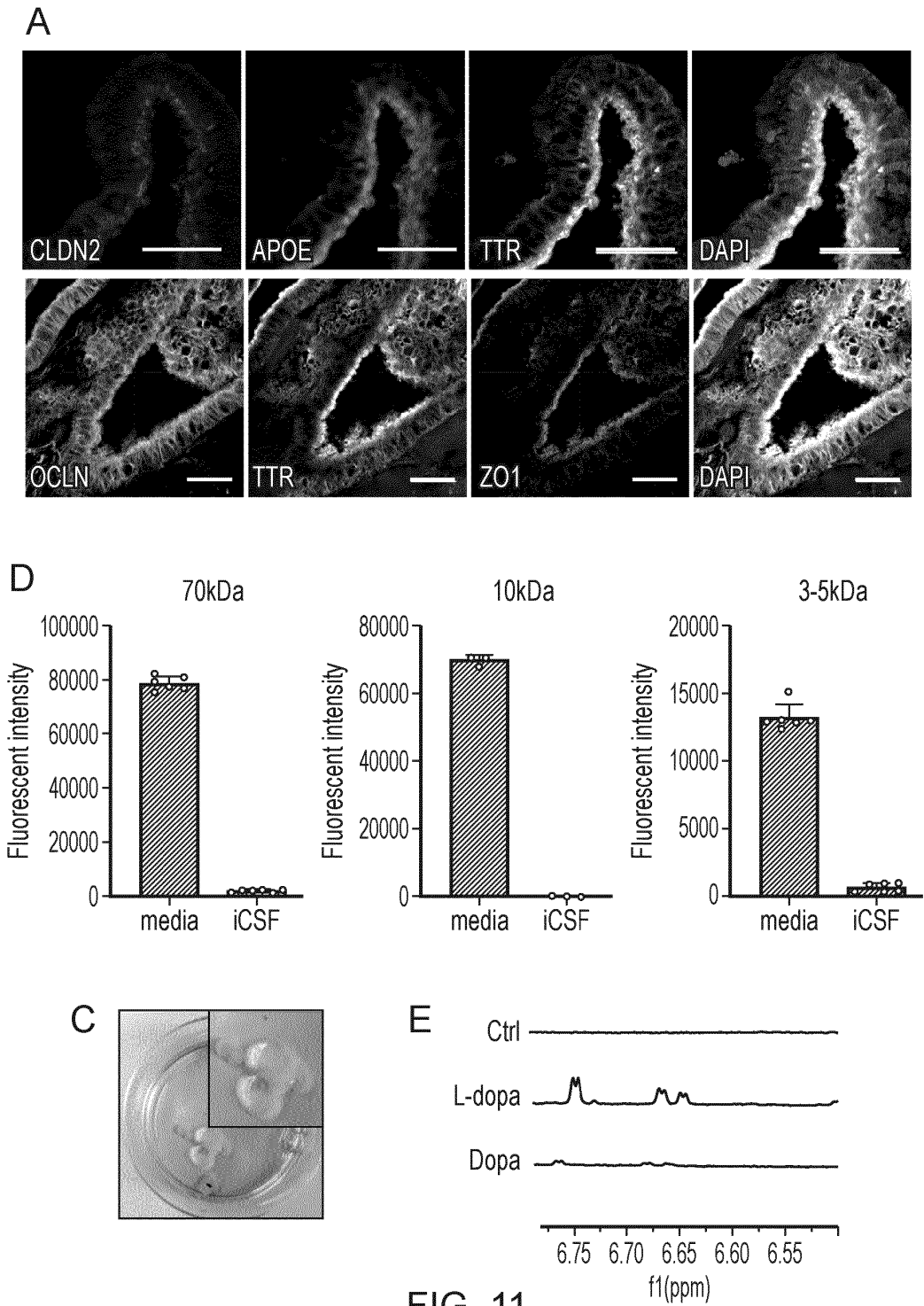


FIG. 11

25/28

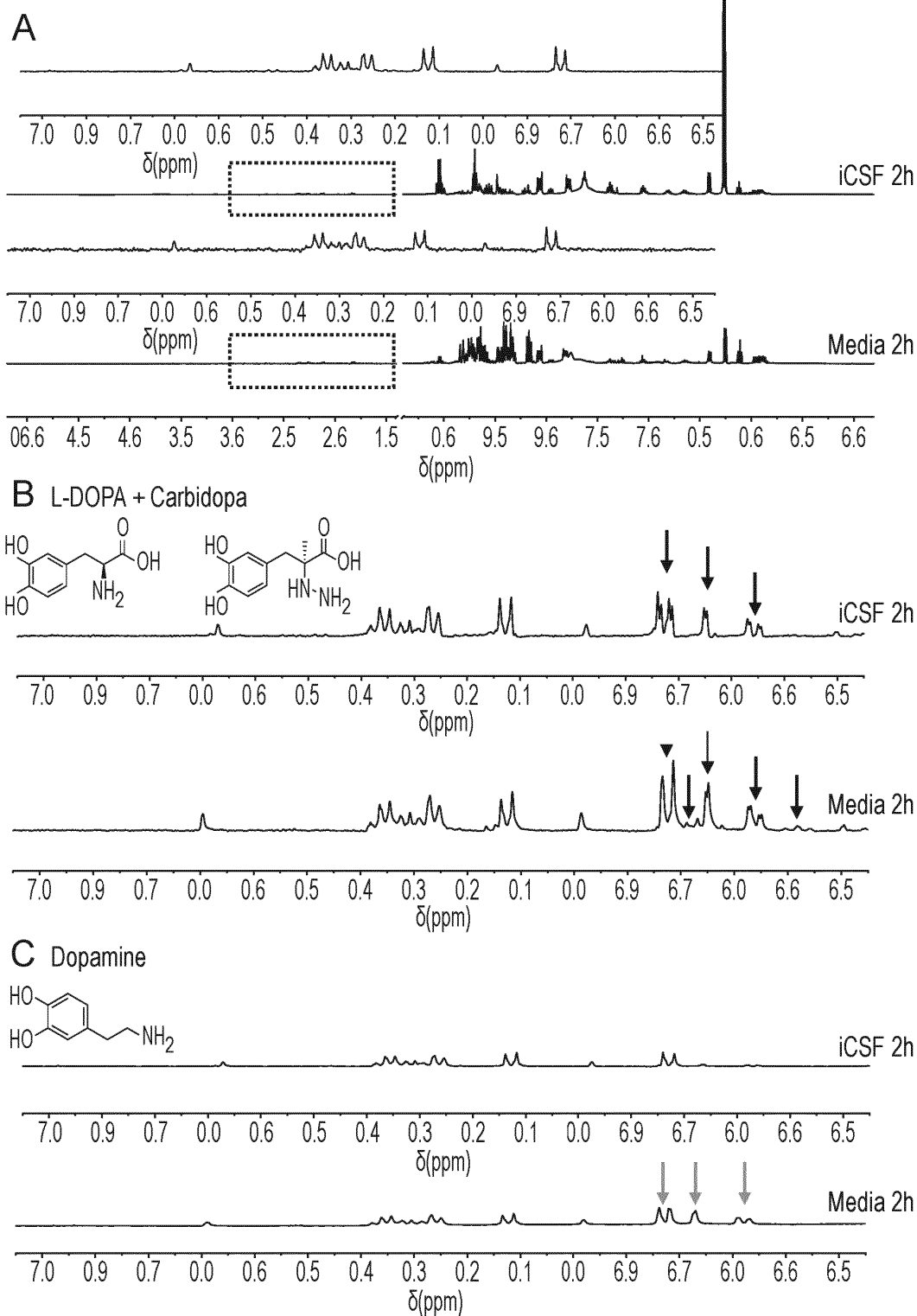
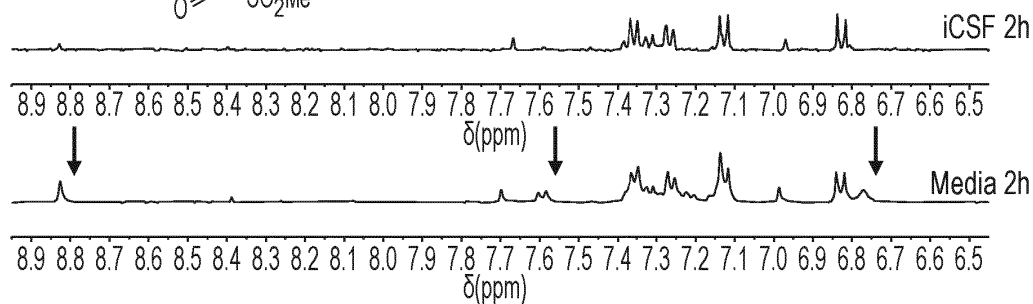
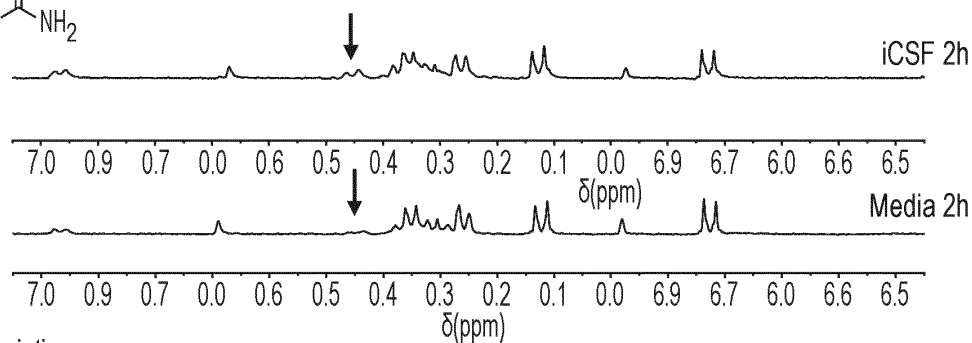
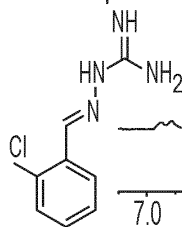
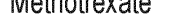


FIG. 12

A Sephin 1



C Methotrexate



The chemical structure of Methotrexate is shown. It consists of a 2,4,6-triaminopteridine ring system. The 7-position of the ring is substituted with a 4-((2S,3S)-2-carboxy-3-hydroxypropyl)amino group. The stereochemistry at the chiral center is indicated with a wedge bond for the hydroxyl group and a dashed bond for the hydrogen atom.

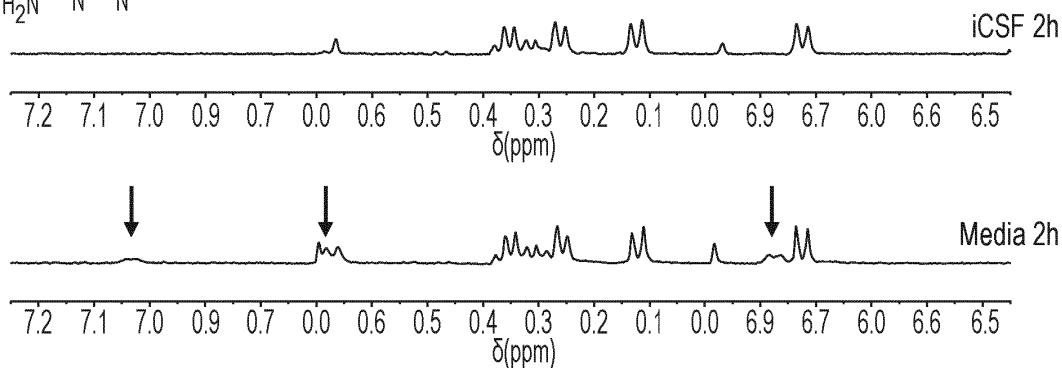
NC1=NC2=C(N)N=CN=C2N1CN(C)Cc3ccc(cc3)NC(=O)O[C@H](C(=O)O)CO

FIG. 13

27/28

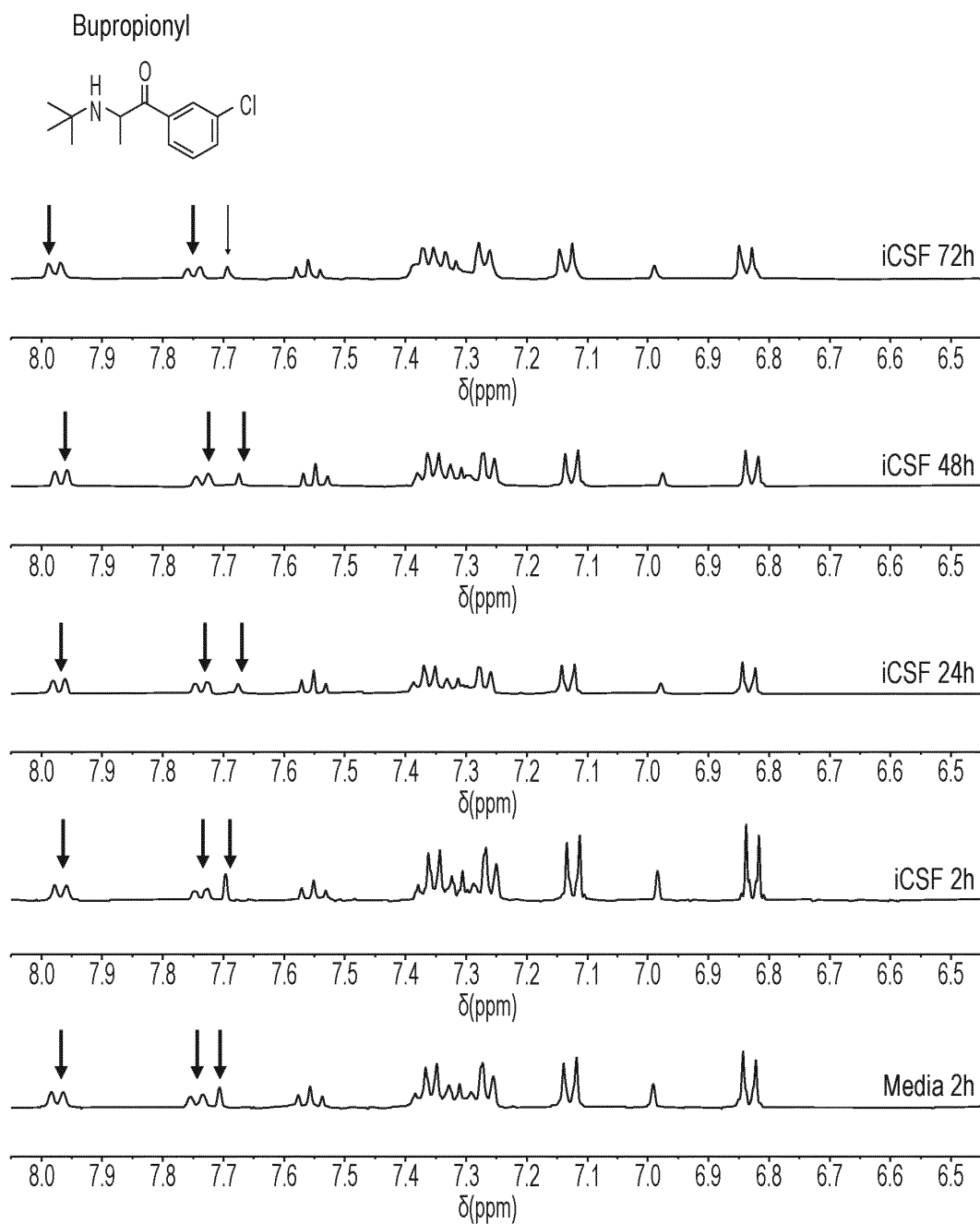


FIG. 14

28/28

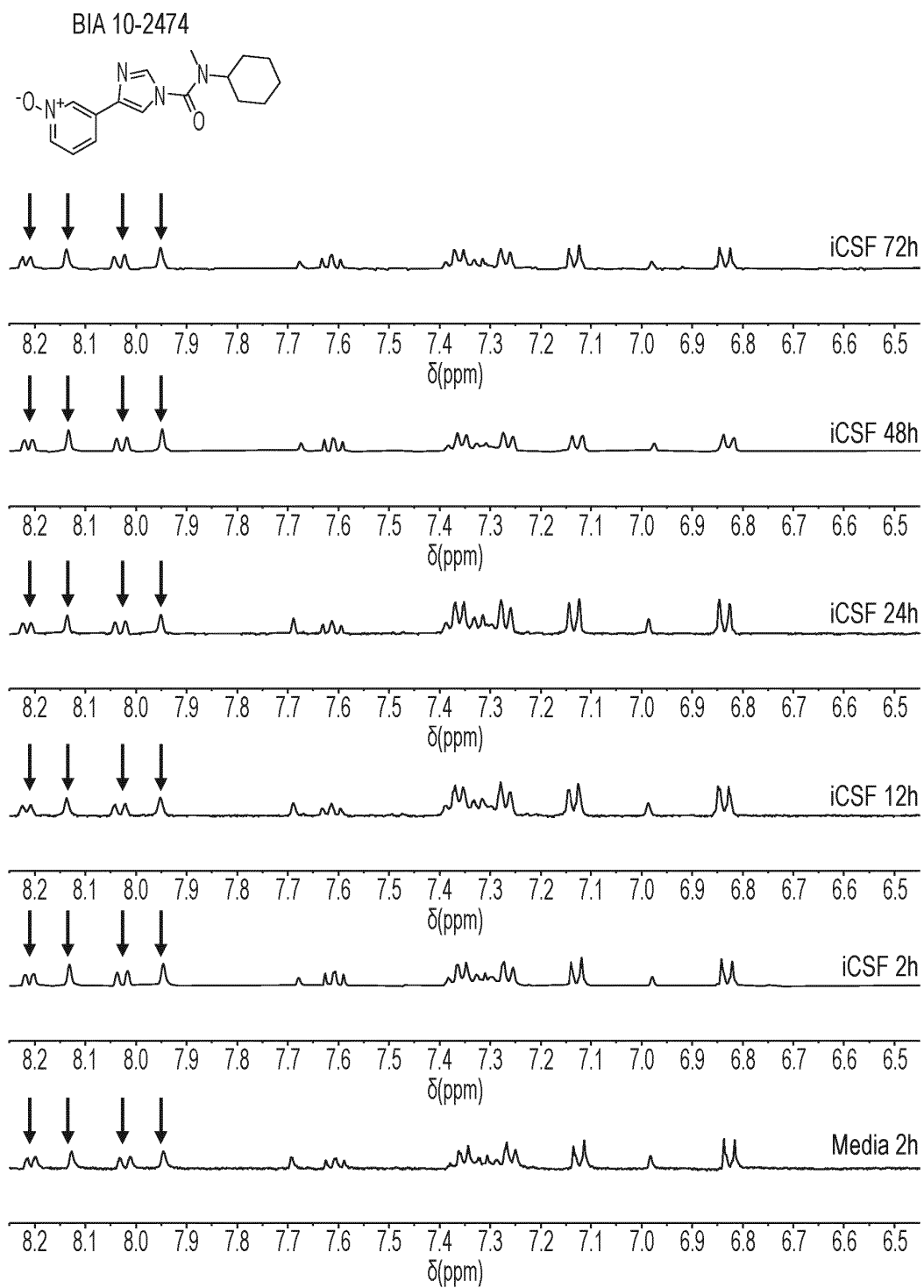


FIG. 15