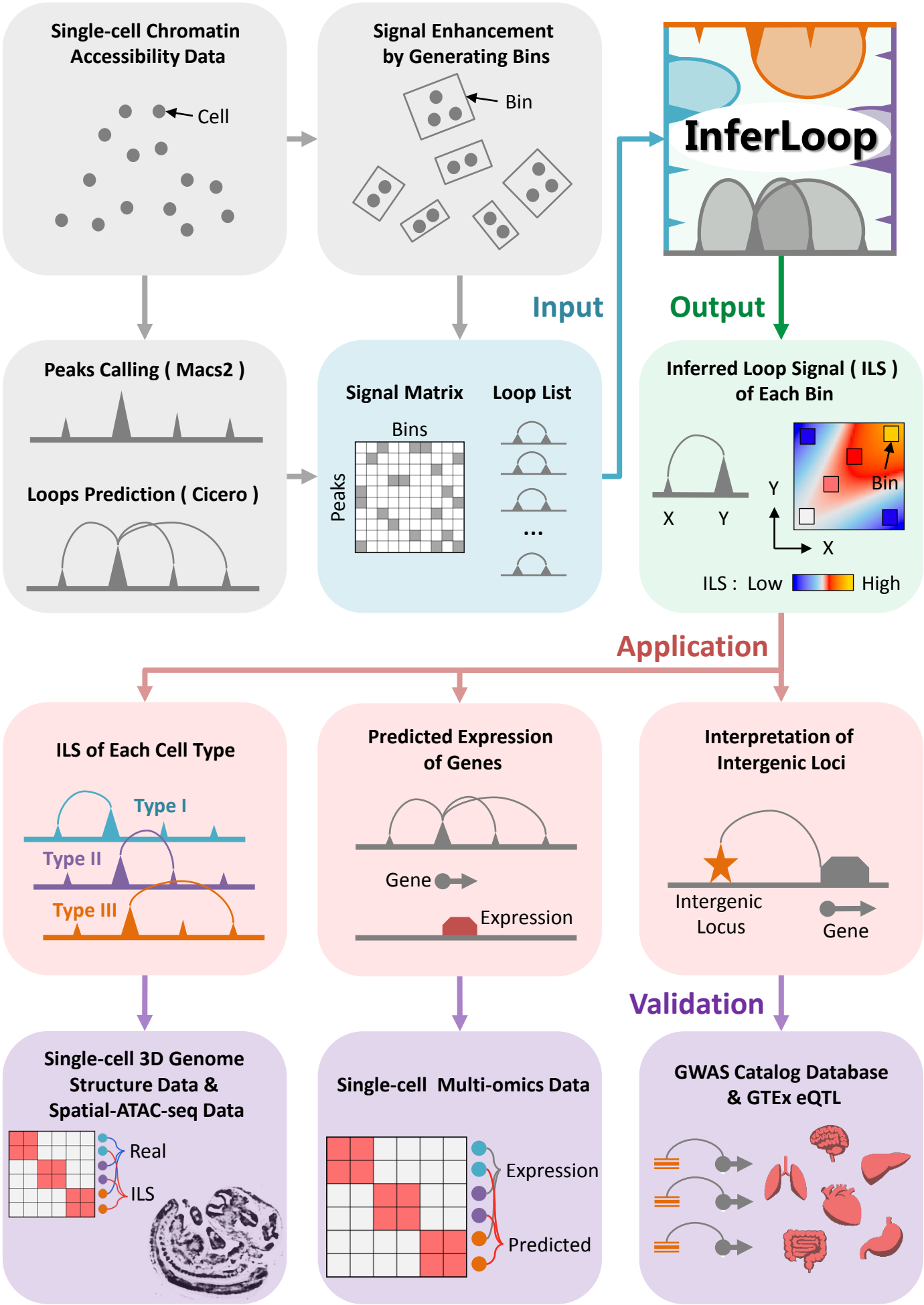
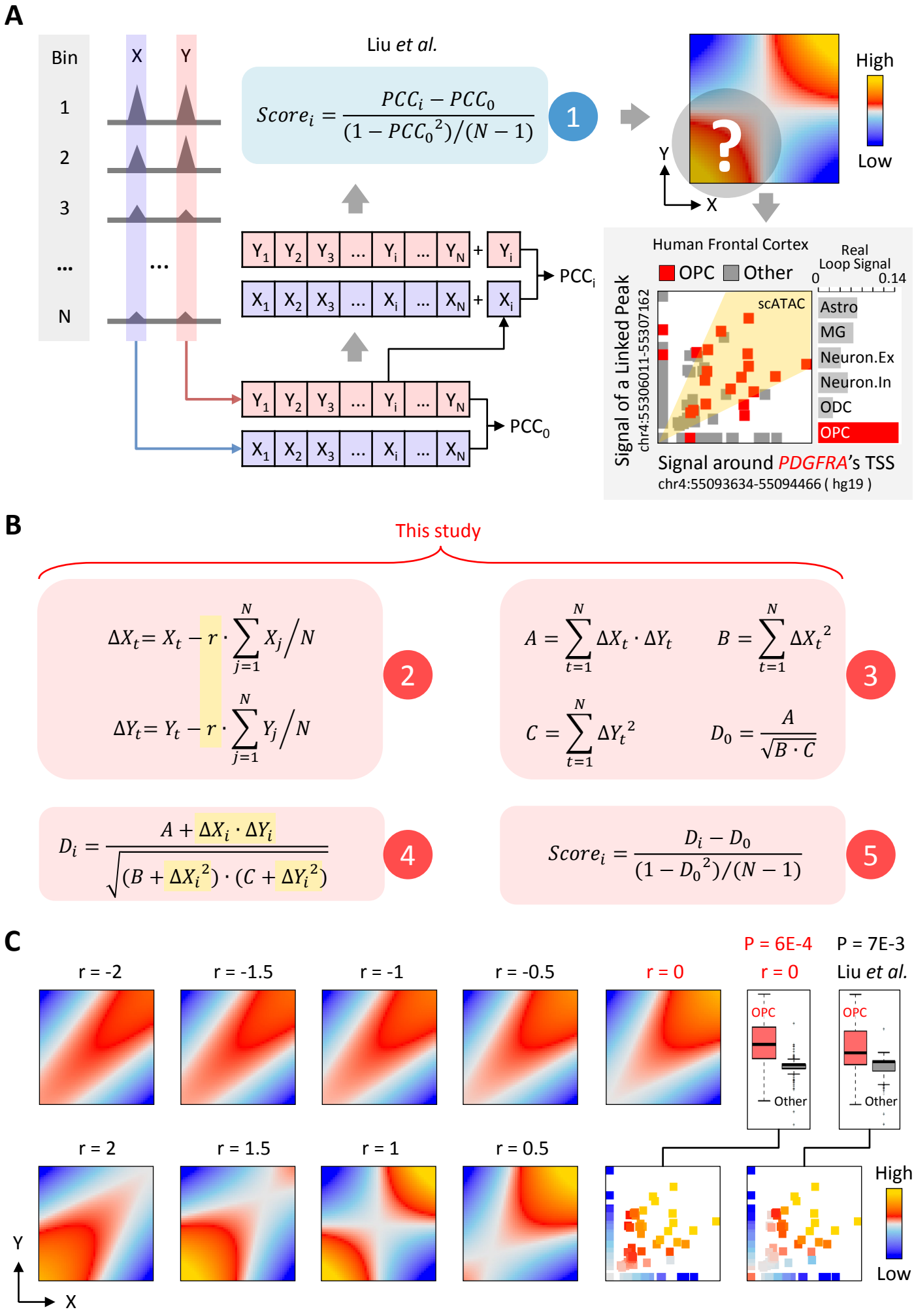
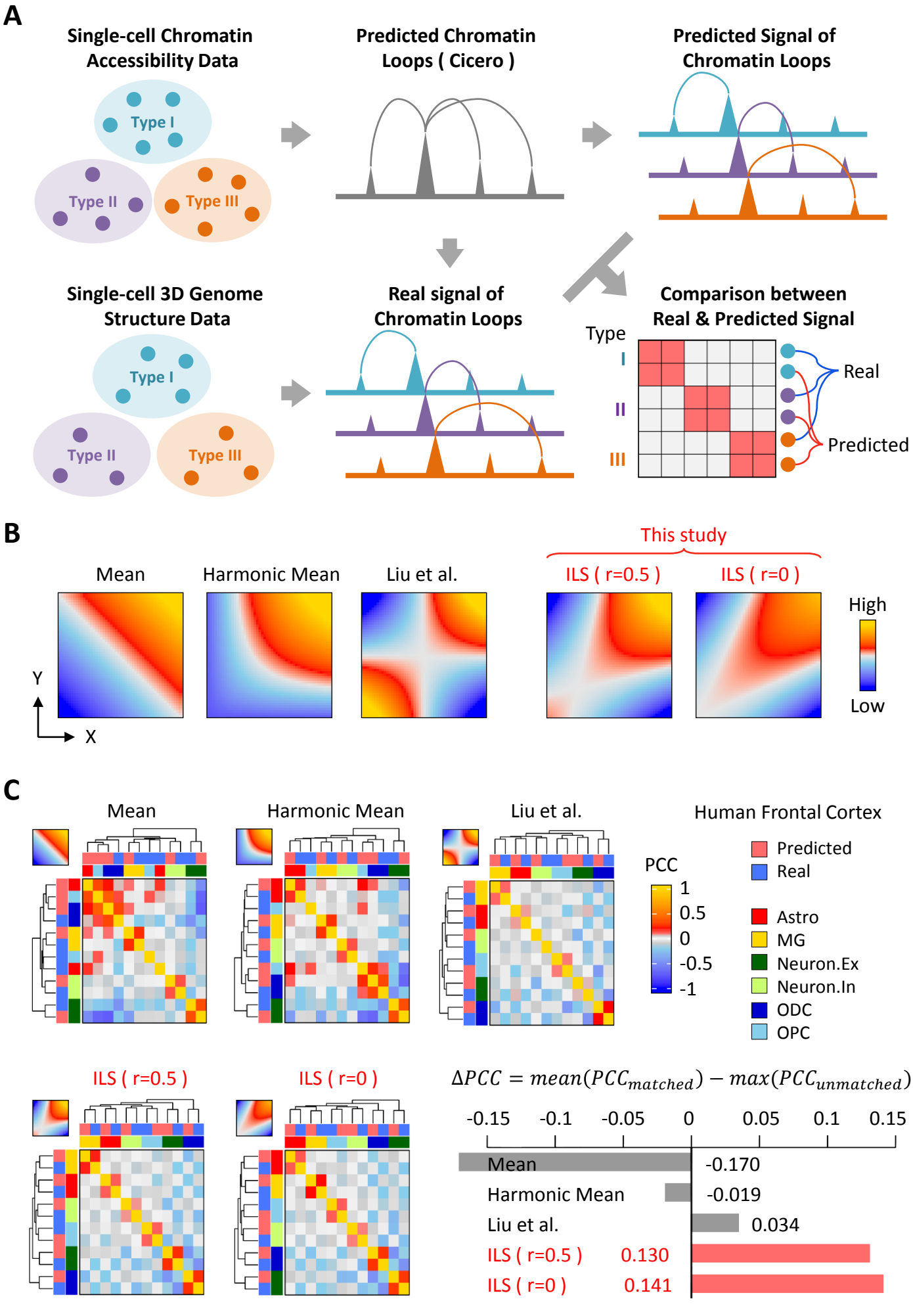
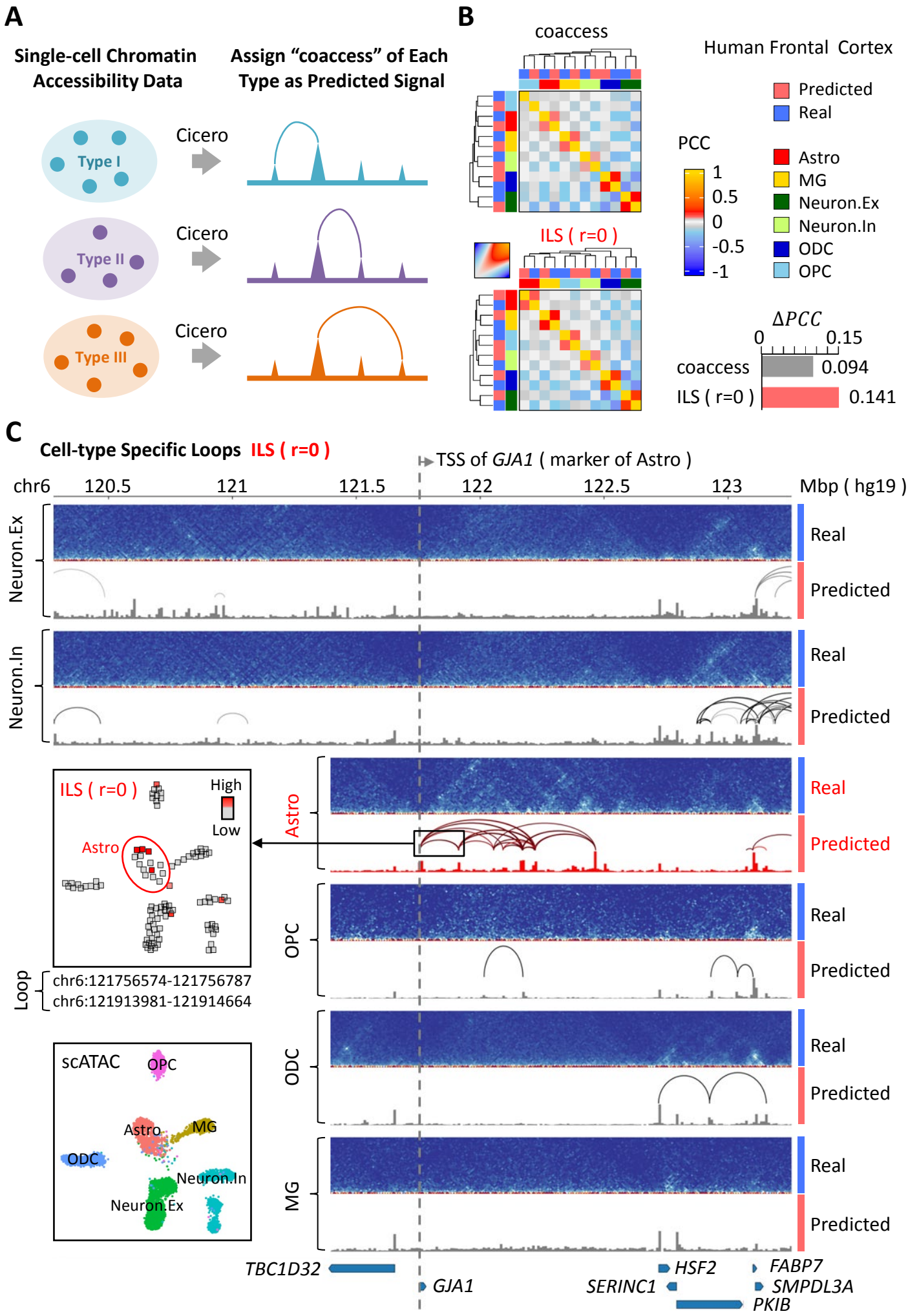
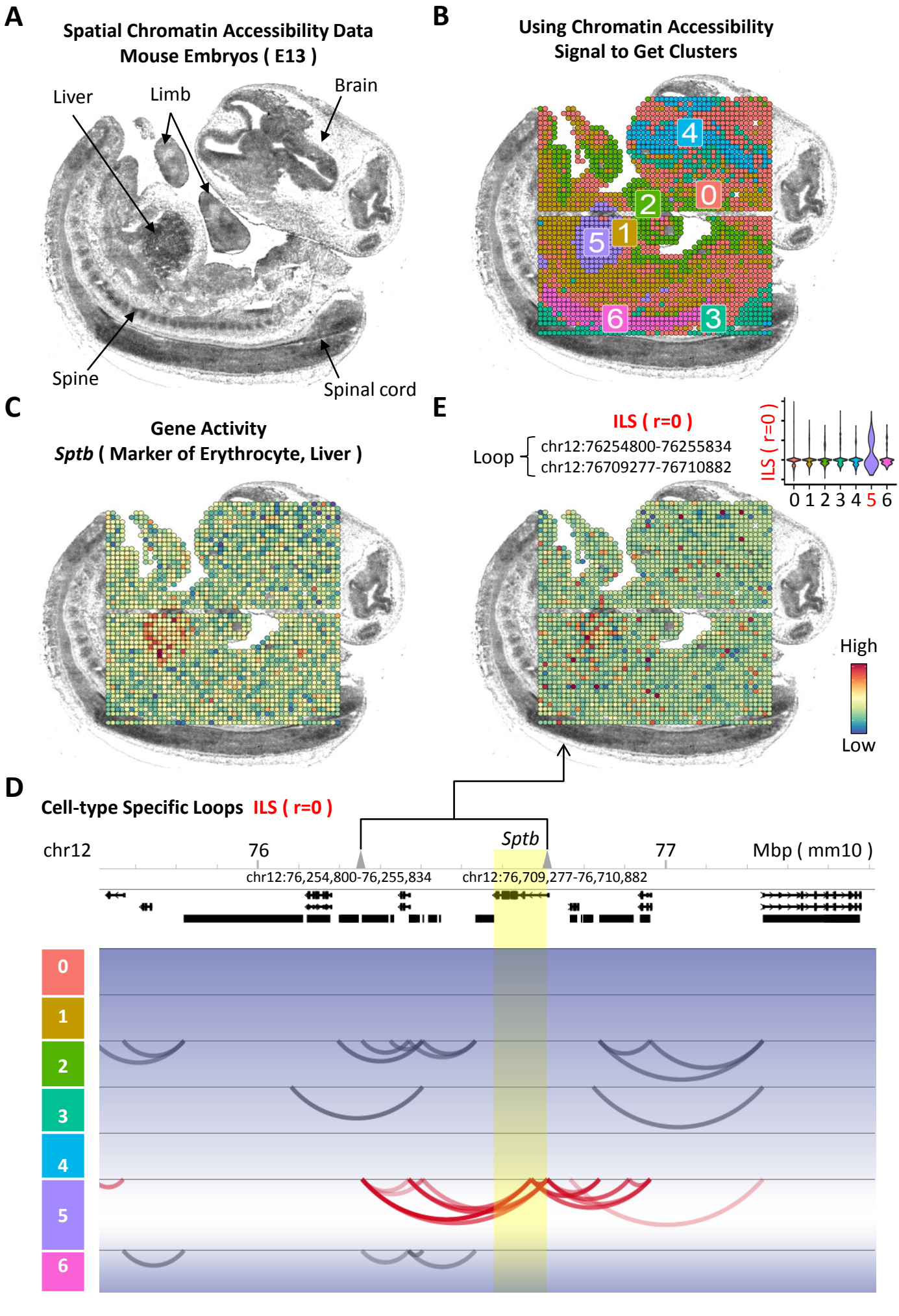
Main Figures

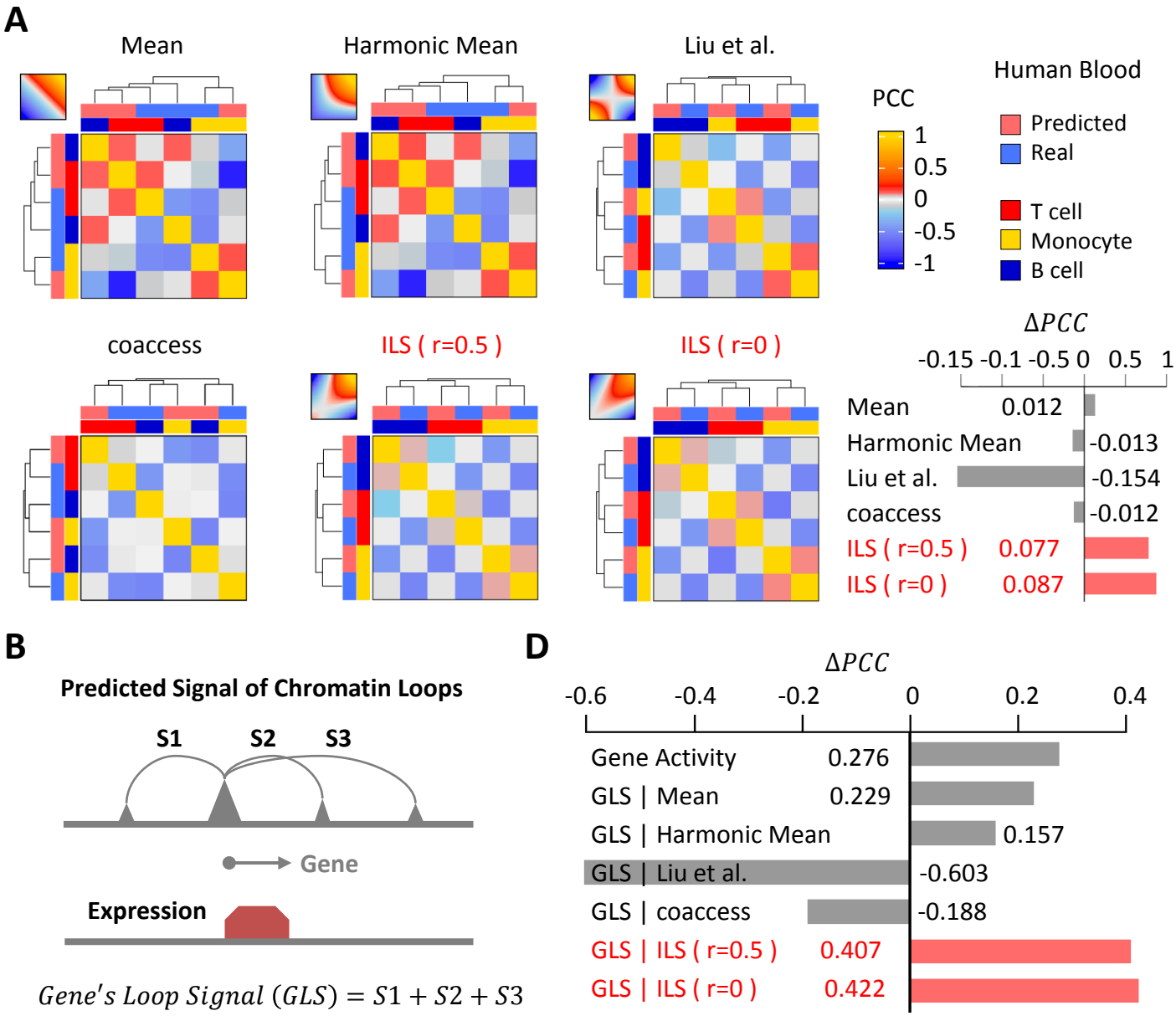

Single-cell Chromatin Accessibility Data
Cell
Signal Enhancement by Generating Bins
Bin
InferLoop
Input
Output
Peaks Calling (Macs2)
Loops Prediction (Cicero)
Signal Matrix
Bins
Peaks
Loop List
...
Inferred Loop Signal (ILS) of Each Bin
X
Y
Y
X
Bin
ILS : Low
High
Application
ILS of Each Cell Type
Type I
Type II
Type III
Predicted Expression of Genes
Gene
Expression
Interpretation of Intergenic Loci
Intergenic Locus
Gene
Validation
Single-cell 3D Genome Structure Data & Spatial-ATAC-seq Data
Real
ILS
Single-cell Multi-omics Data
Expression
Predicted
GWAS Catalog Database & GTEx eQTL


A
Bin
X
Y
1
2
3
...
N
Liu et al.
$Score_i = \frac{PCC_i - PCC_0}{(1 - PCC_0{}^2)/(N-1)}$
1
High
Low
Y
X
Y_1 Y_2 Y_3 ... Y_i ... Y_N + Y_i
X_1 X_2 X_3 ... X_i ... X_N + X_i
PCC_i
PCC_0
Human Frontal Cortex
OPC
Other
Real Loop Signal
0
0.14
scATAC
Astro
MG
Neuron.Ex
Neuron.In
ODC
OPC
Signal of a Linked Peak
chr4:55306011-55307162
Signal around PDGFRA's TSS
chr4:55093634-55094466 (hg19)
B
This study
$\Delta X_t = X_t - r \cdot \sum_{j=1}^{N} X_j / N$
$\Delta Y_t = Y_t - r \cdot \sum_{j=1}^{N} Y_j / N$
2
$A = \sum_{t=1}^{N} \Delta X_t \cdot \Delta Y_t$
$B = \sum_{t=1}^{N} \Delta X_t{}^2$
$C = \sum_{t=1}^{N} \Delta Y_t{}^2$
$D_0 = \frac{A}{\sqrt{B \cdot C}}$
3
$D_i = \frac{A + \Delta X_i \cdot \Delta Y_i}{\sqrt{(B + \Delta X_i{}^2) \cdot (C + \Delta Y_i{}^2)}}$
4
$Score_i = \frac{D_i - D_0}{(1 - D_0{}^2)/(N-1)}$
5
C
r = -2
r = -1.5
r = -1
r = -0.5
r = 0
P = 6E-4
r = 0
P = 7E-3
Liu et al.
OPC
Other
OPC
Other
r = 2
r = 1.5
r = 1
r = 0.5
High
Low
Y
X


A
Single-cell Chromatin Accessibility Data
Type I
Type II
Type III
Predicted Chromatin Loops (Cicero)
Predicted Signal of Chromatin Loops
Single-cell 3D Genome Structure Data
Type I
Type II
Type III
Real signal of Chromatin Loops
Comparison between Real & Predicted Signal
Type
I
II
III
Real
Predicted
B
This study
Mean
Harmonic Mean
Liu et al.
ILS (r=0.5)
ILS (r=0)
High
Low
Y
X
C
Mean
Harmonic Mean
Liu et al.
Human Frontal Cortex
PCC
1
0.5
0
-0.5
-1
Predicted
Real
Astro
MG
Neuron.Ex
Neuron.In
ODC
OPC
ILS (r=0.5)
ILS (r=0)
$\Delta PCC = mean(PCC_{matched}) - max(PCC_{unmatched})$
-0.15
-0.1
-0.05
0
0.05
0.1
0.15
Mean
-0.170
Harmonic Mean
-0.019
Liu et al.
0.034
ILS (r=0.5)
0.130
ILS (r=0)
0.141

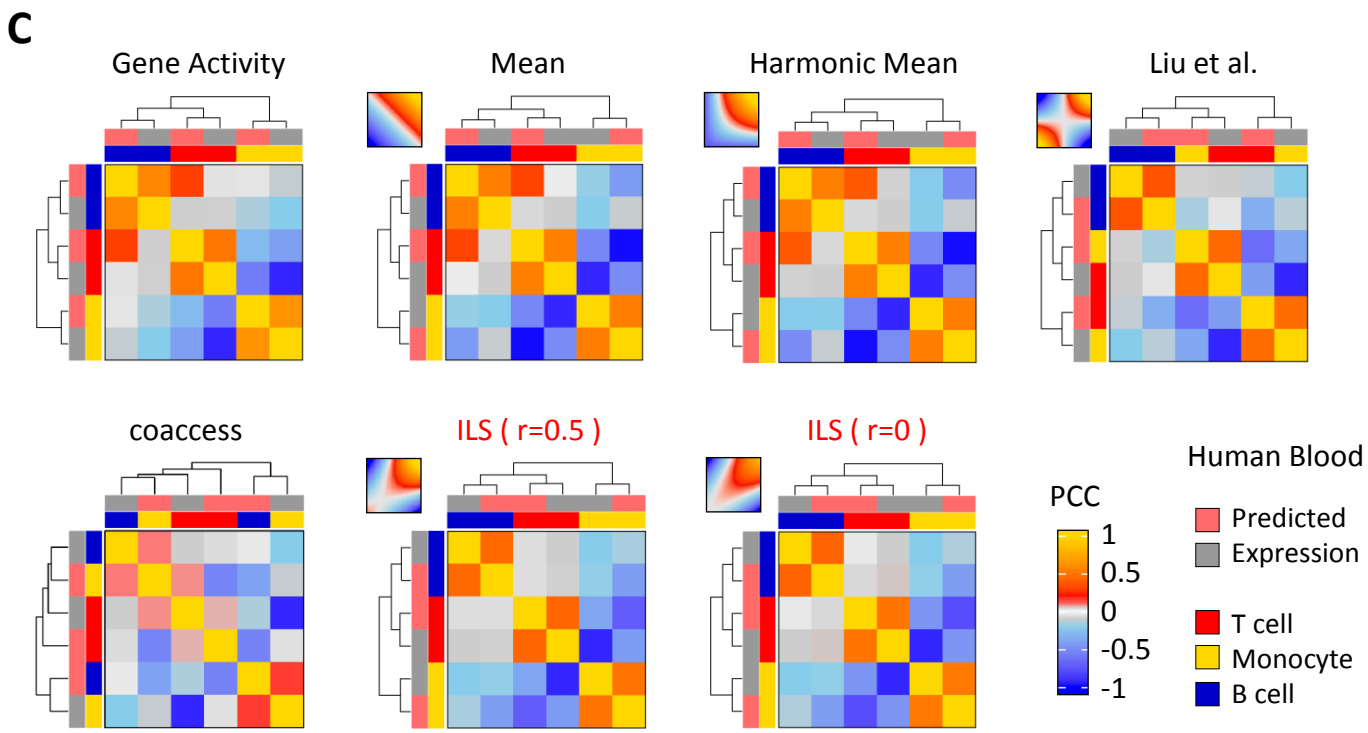

A
Single-cell Chromatin Accessibility Data
Assign "coaccess" of Each Type as Predicted Signal
Type I
Type II
Type III
Cicero
Cicero
Cicero
B
coaccess
ILS (r=0)
Human Frontal Cortex
Predicted
Real
PCC
1
0.5
0
-0.5
-1
Astro
MG
Neuron.Ex
Neuron.In
ODC
OPC
ΔPCC
0
0.15
coaccess
0.094
ILS (r=0)
0.141
C
Cell-type Specific Loops ILS (r=0)
TSS of GJA1 (marker of Astro)
chr6
120.5
121
121.5
122
122.5
123
Mbp (hg19)
Neuron.Ex
Neuron.In
Real
Predicted
ILS (r=0)
High
Low
Astro
Loop
chr6:121756574-121756787
chr6:121913981-121914664
scATAC
OPC
Astro
MG
ODC
Neuron.In
Neuron.Ex
OPC
ODC
MG
TBC1D32
GJA1
HSF2
FABP7
SERINC1
SMPDL3A
PKIB

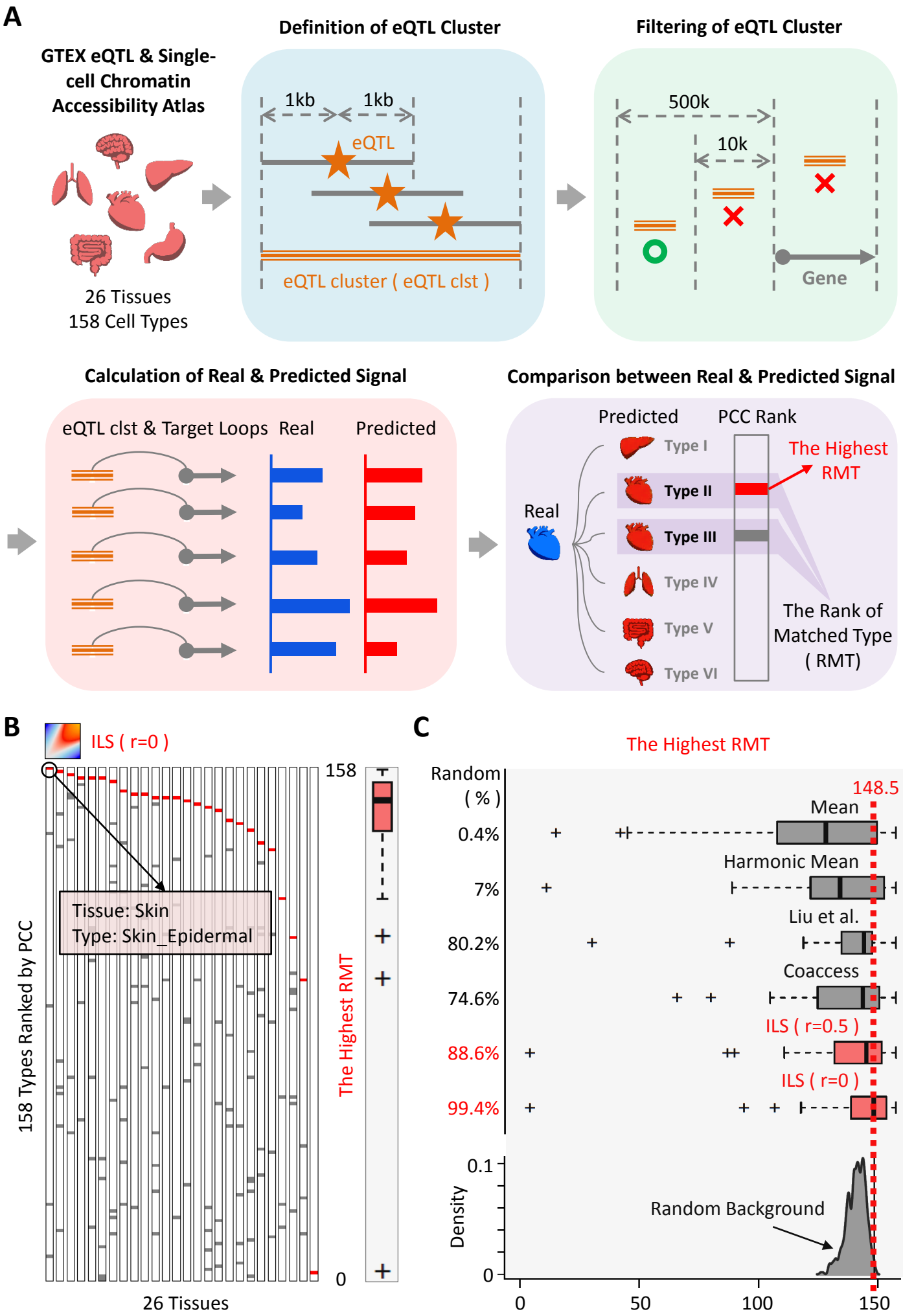

A
Spatial Chromatin Accessibility Data
Mouse Embryos (E13)
Liver
Limb
Brain
Spine
Spinal cord
B
Using Chromatin Accessibility
Signal to Get Clusters
4
0
2
1
5
6
3
C
Gene Activity
Sptb (Marker of Erythrocyte, Liver)
E
ILS (r=0)
Loop
chr12:76254800-76255834
chr12:76709277-76710882
ILS (r=0)
0 1 2 3 4 5 6
High
Low
D
Cell-type Specific Loops ILS (r=0)
chr12
76
Sptb
77
Mbp (mm10)
chr12:76,254,800-76,255,834
chr12:76,709,277-76,710,882
0
1
2
3
4
5
6


A
Mean
Harmonic Mean
Liu et al.
PCC
1
0.5
0
-0.5
-1
Human Blood
Predicted
Real
T cell
Monocyte
B cell
coaccess
ILS (r=0.5)
ILS (r=0)
ΔPCC
-0.15 -0.1 -0.5 0 0.5 1
Mean 0.012
Harmonic Mean -0.013
Liu et al. -0.154
coaccess -0.012
ILS (r=0.5) 0.077
ILS (r=0) 0.087

B
Predicted Signal of Chromatin Loops
S1
S2
S3
Gene
Expression
Gene's Loop Signal (GLS) = S1 + S2 + S3

D
ΔPCC
-0.6 -0.4 -0.2 0 0.2 0.4
Gene Activity 0.276
GLS | Mean 0.229
GLS | Harmonic Mean 0.157
GLS | Liu et al. -0.603
GLS | coaccess -0.188
GLS | ILS (r=0.5) 0.407
GLS | ILS (r=0) 0.422


C
Gene Activity
Mean
Harmonic Mean
Liu et al.
coaccess
ILS (r=0.5)
ILS (r=0)
PCC
1
0.5
0
-0.5
-1
Human Blood
Predicted
Expression
T cell
Monocyte
B cell


A
GTEX eQTL & Single-cell Chromatin Accessibility Atlas
26 Tissues
158 Cell Types
Definition of eQTL Cluster
1kb
1kb
eQTL
eQTL cluster (eQTL clst)
Filtering of eQTL Cluster
500k
10k
Gene
Calculation of Real & Predicted Signal
eQTL clst & Target Loops
Real
Predicted
Comparison between Real & Predicted Signal
Predicted
PCC Rank
Real
Type I
Type II
Type III
Type IV
Type V
Type VI
The Highest RMT
The Rank of Matched Type (RMT)
B
ILS (r=0)
Tissue: Skin
Type: Skin_Epidermal
158 Types Ranked by PCC
158
0
The Highest RMT
26 Tissues
C
The Highest RMT
Random (%)
148.5
Mean
0.4%
Harmonic Mean
7%
Liu et al.
80.2%
Coaccess
74.6%
ILS (r=0.5)
88.6%
ILS (r=0)
99.4%
Density
0.1
0
Random Background
0
50
100
150