

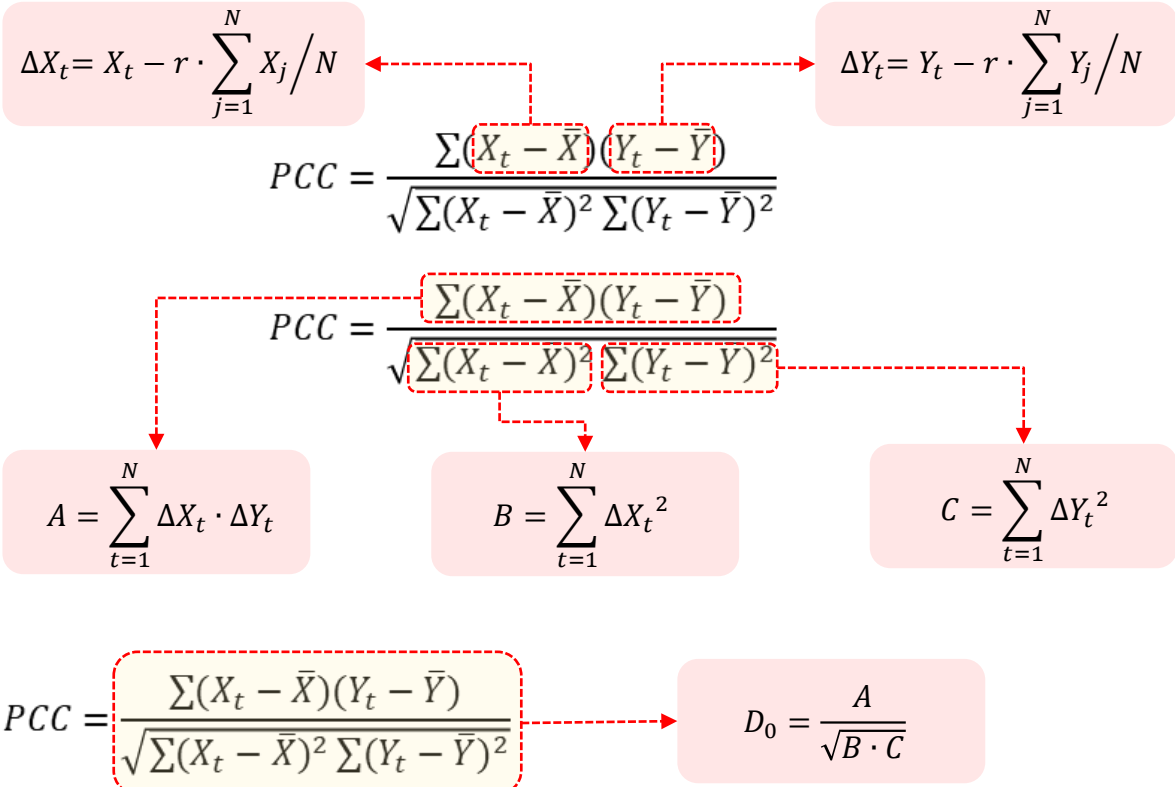
Supp. Figures

Supplementary Figure 1

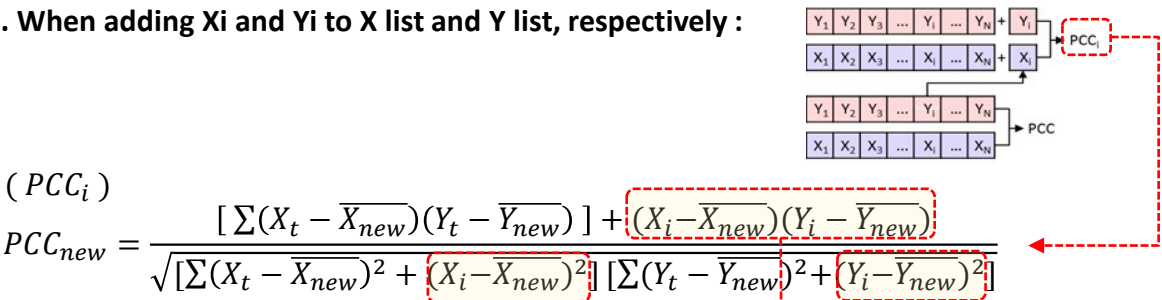
1. The formula of Pearson Correlation Coefficient (PCC):

$$PCC = \frac{\sum(X_t - \bar{X})(Y_t - \bar{Y})}{\sqrt{\sum(X_t - \bar{X})^2 \sum(Y_t - \bar{Y})^2}}$$

2. When r = 1 :



3. When adding Xi and Yi to X list and Y list, respectively :



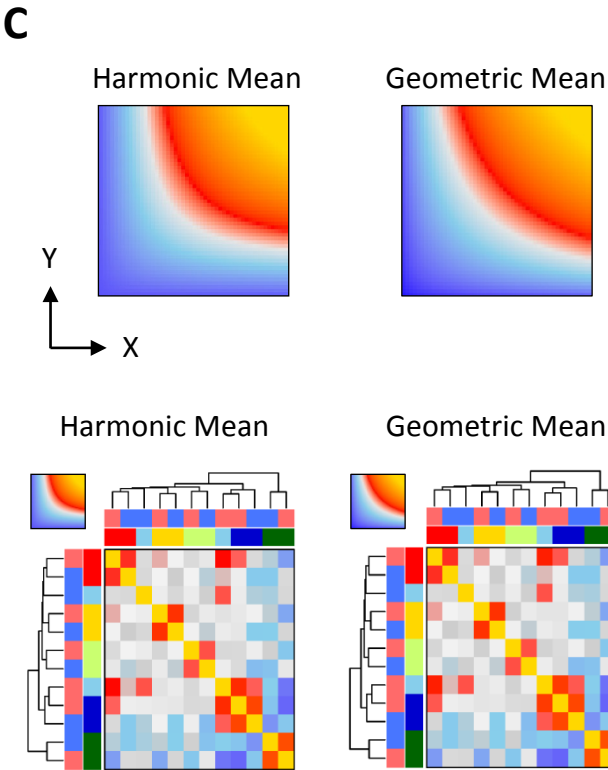
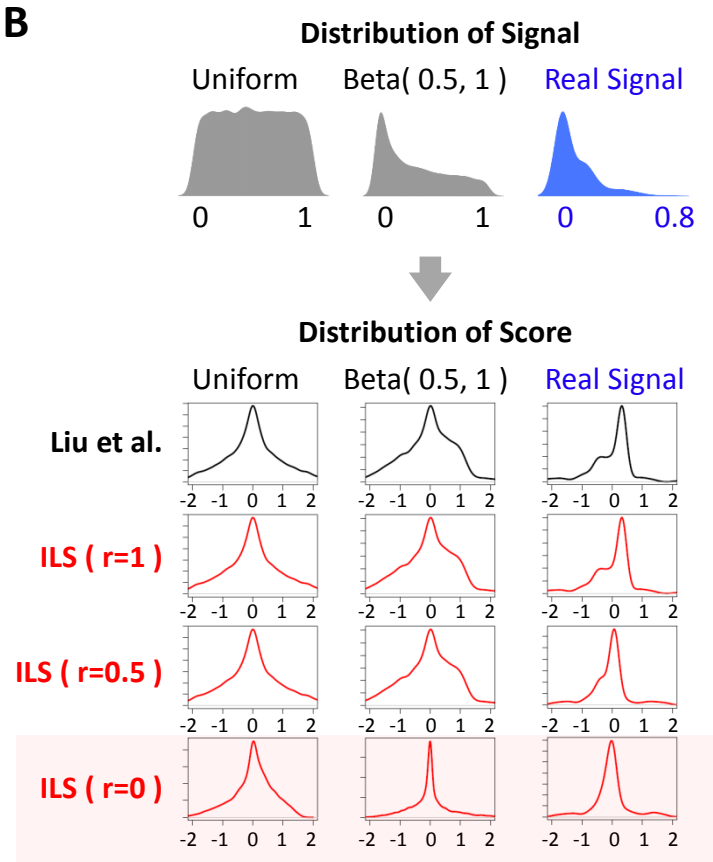
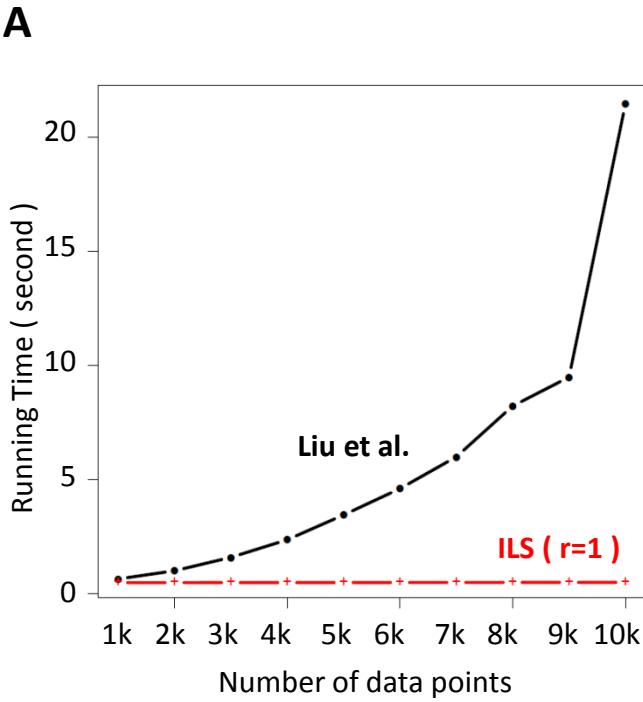
4. Because $\bar{X}_{new} \sim \bar{X}$ and $\bar{Y}_{new} \sim \bar{Y}$:

$$PCC_{new} \sim D_i = \frac{A + \Delta X_i \cdot \Delta Y_i}{\sqrt{(B + \Delta X_i^2) \cdot (C + \Delta Y_i^2)}}$$

5. Calculation of ILS (r=1):

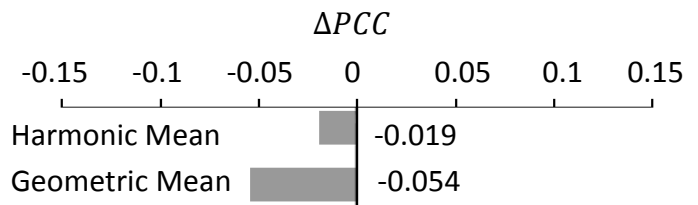
$$ILS_i = Score_i = \frac{D_i - D_0}{(1 - D_0^2)/(N - 1)} \sim Score_i \text{ of Liu et al.} = \frac{PCC_i - PCC_0}{(1 - PCC_0^2)/(N - 1)}$$

Supplementary Figure 2



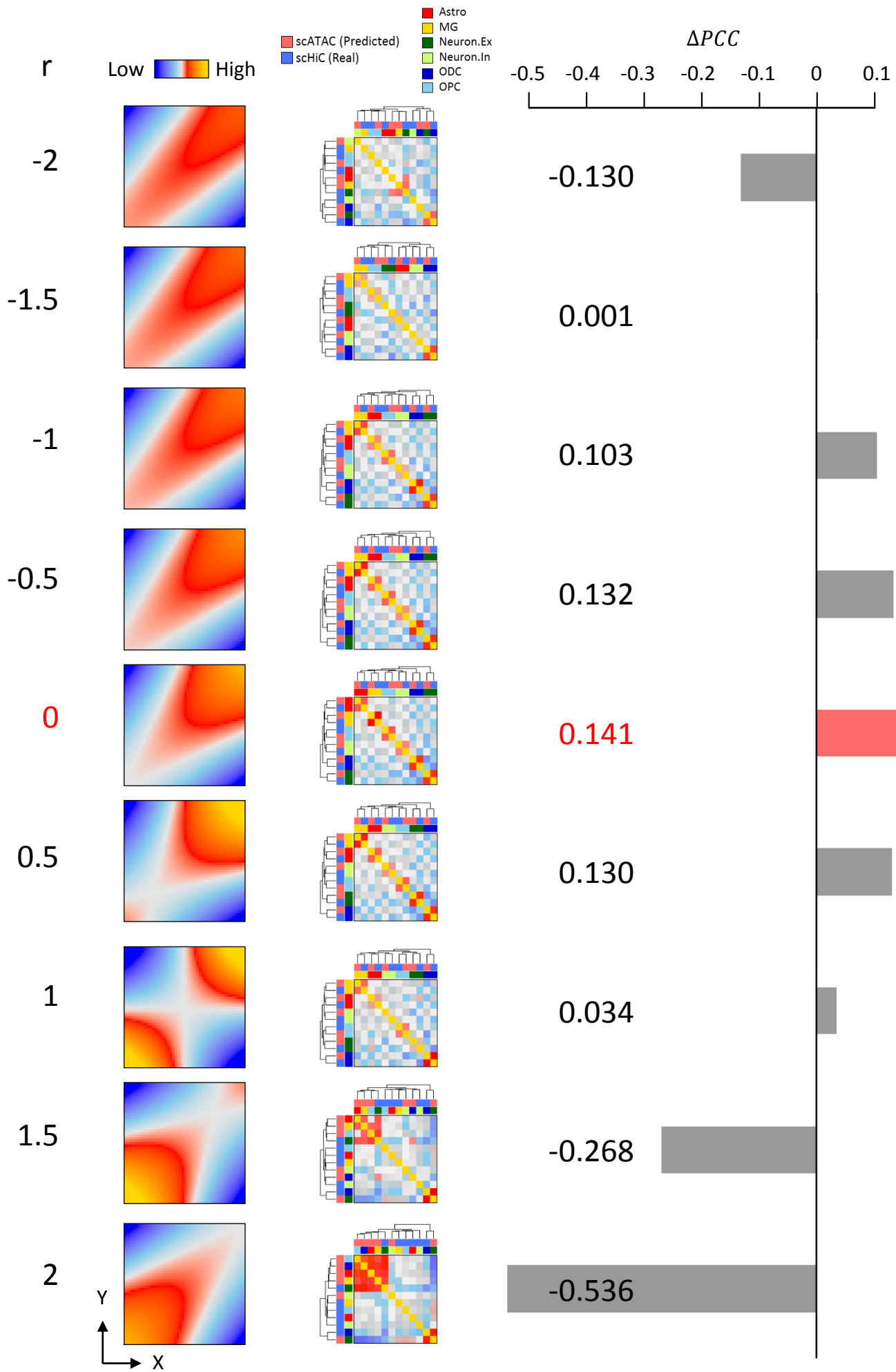
$$\text{Harmonic Mean} = \frac{2 \cdot X \cdot Y}{X + Y + 1}$$

$$\text{Geometric Mean} = \sqrt{X \cdot Y}$$



Supplementary Figure 3

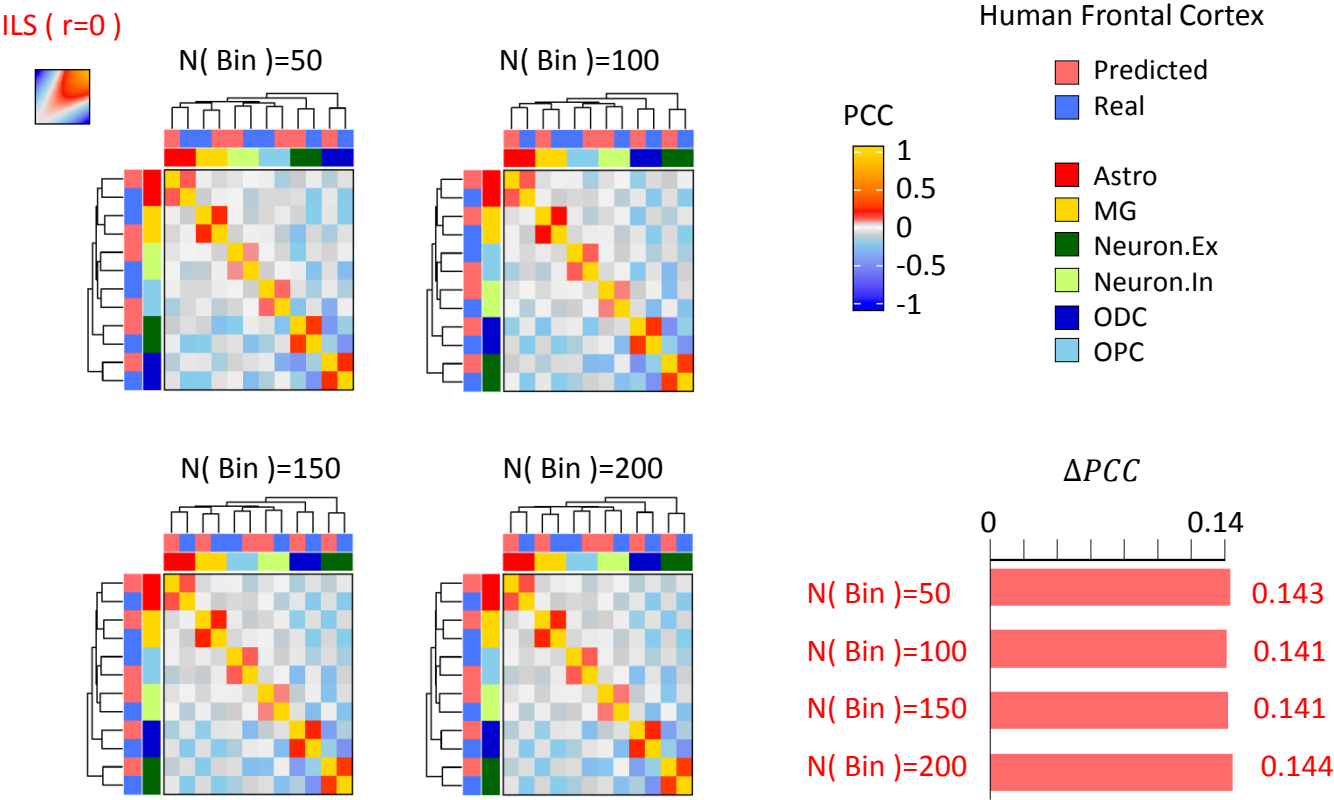
Human Frontal Cortex



Supplementary Figure 4

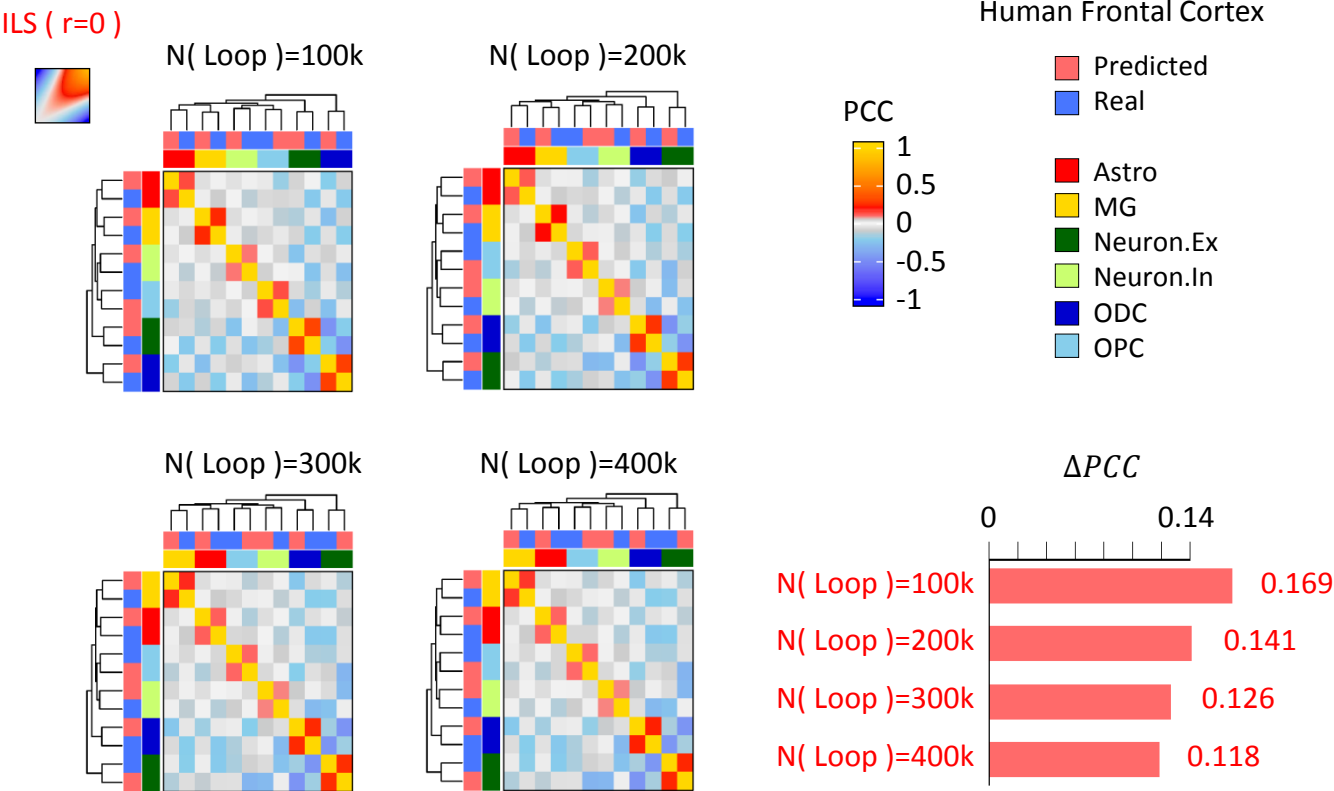
A

Using different number of bins, N(Loop)=200k

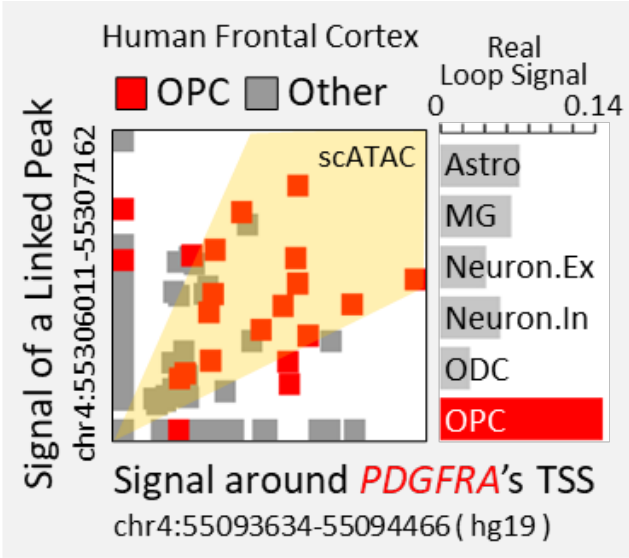
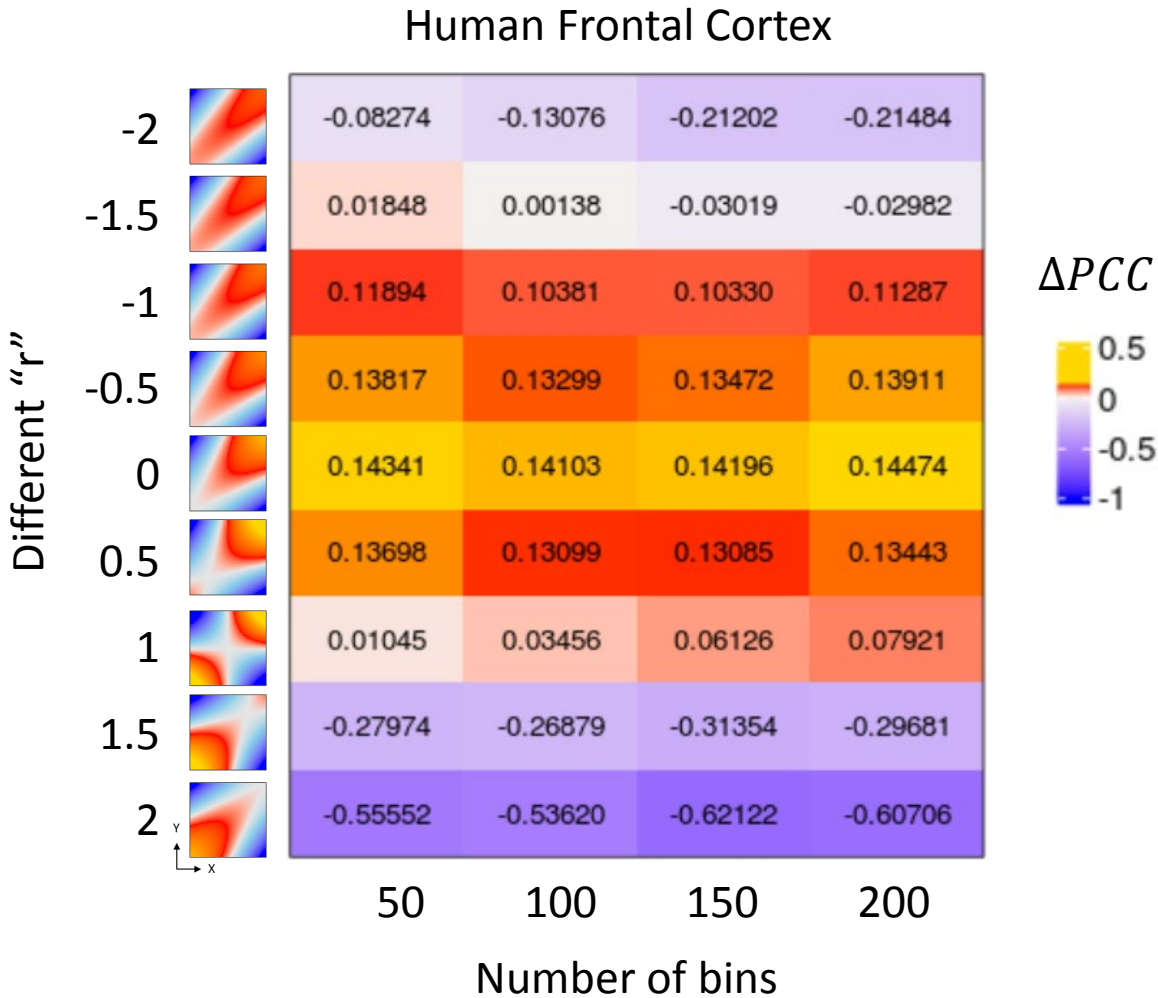


B

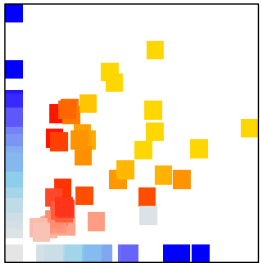
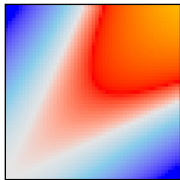
Using different number of top loops of Cicero, N(Bin)=100



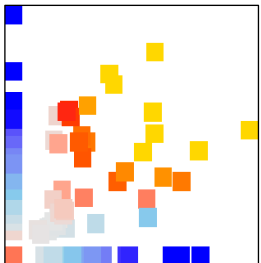
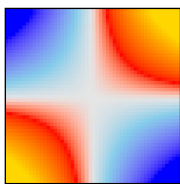
Number of bins & different “r”



r = 0



r = 1



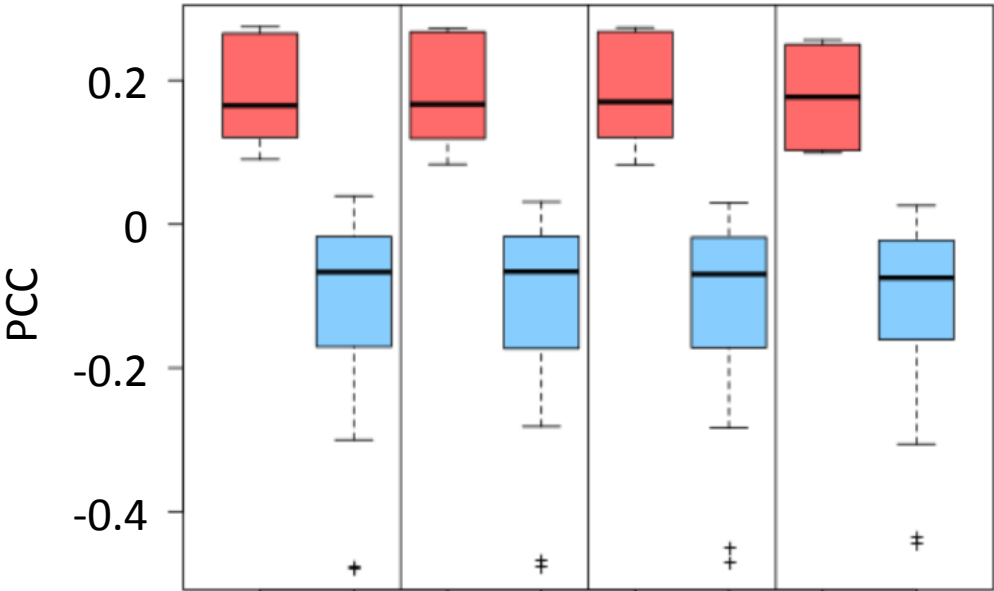
Number of bins & peak calling

Peaks are called independently on each bin of cells and then combined:

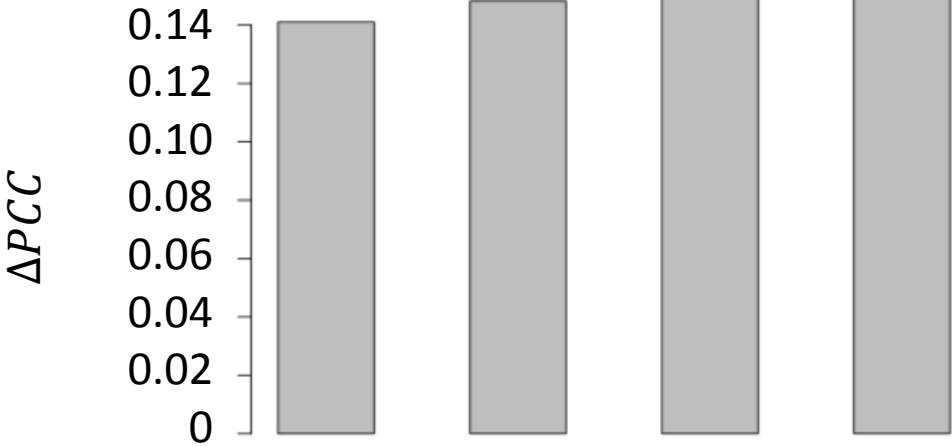
```
CallPeaks(..., group.by="bin", ...) in Signac
```

Human Frontal Cortex

Matched Un-matched



0.141 0.148 0.150 0.151



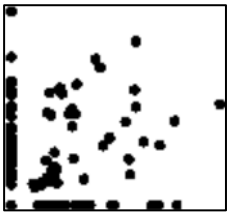
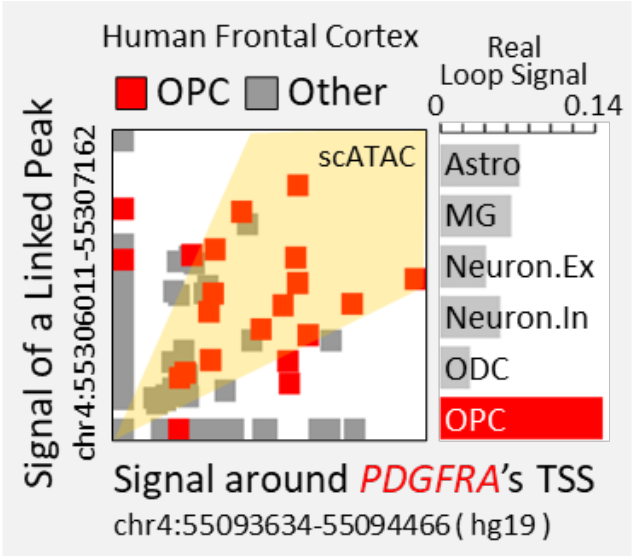
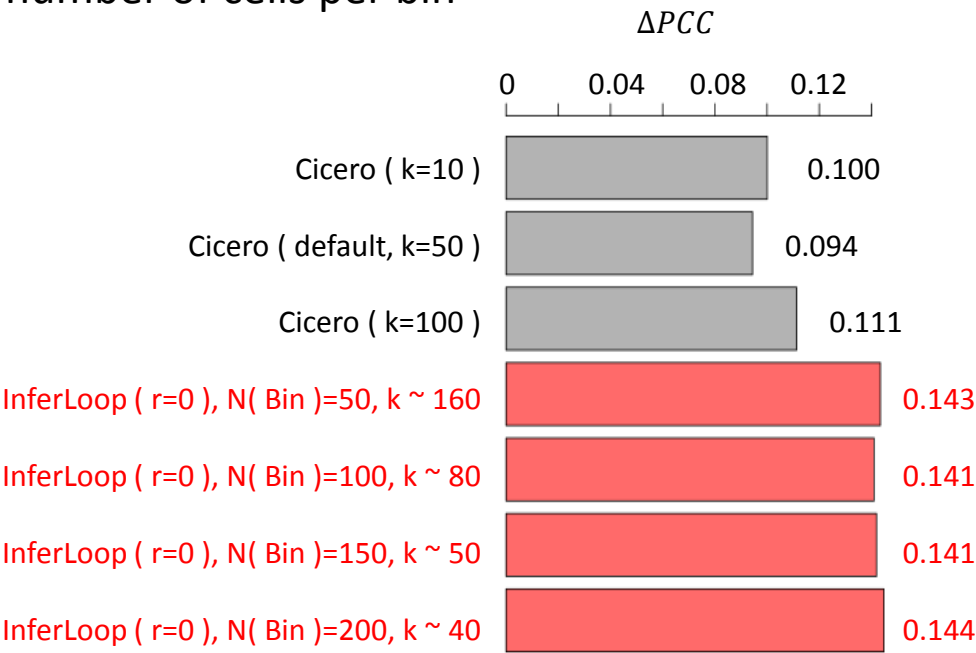
Number pf bins for calling peaks

All (1 bin) 5 bins 10 bins 50 bins

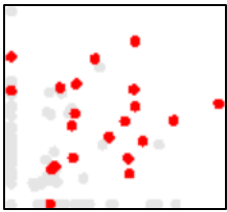
Using different k to run Cicero

Human Frontal Cortex: ~8000 cells

k: number of cells per bin

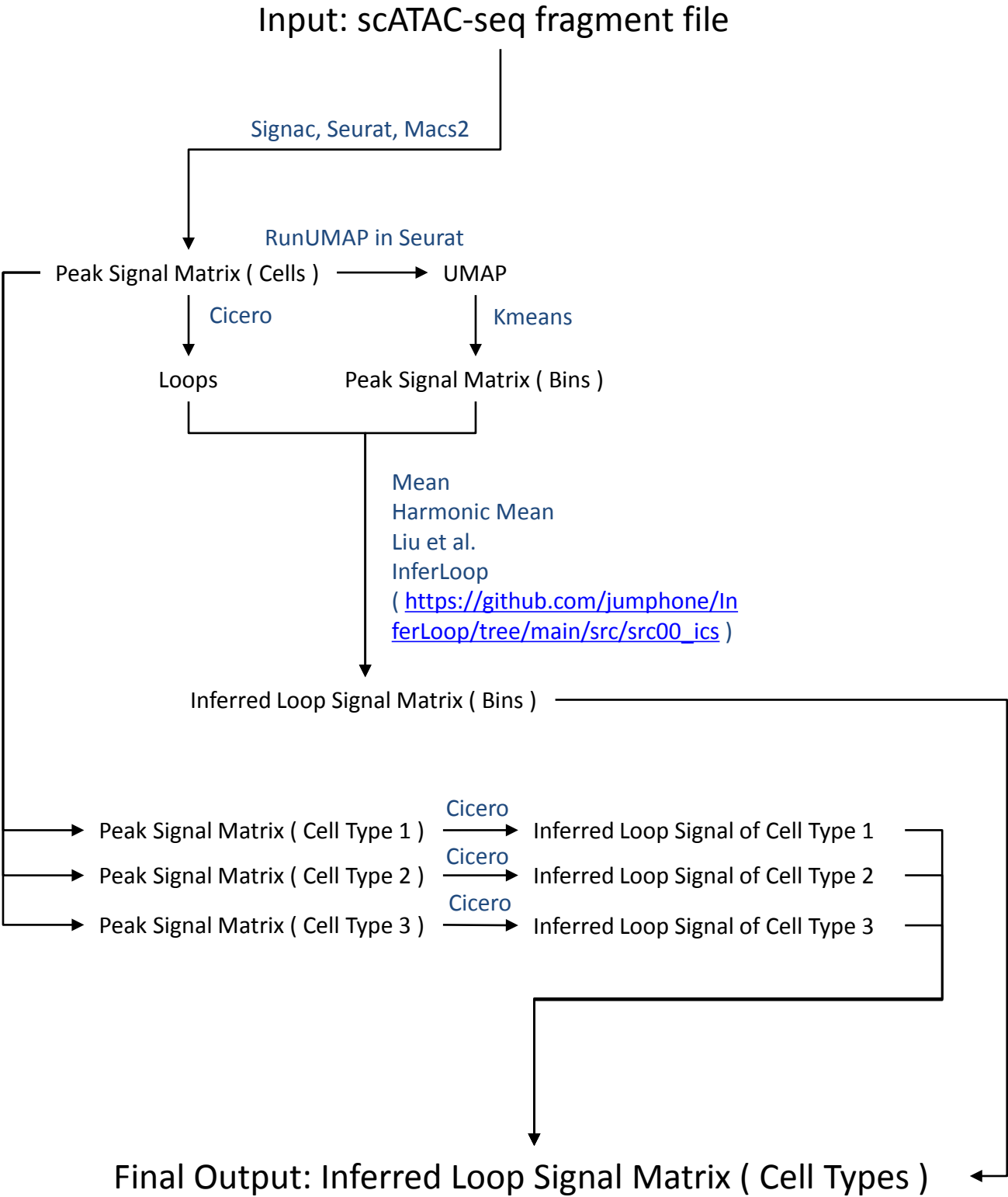


PCC (all bins)
= 0.27

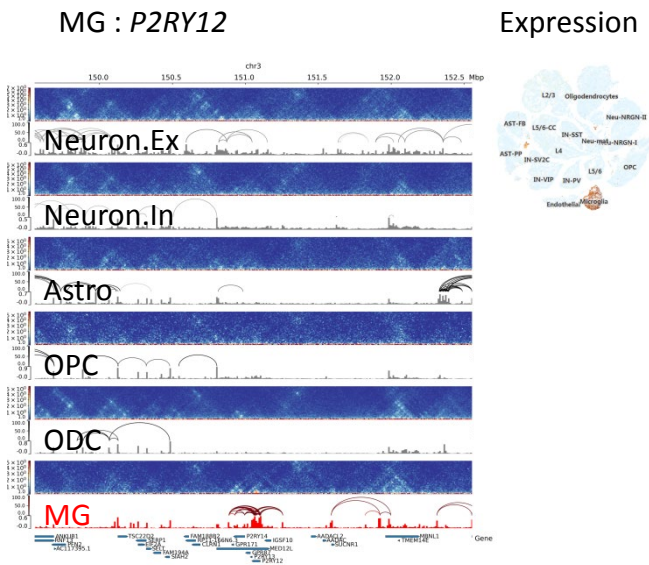
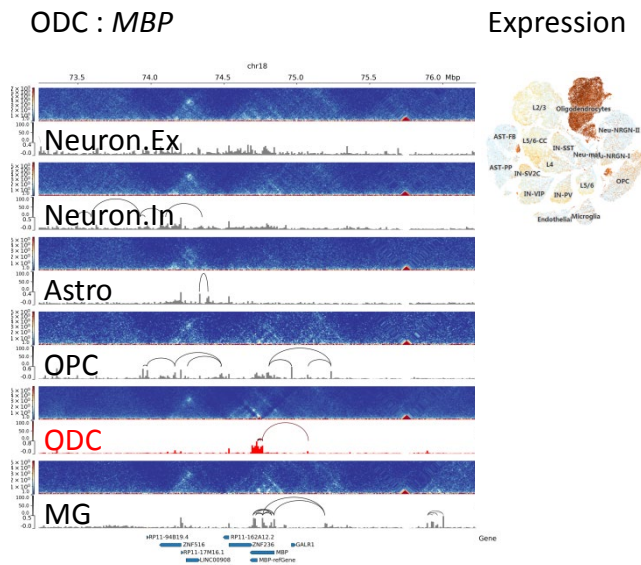
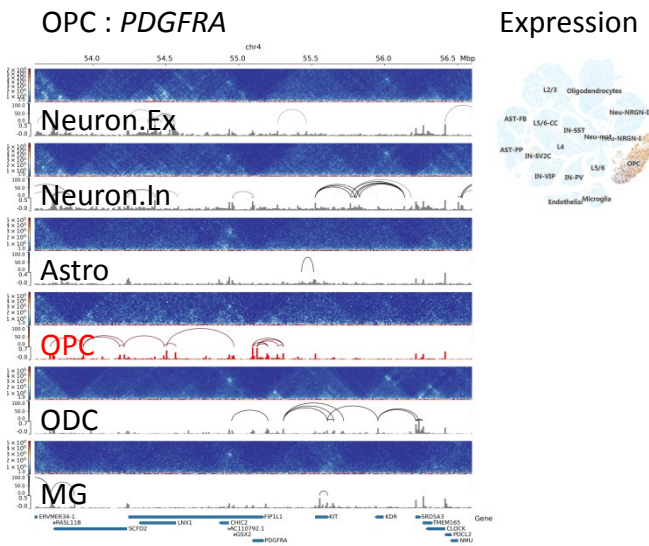
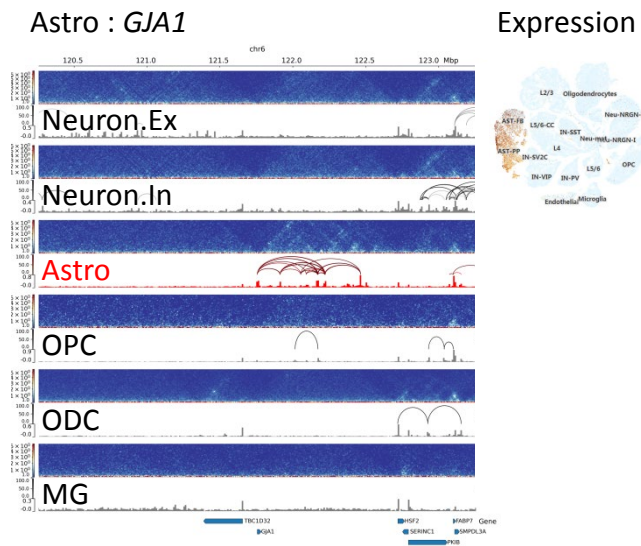
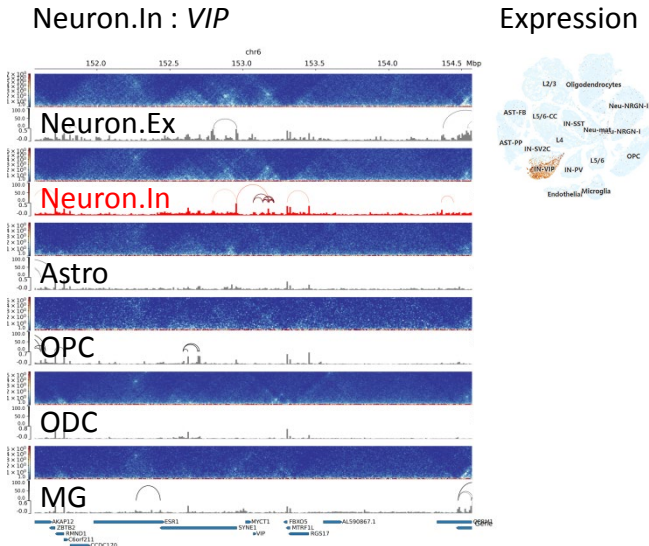
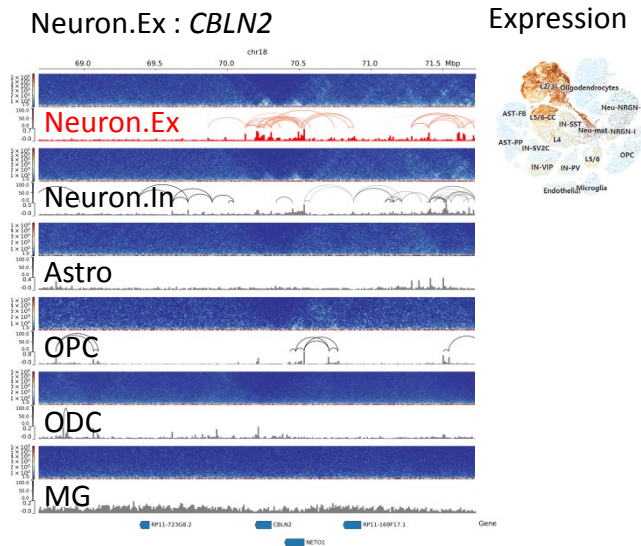


PCC (bins of OPC)
= 0.03

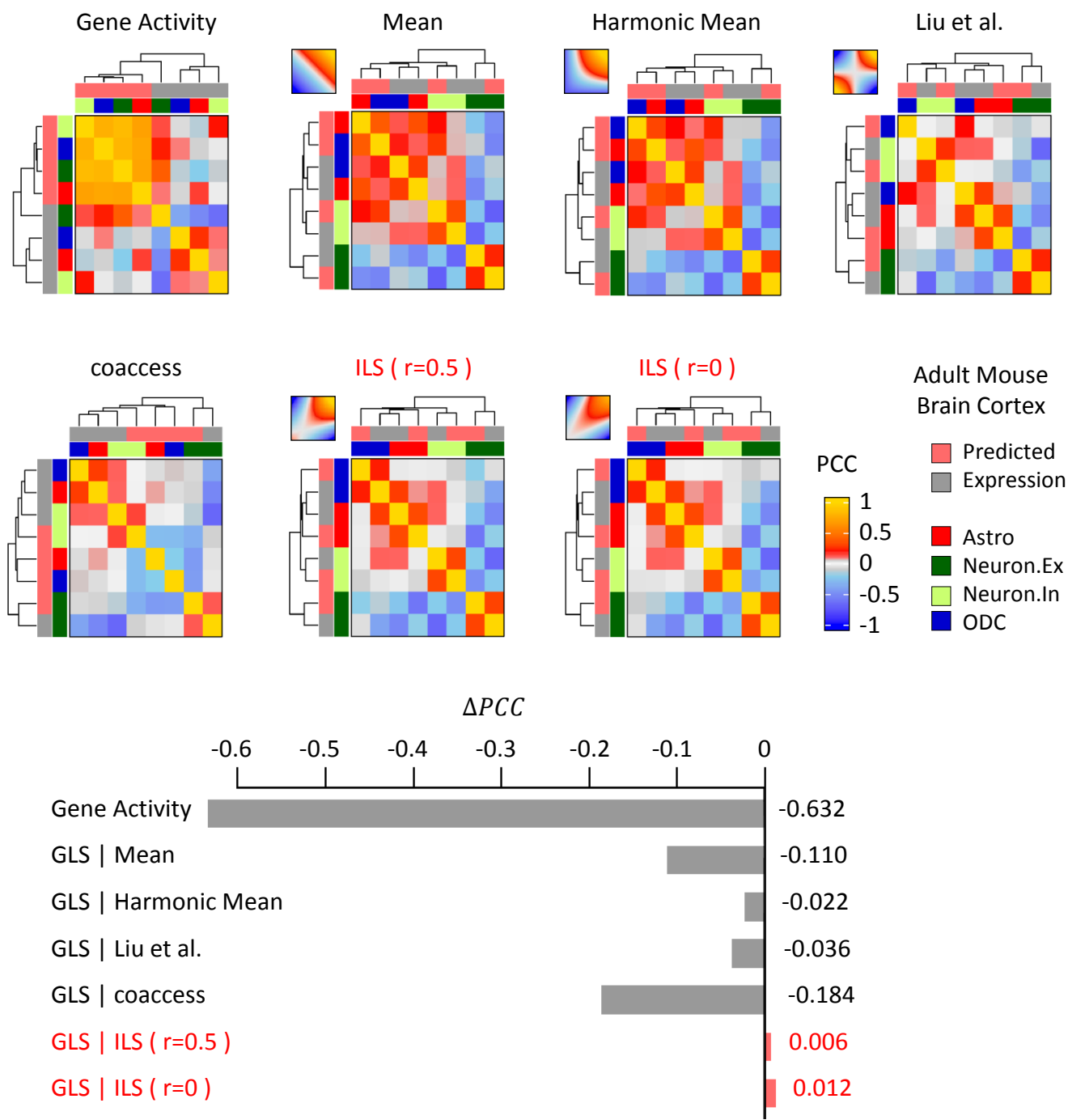
Supplementary Figure 8



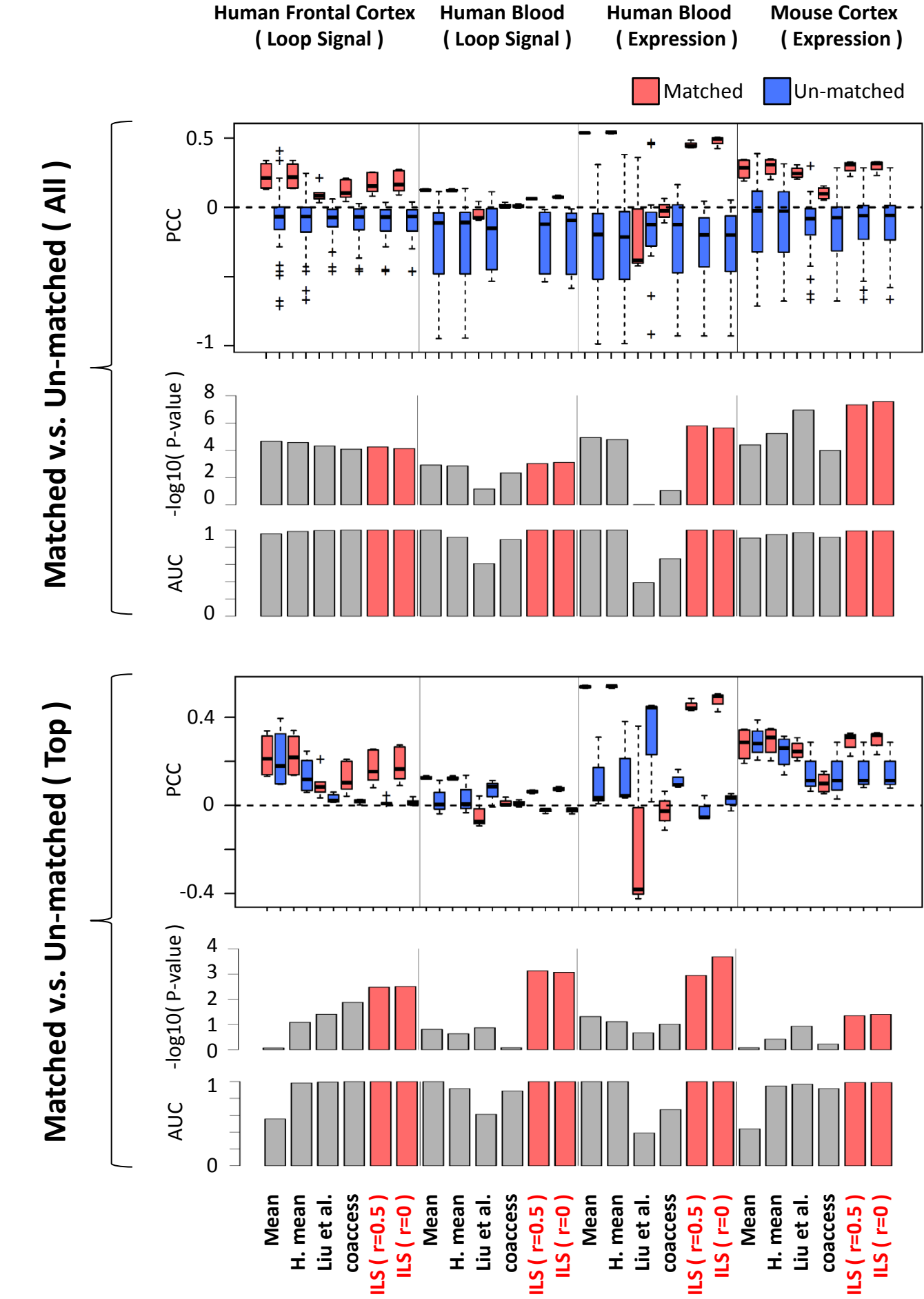
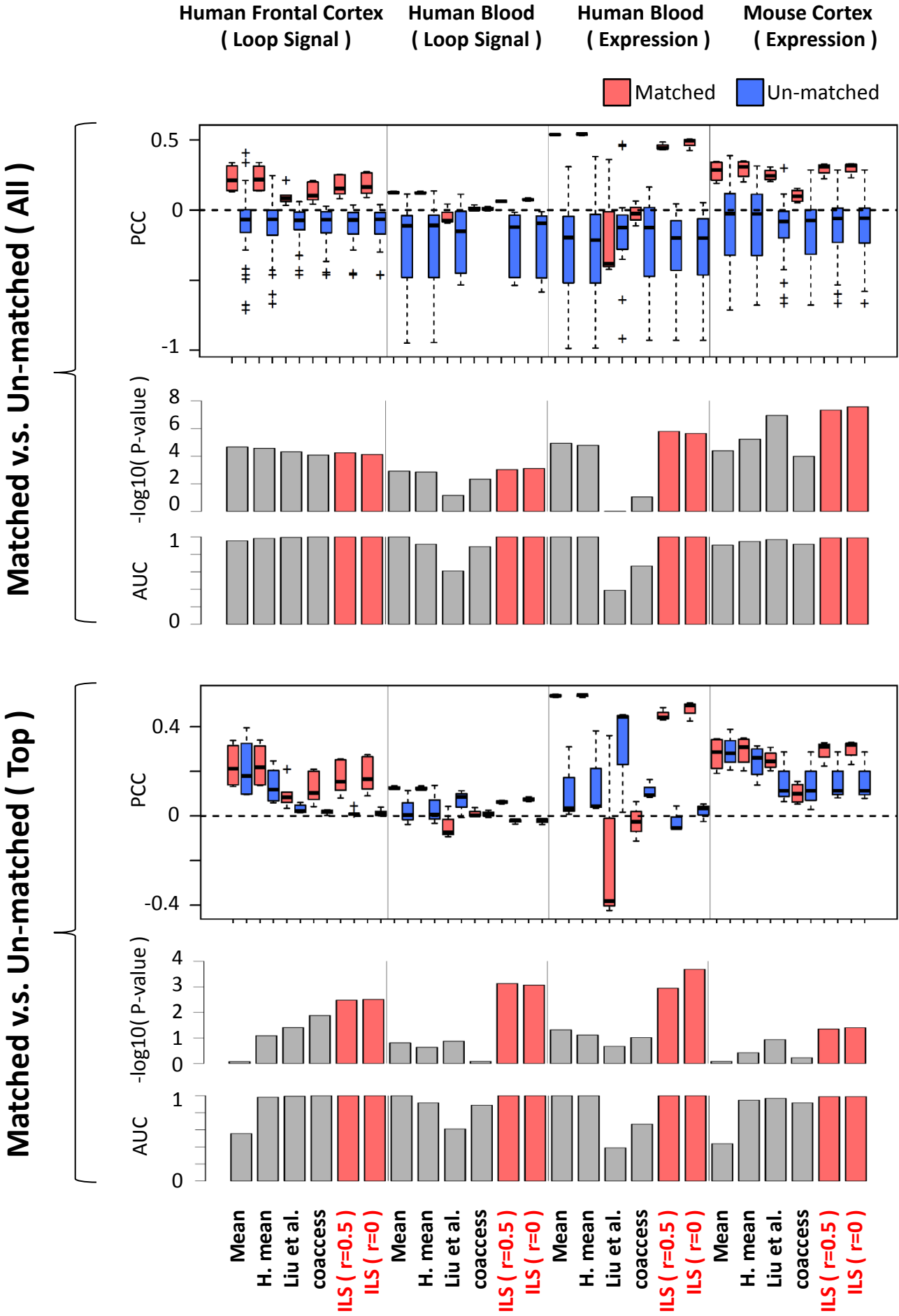
Supplementary Figure 9



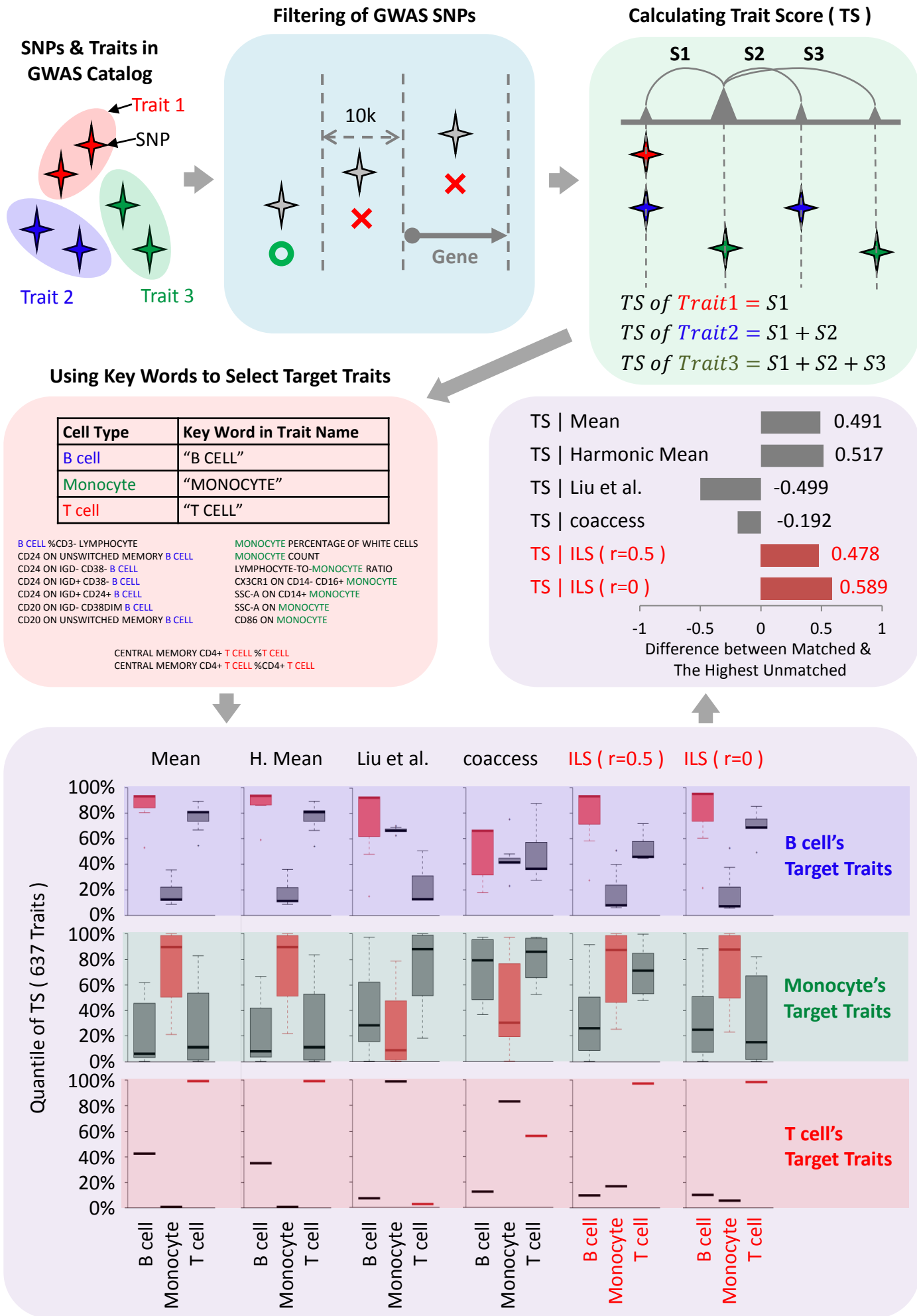
Supplementary Figure 10



Supplementary Figure 11

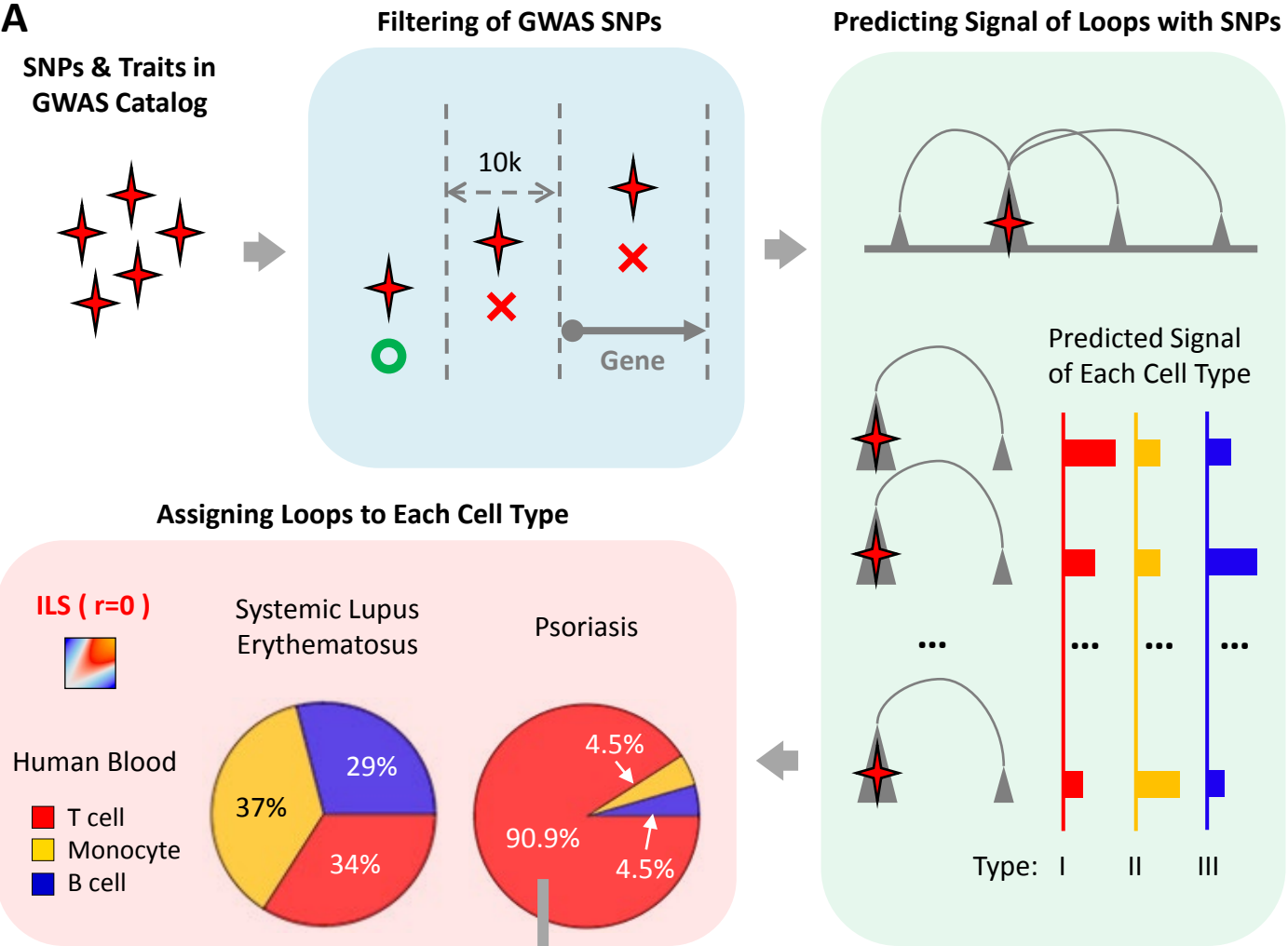


Supplementary Figure 12

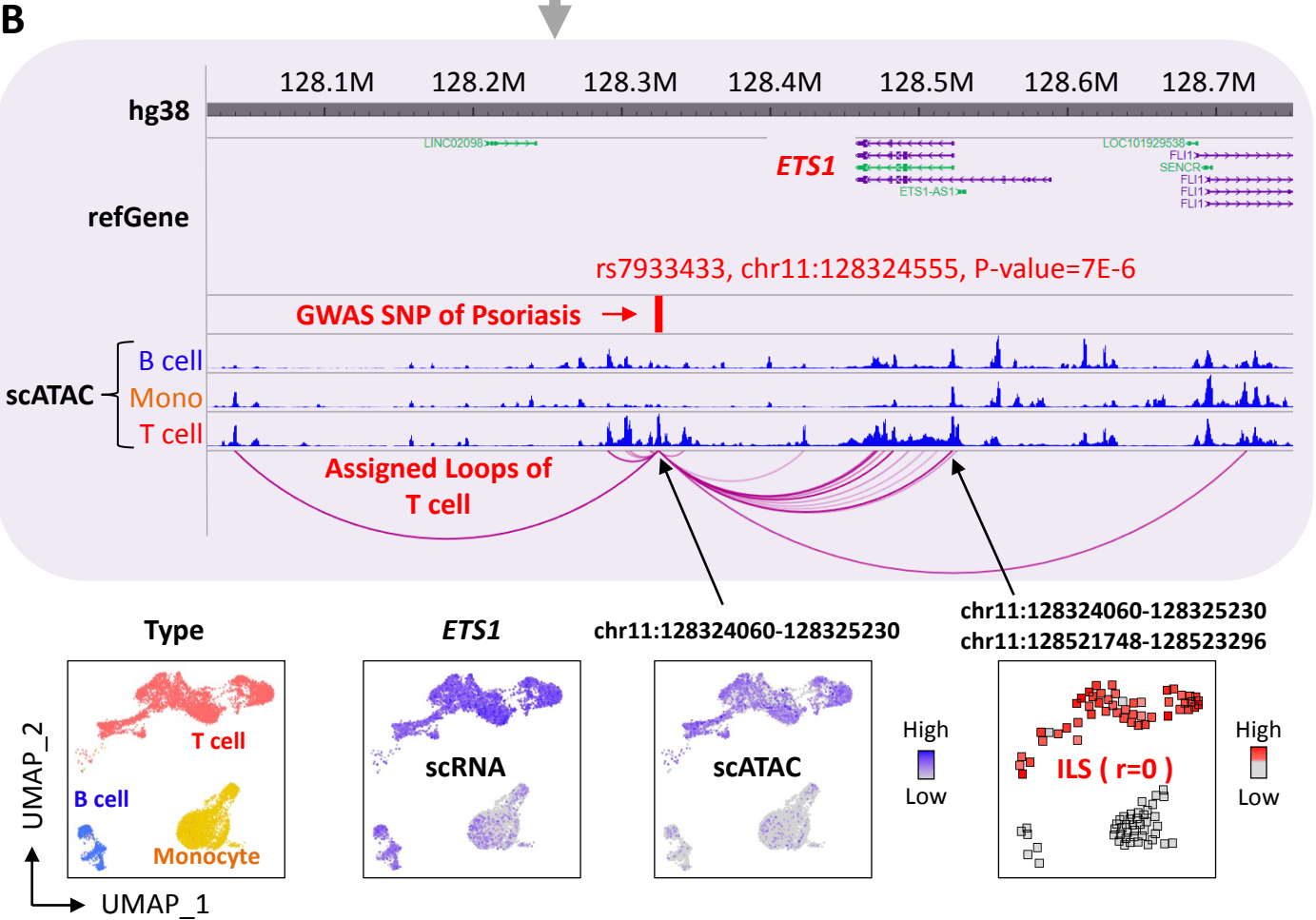


Supplementary Figure 13

A



B



Our study (hg38)

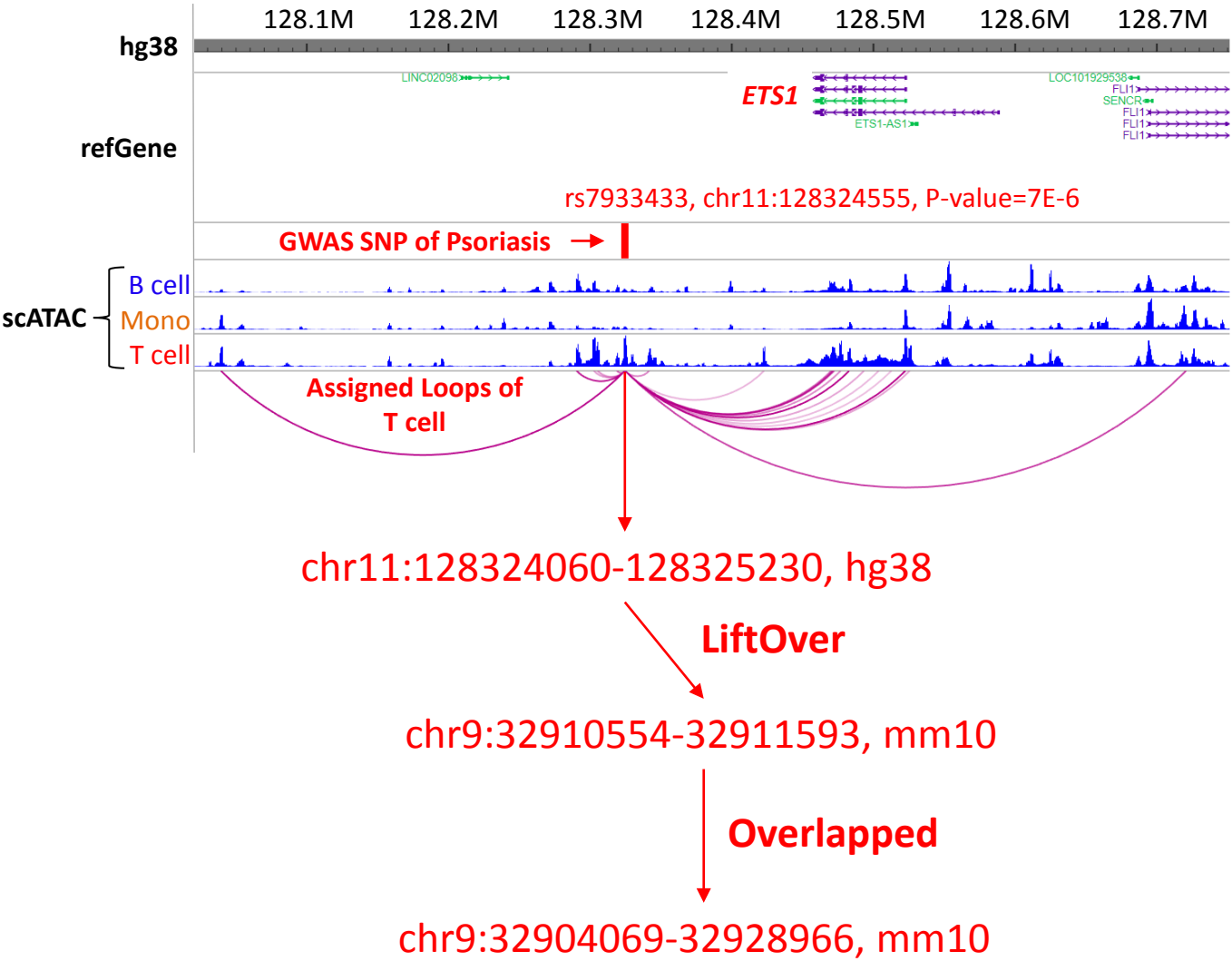
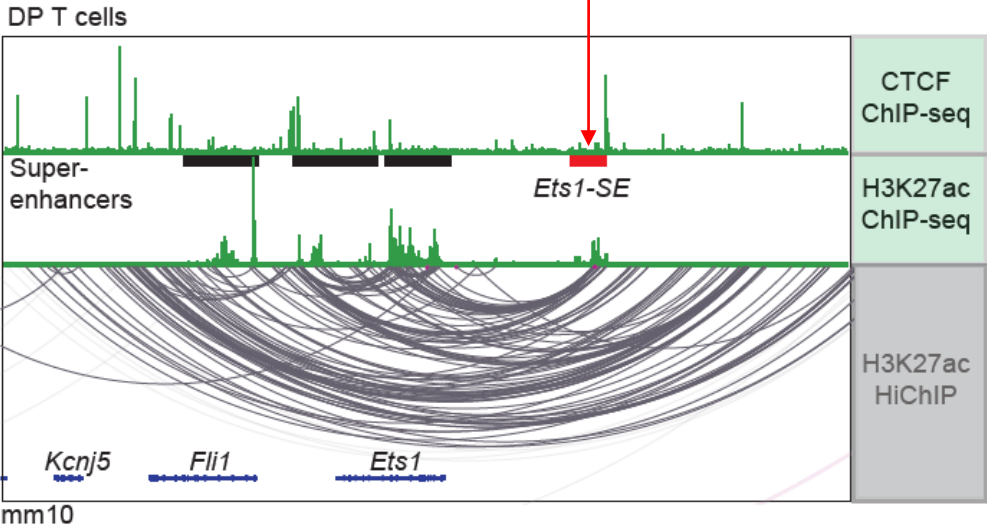


Figure 1d in Chandra's paper (mm10)



A multi-enhancer hub at the Ets1 locus controls T cell differentiation and allergic inflammation through 3D genome topology, *bioRxiv*, 2022.10.28, <https://doi.org/10.1101/2022.10.28.514213>