Supplemental Material

Combined analysis of single cell RNA-Seq and ATAC-Seq data reveals regulatory toggles operating in native and iPS-derived retina.

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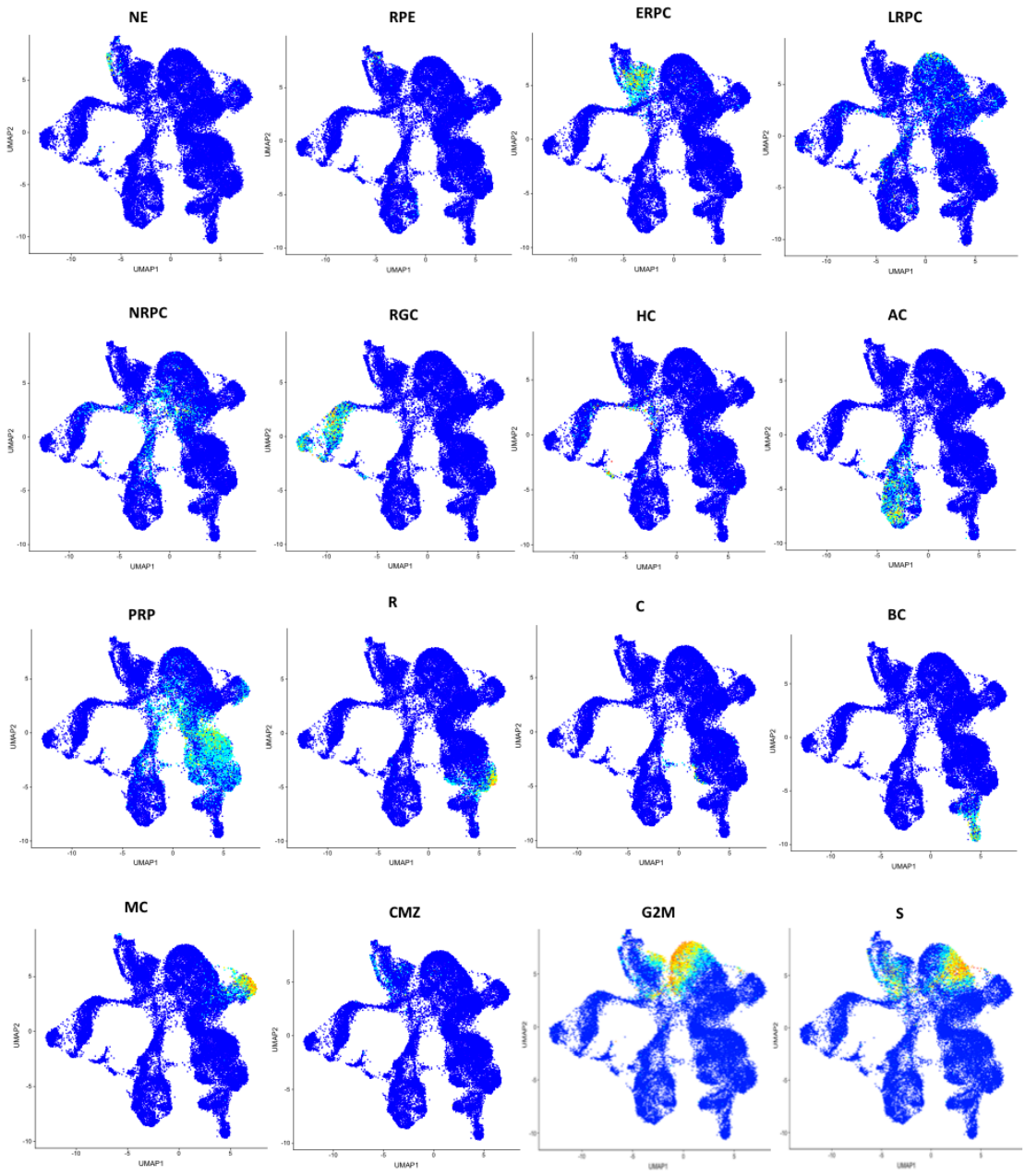
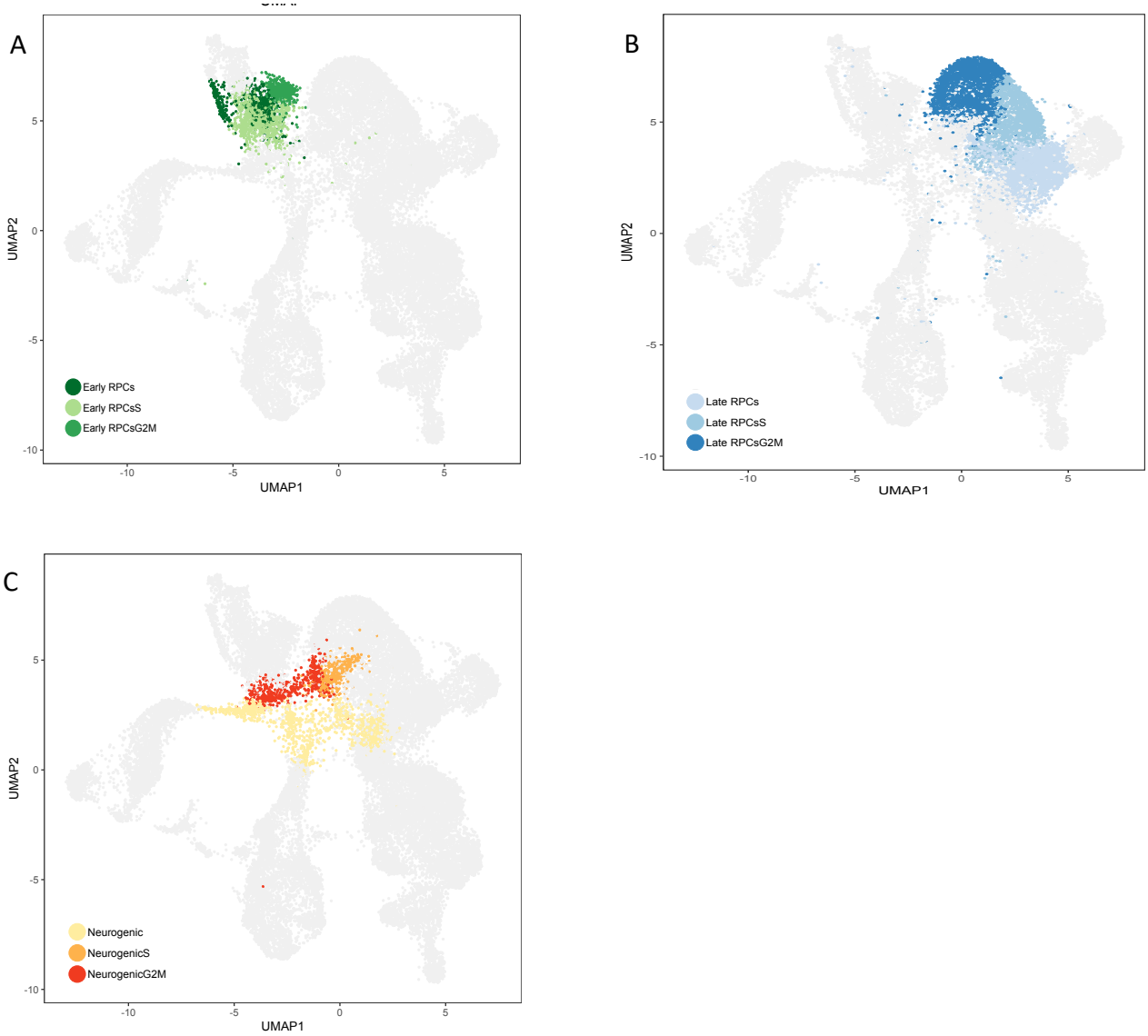
Supplemental figure 1:



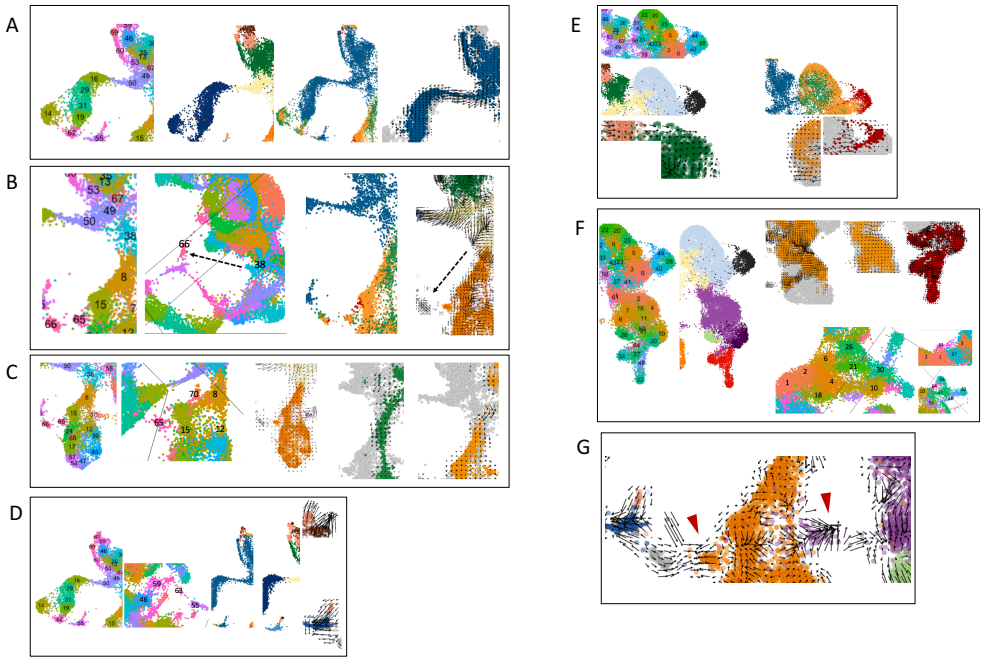
UMAP manifolds showing (from upper left to lower right): (i) gene expression signatures for 13 previously recognized retinal cell types: NE, RPE, ERPCs, LRPCs, NRPCs, RGC, AC, HC, PRP, R, C, BC and MC; (ii) gene expression signature typical of the NE/ciliary marginal zone (CMZ), and (iii) gene expression signatures specific for the S and G2-M phases of the cell cycle. The genes underlying each signature are as in Suppl. Table 3.

Supplemental figure 2



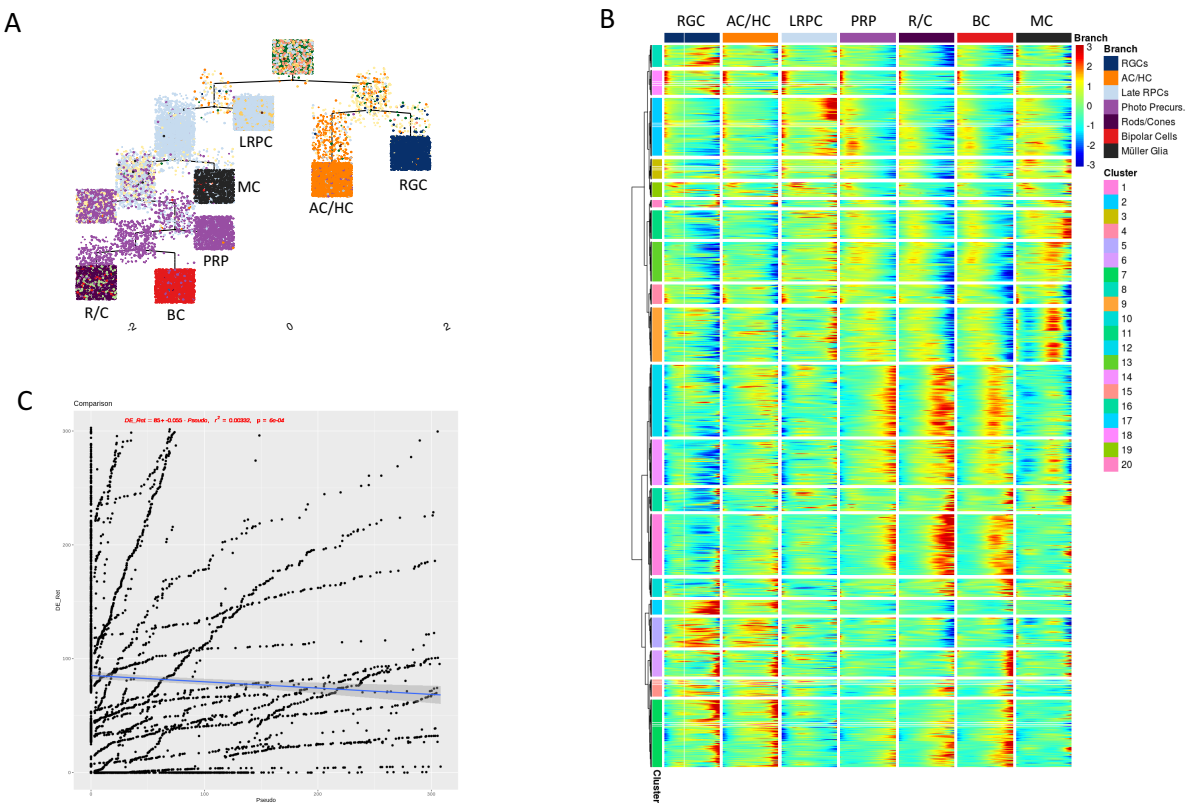
Separating dividing early (ERPC) (A), late (LRPC) (B) and neurogenic (NRPC) (C) retinal precursor cells by cell cycle stage (G1, S, G2M) based on the expression of genes that are specific for the S and G2M stage (Tirosh et al, 2016).

Supplemental figure 3



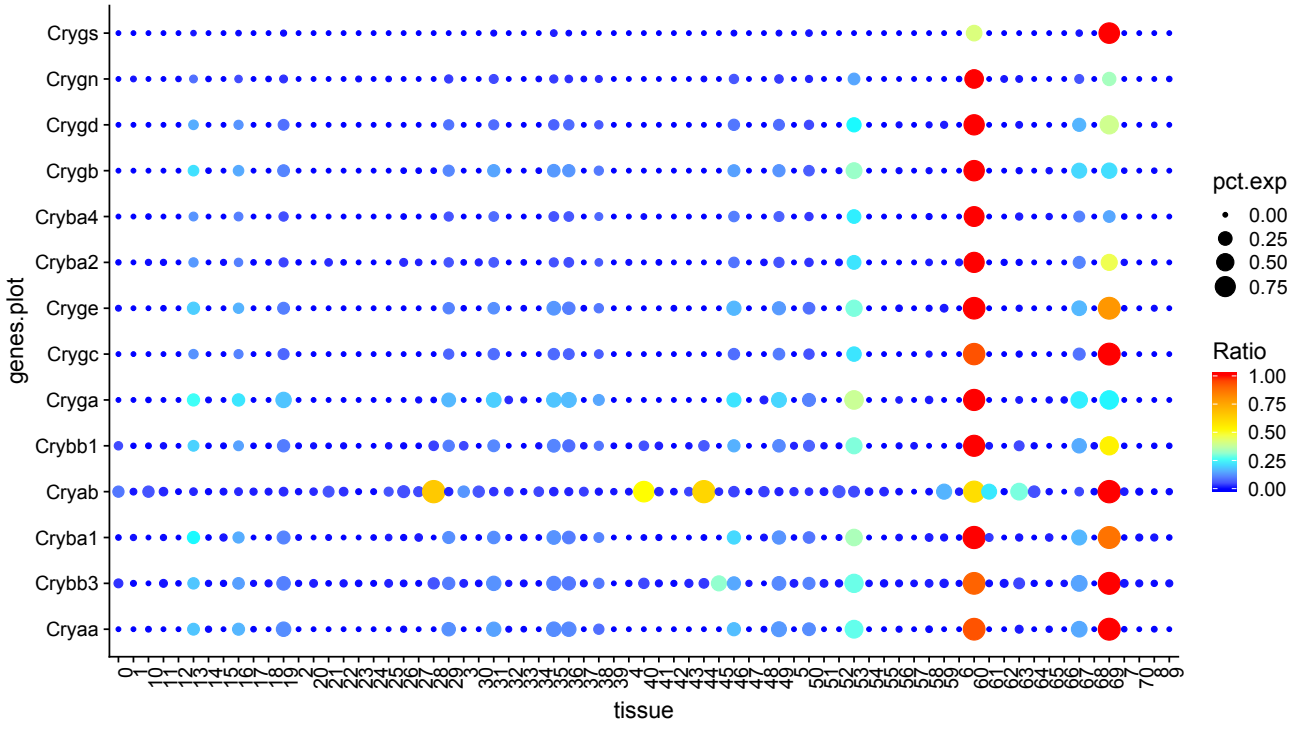
Combining information from (i) the cells' developmental stage, (ii) RNA velocity analyses, and (iii) the 3D UMAP manifold, to deduce developmental trajectories for (A) RGC; (B) HC; (C) AC; (D) Tbr1^{+}RGC and RPE; (E) NE, ERPC, LRPC, NRPC and MC; (F) PRP, R, C and BC; (G) red arrows show "re-specification" of AC into HC and into PRP. Consult videos (http://www.sig.hec.ulg.ac.be/giga) for visit in 3D.

Supplemental figure 4



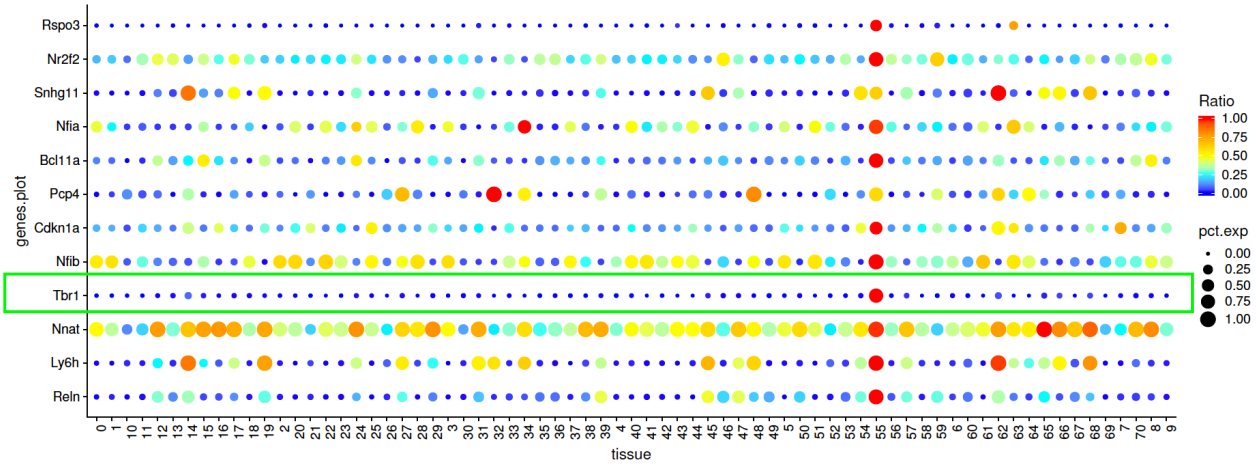
(A) Developmental trajectory obtained without supervision with Monocle 2 (Trapnell et al., 2014) using NaR cells only. Colors correspond to "cliques" as defined in the main text and color-coded as in the main figures. As expected, terminal leaves correspond to terminally differentiated cell types (from left to right: R/C, BC, MC, AC/HC and RGC) or to niches of progenitor cells (LRPC, PRP). **(B)** Expression levels (in pseudo-color) along the seven branches of the Monocole 2 tree (X axis) of 10,269 genes that are dynamically regulated as a function of pseudo-time ($q < 0.0001$) and grouped in 20 clusters according to their expression pattern (Y axis). **(C)** Log(1/p) values of all genes in the differential expression analysis (each clique versus all others; see main text) (X axis) and the Monocle 2 analysis (Y axis), showing the strong concordance between the two approaches

Supplemental figure 5:



Level of expression in all 70 clusters of 14 crystallin genes. The 14 chosen crystallin genes are the ones ranked amongst the top 24 genes differentially expressed in the CMZ (=cluster 60 + cluster 69) compared to all other cliques.

Supplemental figure 6:



Level of expression in all 70 clusters of the top-ranked genes differentially expressed in Tbr1+RGC clique (=cluster 55) compared to all other clusters. Tbr1 transcription factor is exclusively expressed cluster 55 hence identifying it as a recently described subgroup of Tbr1^{+}RGC.