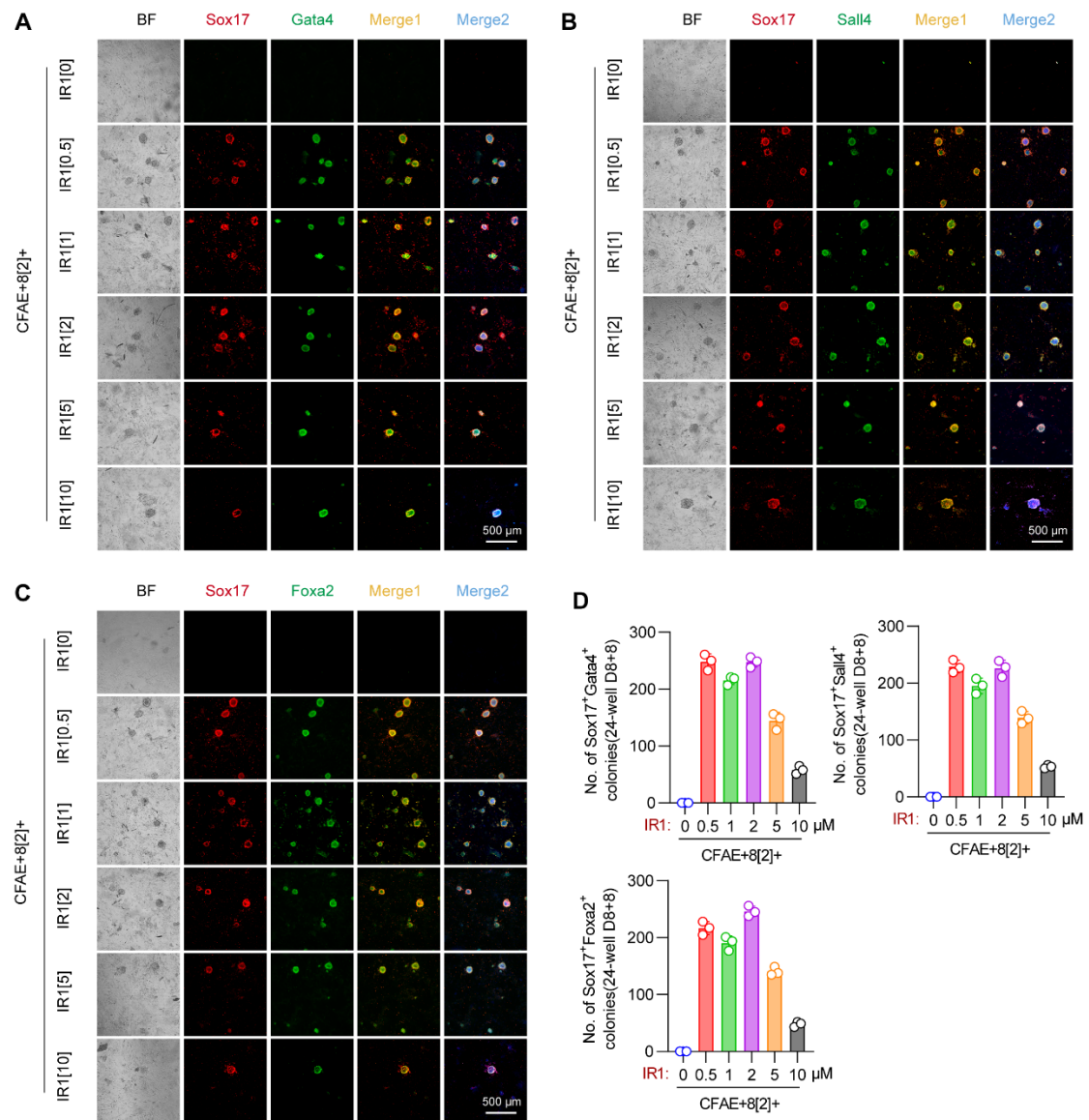
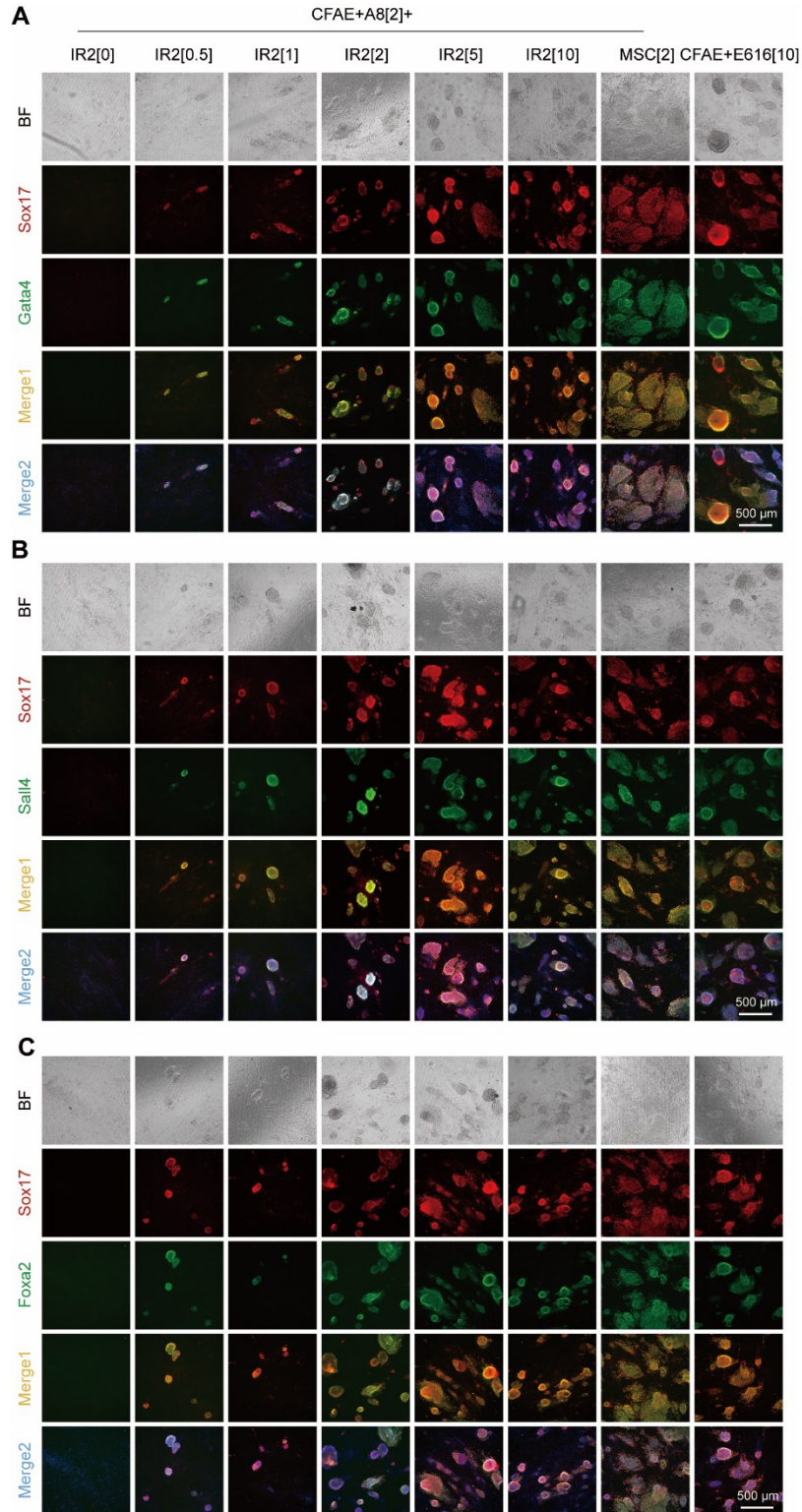


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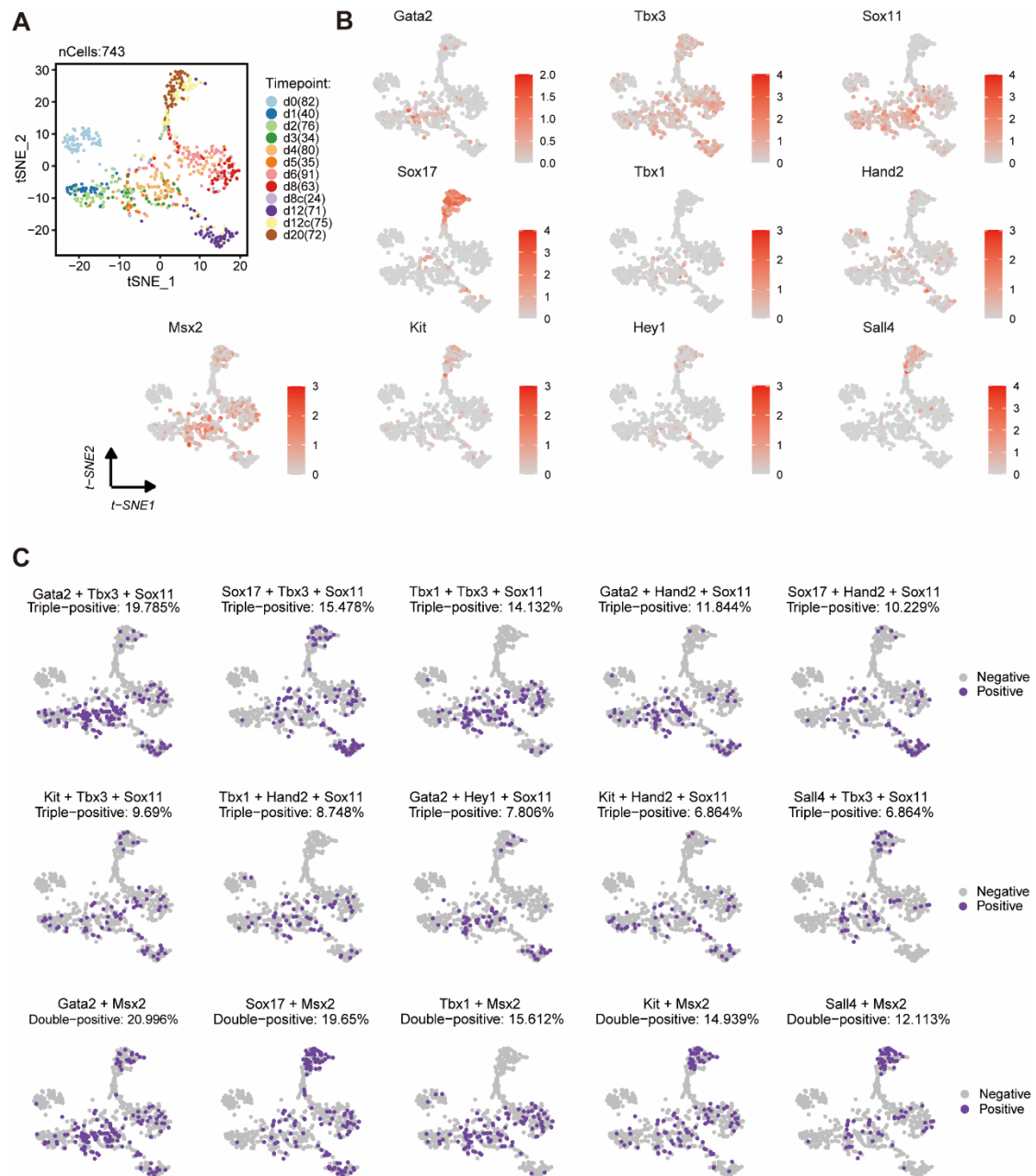
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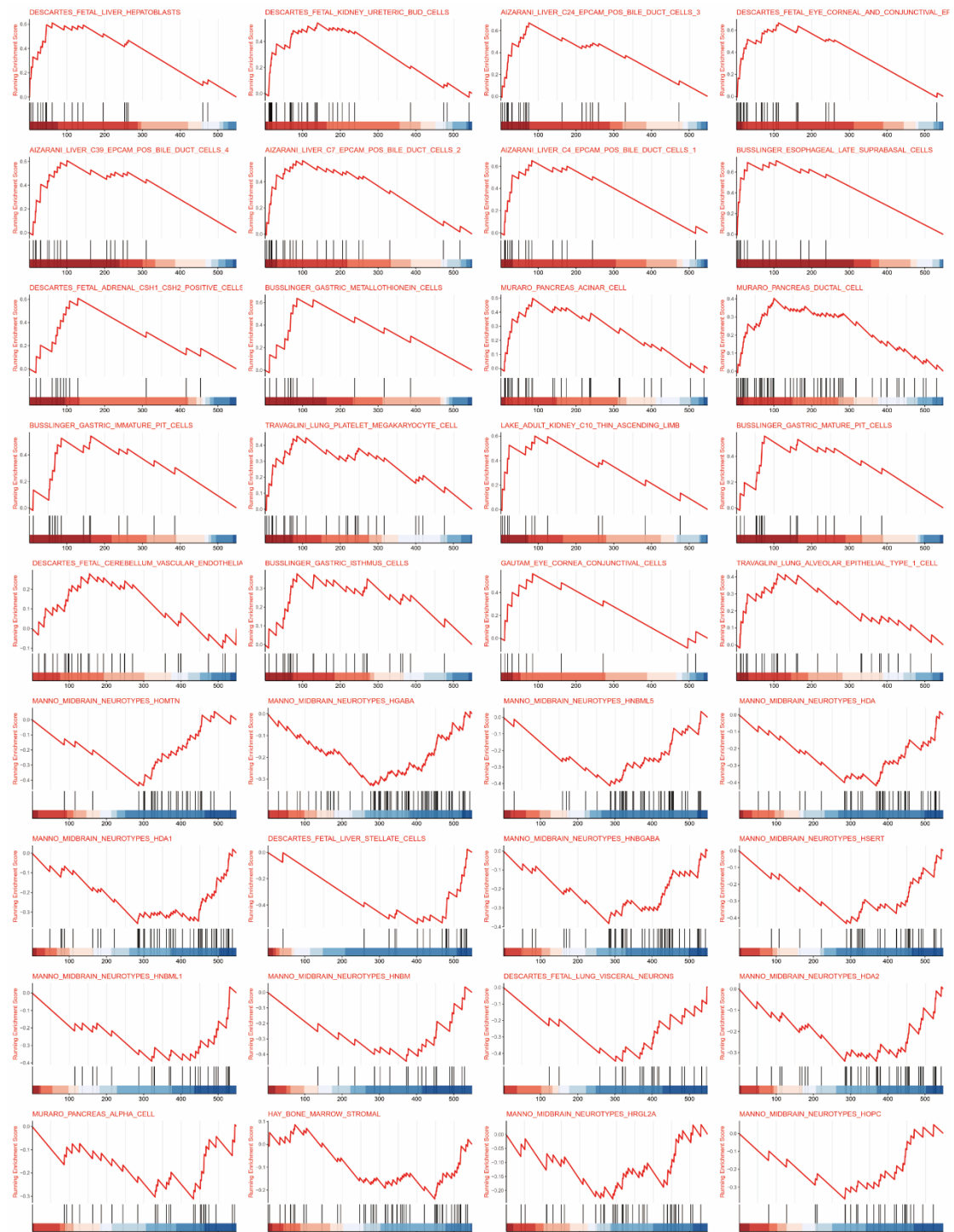
Appendix Figure S1. Optimal concentration determination of IR1 during MEF-XEN reprogramming. Related to Figure 2. (A)-(C) Immunofluorescence staining of XEN master regulators Sox17, Gata4, Sall4, and Foxa2 under CFAE+8 medium with a series of doses of IR1 induction for 16 days, respectively. Scale bar: 500 μ m. (D) The number of Sox17⁺Gata4⁺, Sox17⁺Sall4⁺, and Sox17⁺Foxa2⁺ colonies in (A)-(C). Data are represented as mean $\pm$ SD. n=3 biological replicates, respectively.



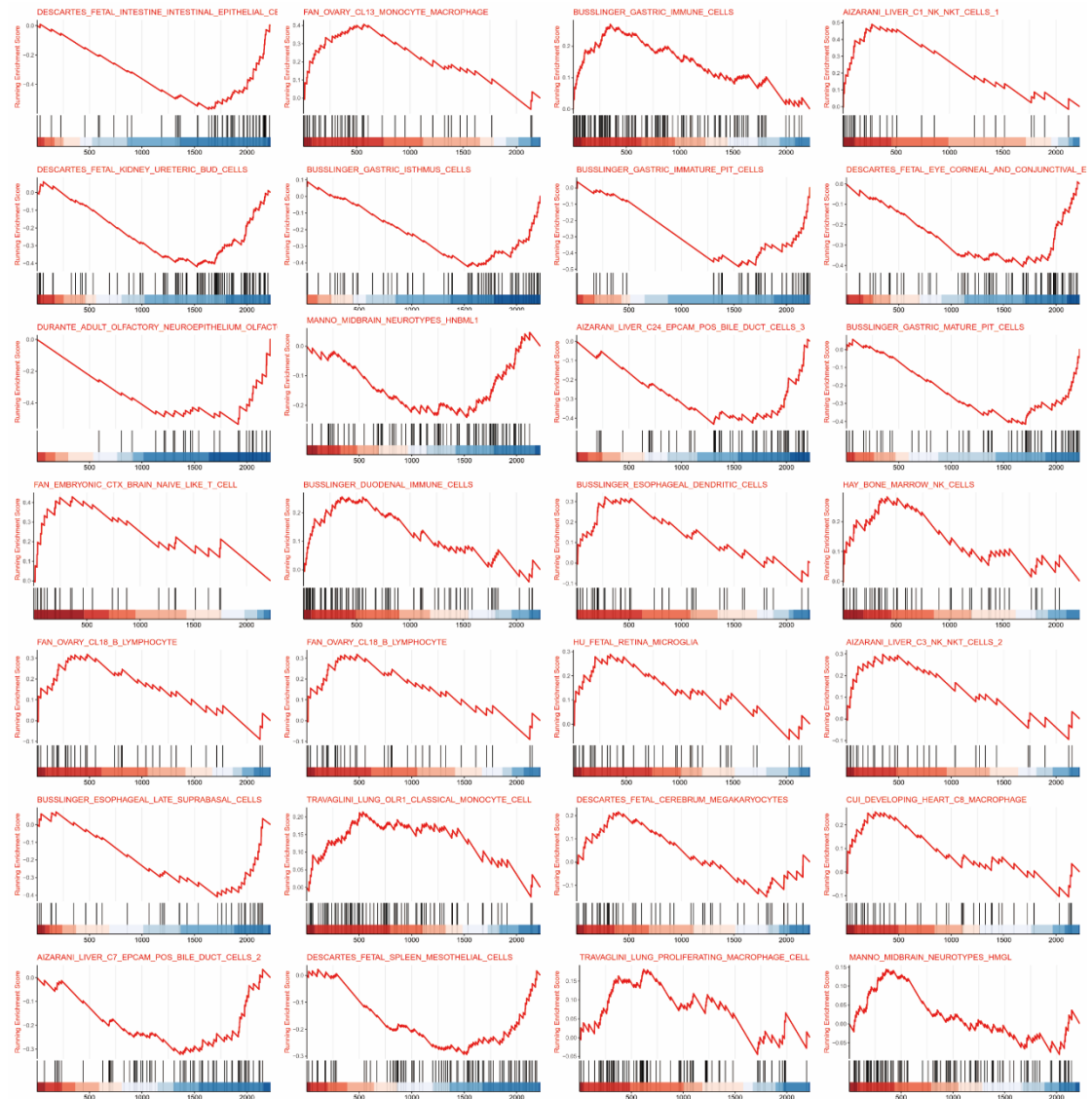
Appendix Figure S2. Optimal concentration determination of IR2 during MEF-XEN reprogramming. Individual raw images and merged panel related to **Figure 2A**. (A)-(C) Immunofluorescence staining of XEN master regulators Sox17, Gata4, Sall4, and Foxa2 under CFAE+8 medium with a series of doses of IR2 induction for 12 days, respectively. Scale bar: 500 μ m.



Appendix Figure S3 (A) t-SNE visualization of single cells from the MEF-to-XEN reprogramming time course. Cells were collected at indicated time points (d0 to d20) and analyzed by Smart-seq2. **(B)** Expression patterns of representative marker genes for the three germ layers. **(C)** Co-expression patterns of the top-ranked gene combinations.



Appendix Figure S4 GSEA enrichments of multi-lineage cell fates in shlrak4 versus scramble.



Appendix Figure S5 GSEA enrichments of multi-lineage cell fates in *Tetone-Irak4* versus vector.