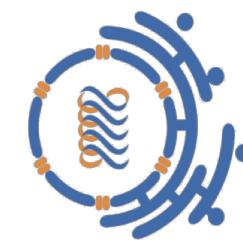




UNIVERSIDAD AUTÓNOMA DEL
ESTADO DE MORELOS



Instituto de
Investigación en
Ciencias
Básicas y
Aplicadas



Centro de
Investigación en
Dinámica Celular

Transcriptional Factors associated with epigenome regulatory regions from neonates and adults CD8+ T cells.

Tutors:

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Laboratorio de Inmunología Celular.
UAEM,CIDC.

Dra. Alejandra Eugenia Medina Rivera
Laboratorio Internacional del Genoma Humano,
UNAM

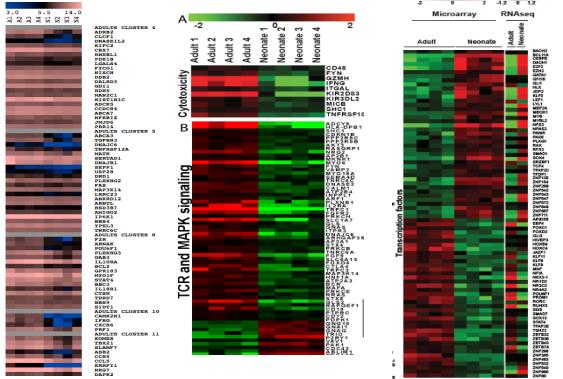
Colaborators:

Dr. Salvatore Spicuglia
Technical Advances for Genomics and Clinics (TAGC)

Dra. Morgane Thomas-Chollier
Dr. Denis Thieffry
Ecole Normale Supérieure Paris

TWO STORIES

Signature gene Clusters

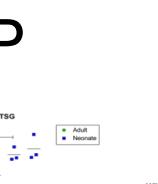
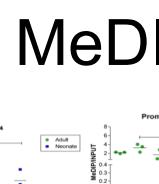
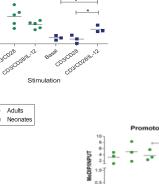
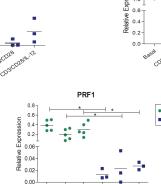


CD3/CD28/IL-12

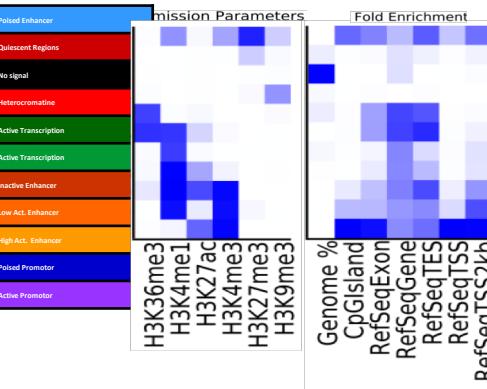
Expression

MeDIP

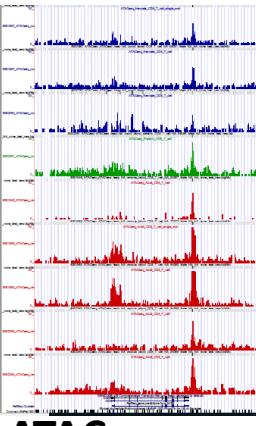
RSAT: Matrix-enrichment



Genome-Wide

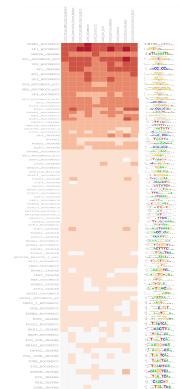


Chromatin States

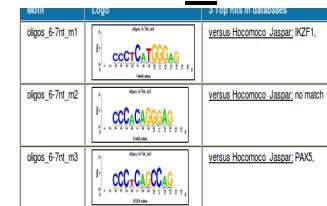
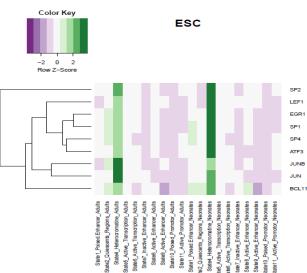


ATAC-seq

RSAT: Matrix-enrichment



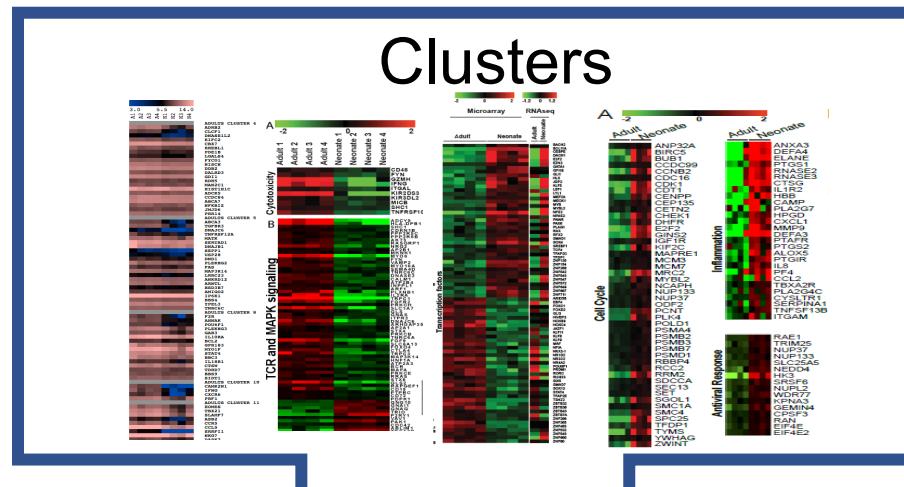
GAT: Overlap ChIP-seq



IL-12 signals induce the maturation of neonatal CD8+ T cells through epigenetic mechanisms.

Abstract

It has been reported that treatment of neonatal CD8+ T cells with IL-12 induces their cytotoxic response. We have previously reported that neonatal CD8+ T cells express innate response inflammatory genes. In this work we evaluated the genome wide presence of the IL-12 response transcription factor, STAT4 in neonatal and adult CD8+ T cells. We found that STAT4 is present in both the cytotoxicity cluster and the neutrophil-like inflammatory genes. We thus activated neonatal and adult CD8+ T cells with CD3/CD28 signals in the presence and absence of IL-12 and evaluated the methylation of promoter DNA and gene expression in a selection of representative genes of both clusters. It was clearly shown that IL-12 signals promote the methylation of neonatal neutrophil-like genes and the demethylation of cytotoxicity genes in the neonatal cells. This suggest that STAT4 may have a dual role in the epigenetic control of gene expression, controlling both the closing and opening of chromatin.

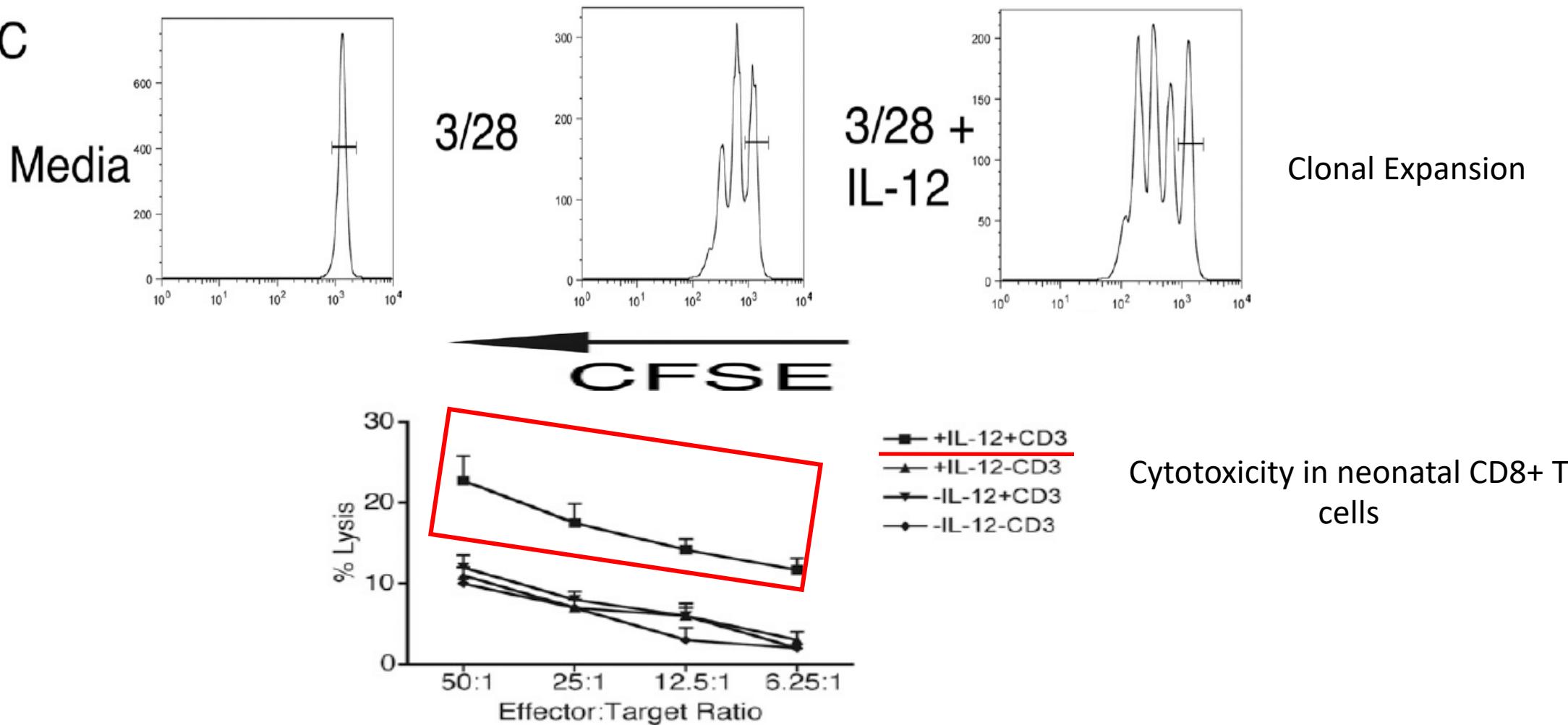


CD3/CD28/IL-12

Background

IL-12 is necessary as a third signal for enhanced cytotoxicity, survival and expansion in neonatal CD8+ T cell.

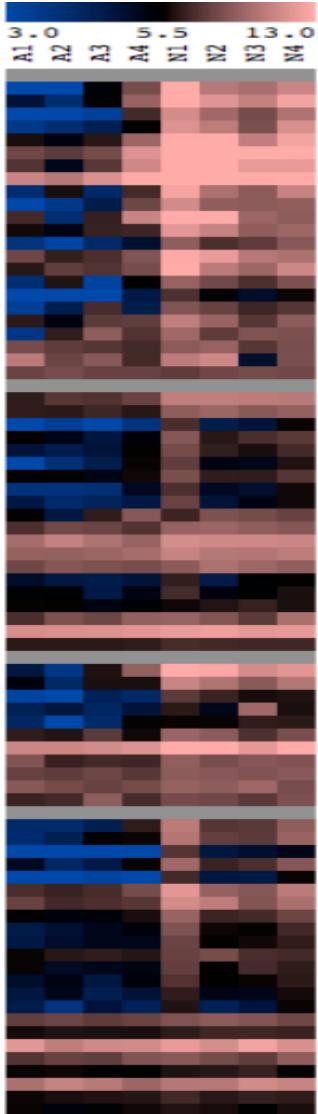
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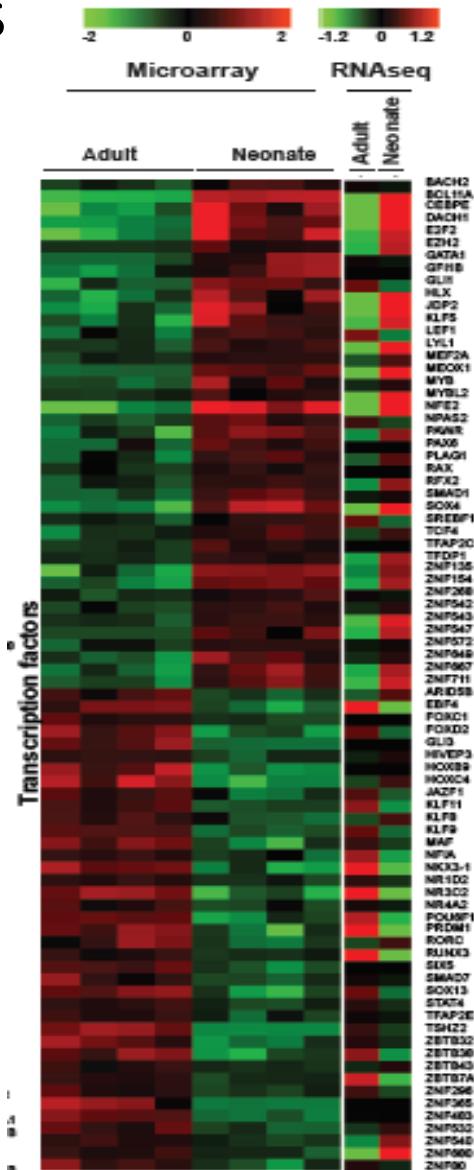
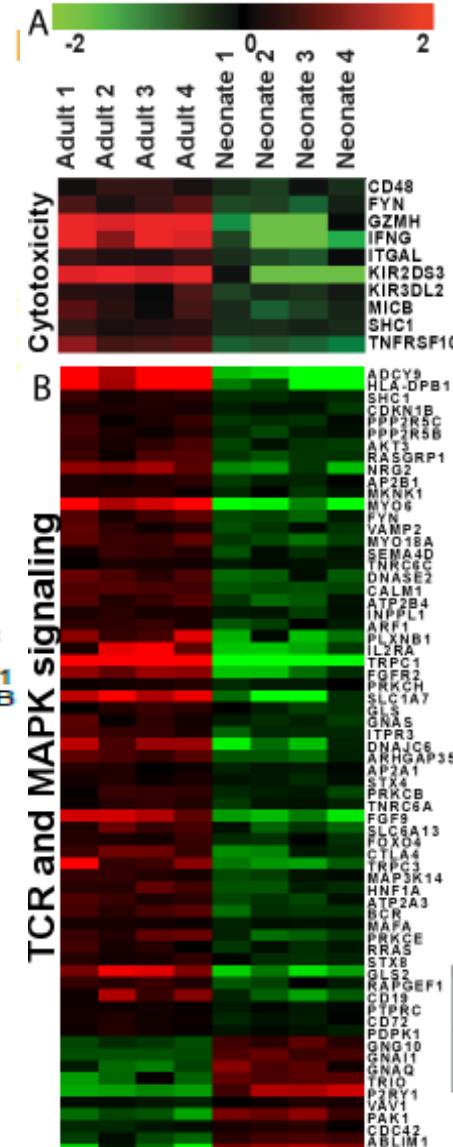
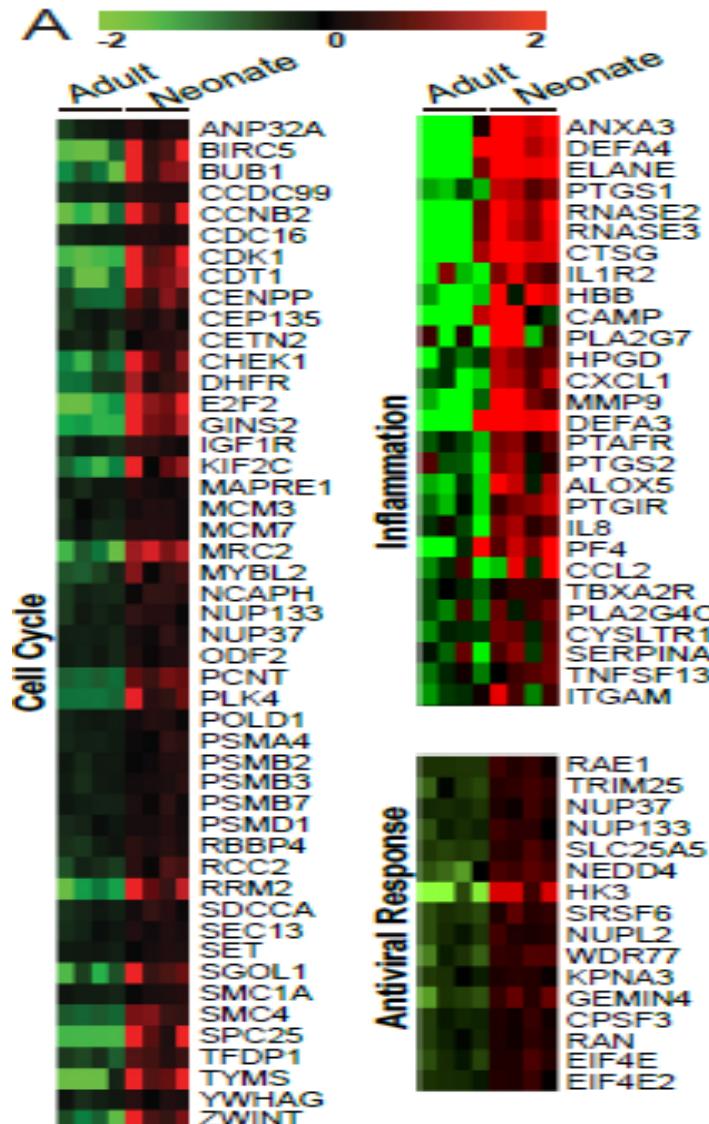
Background

DIFERENTIAL EXPRESSION FROM NEONATAL AND ADULTS NAIVE CD8+T CELLS

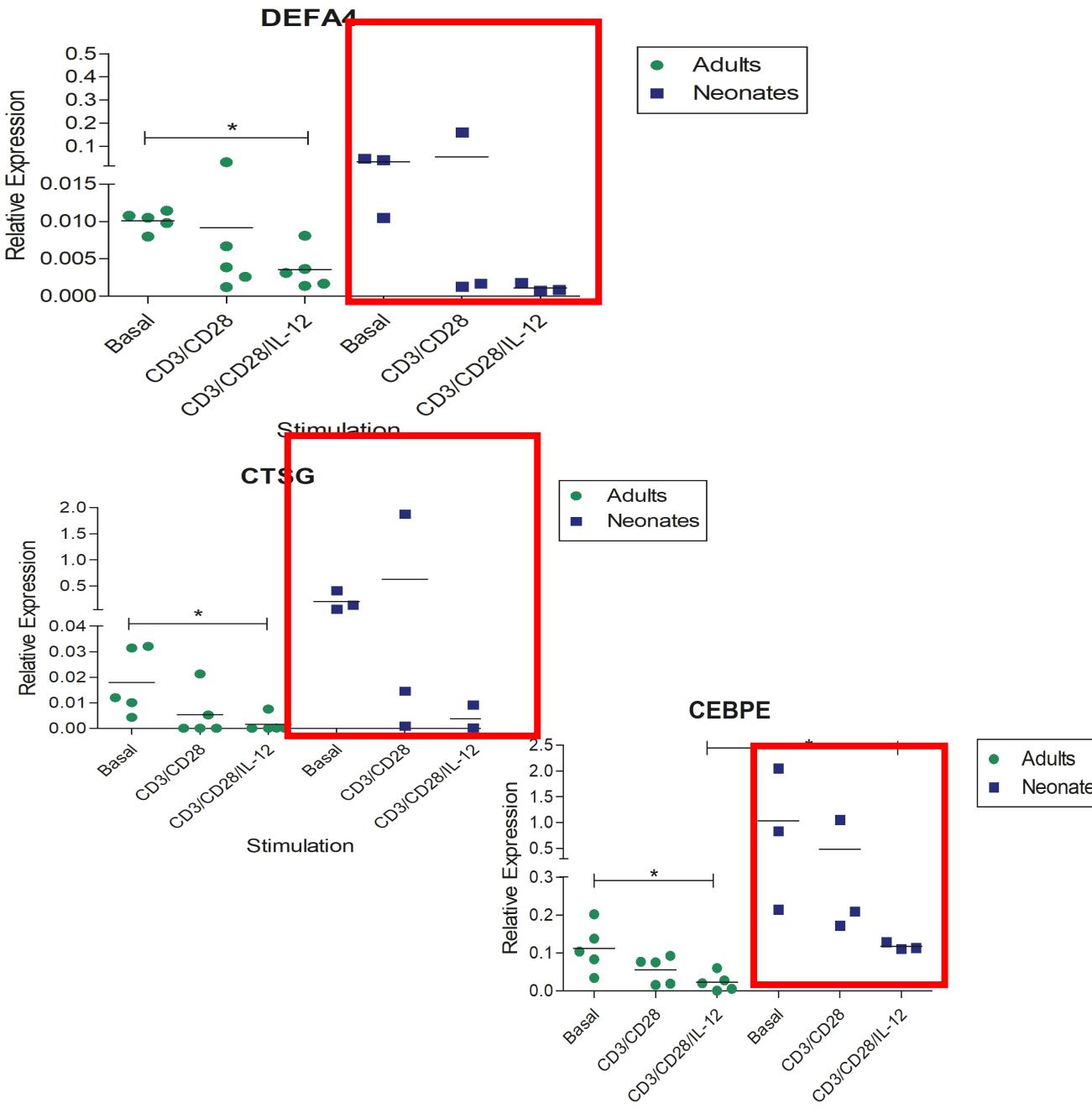
Tolerance



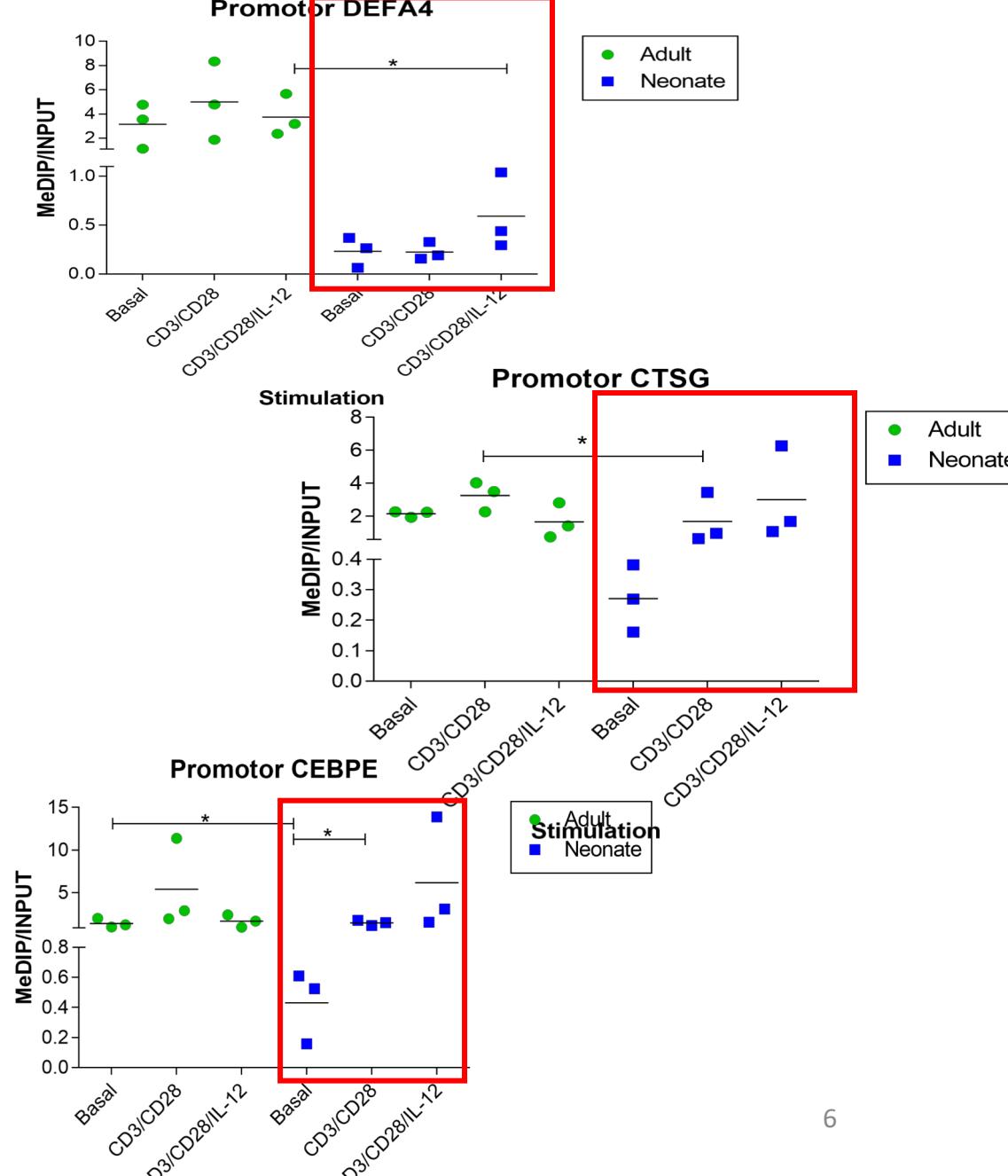
NEONATE CLUSTER 7
MPO
LCN2
ANXA3
CD177
HP
S100A9
LTC
S100A8
CHI3L1
ELANE
CAMP
PYGL
PRTN3
MMP9
CEBPE
LRG1
MGST1
SORT1
CB31
C3
SLC11A1
TGFB1
HDC
NEONATE CLUSTER 9
IGF2BP3
CDC47
KIF15
KIF2C
CDC45
ESO1
ESPL1
BUB1B
RAD54L
NRGN
PTPRS
STMN1
HIST1H3E
MARCKSL1
CDC20
AURKA
ZRANB3
CHST2
HIST1H3A
CCDC99
NEONATE CLUSTER 12
PGLYRP1
NFE2
RAB32
ALAS2
SNCA
SIRPA
FCER1G
GAD155G
GAP1
CRTAM
IL3RA
NEONATE CLUSTER 13
TYSM
E2F2
UHRF1
BIRC5
RRM2
TK1
CAPG
MMP5
NUASP1
KIF11
PSAT1
CCNB1
CDC43
CDC20
PLK1
MCM2
NCAPH
ITM2A
LMNBN1
CINTH
PPA1
FEN1
E2F1



TRANSCRIPTION



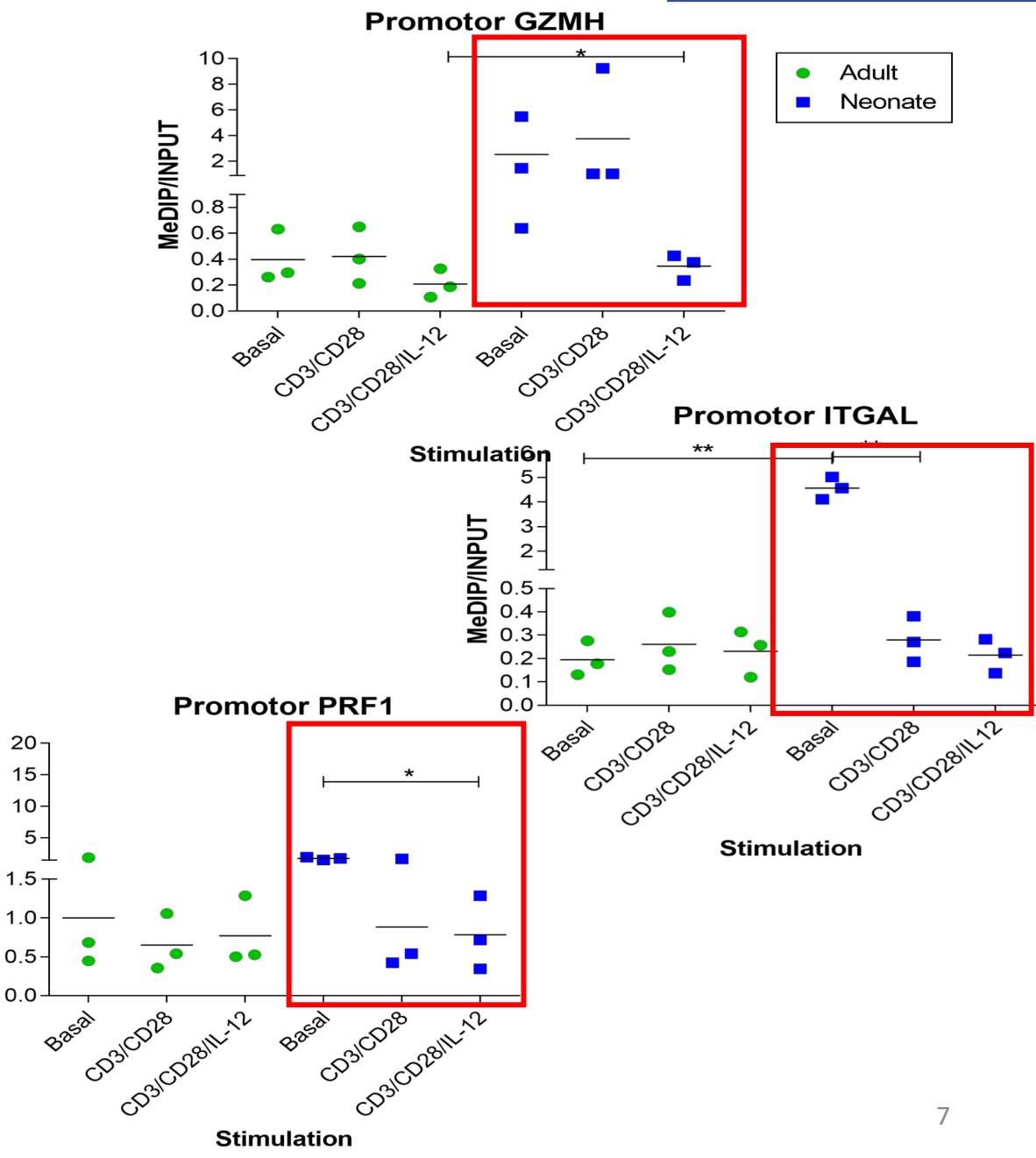
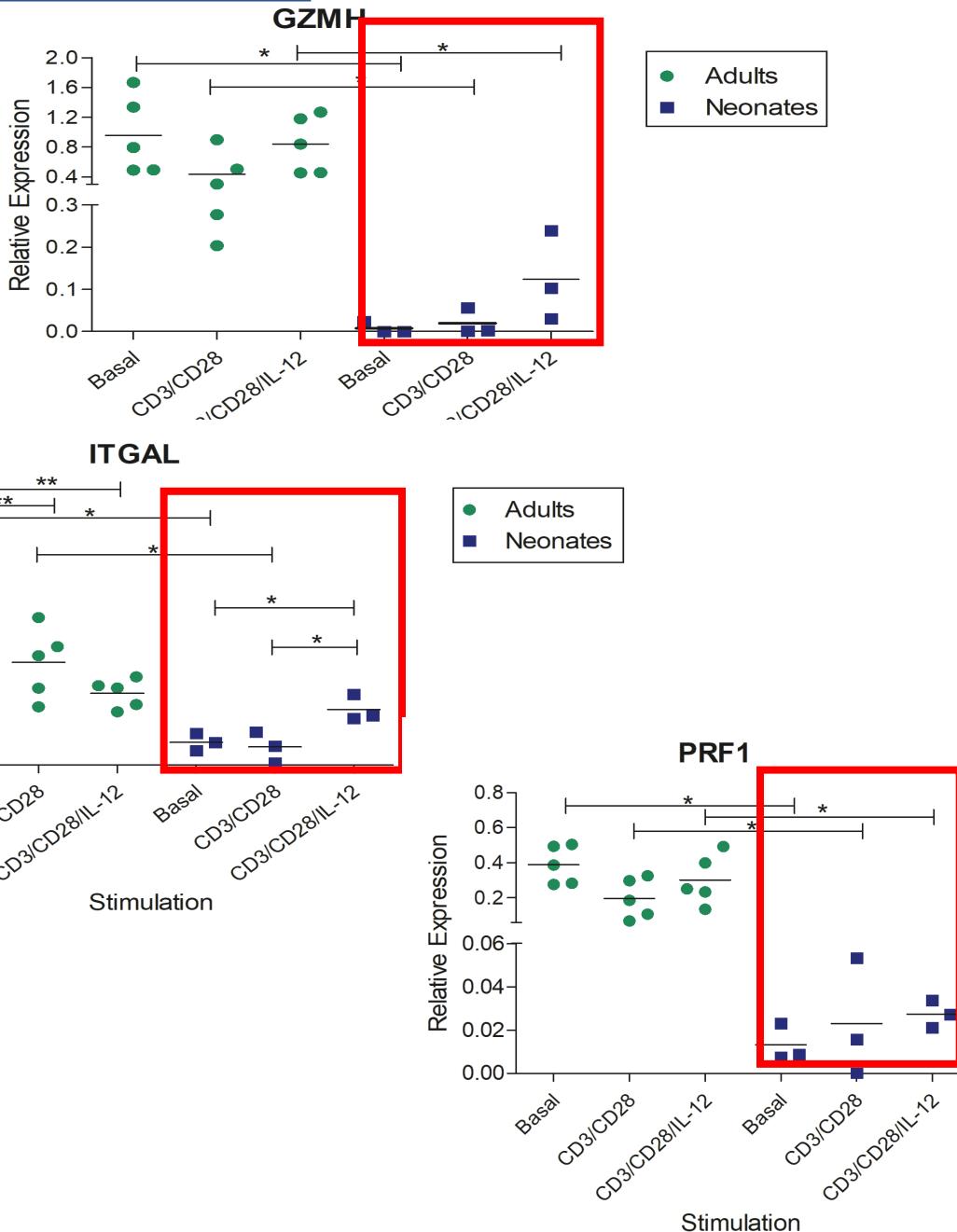
INFLAMMATION



TRANSCRIPTION

Cytotoxicity

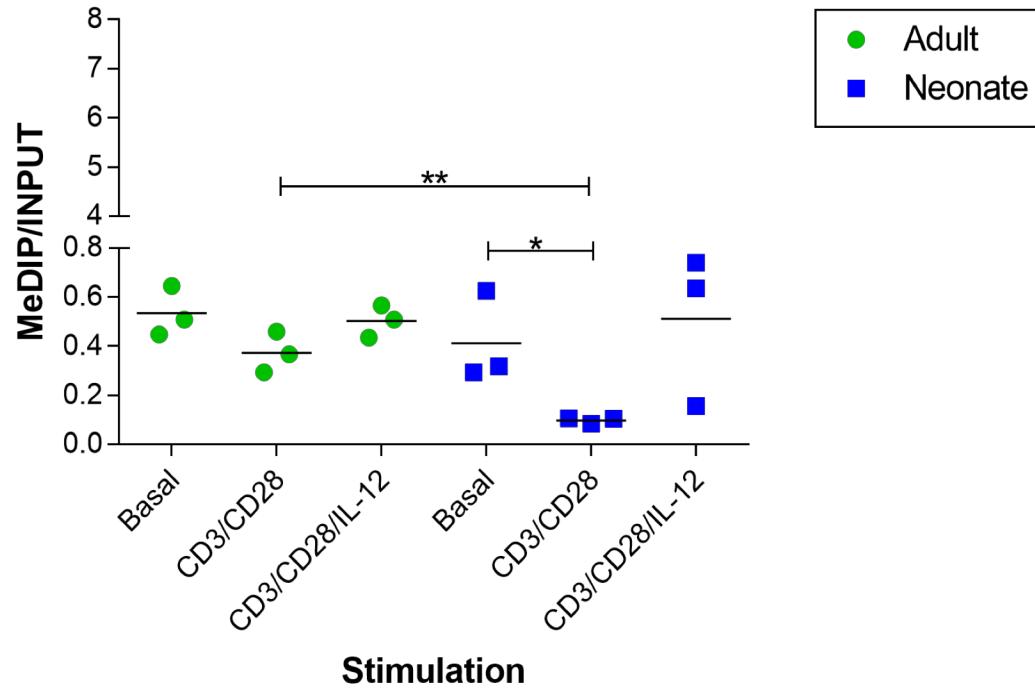
MeDIP



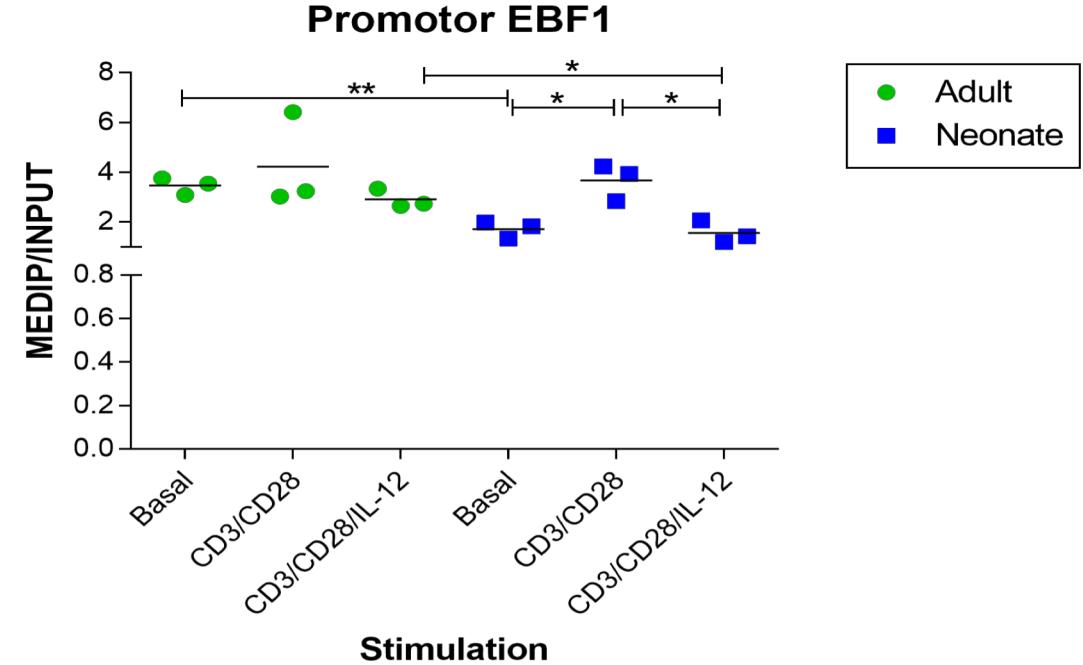
Controls genes

METILACIÓN

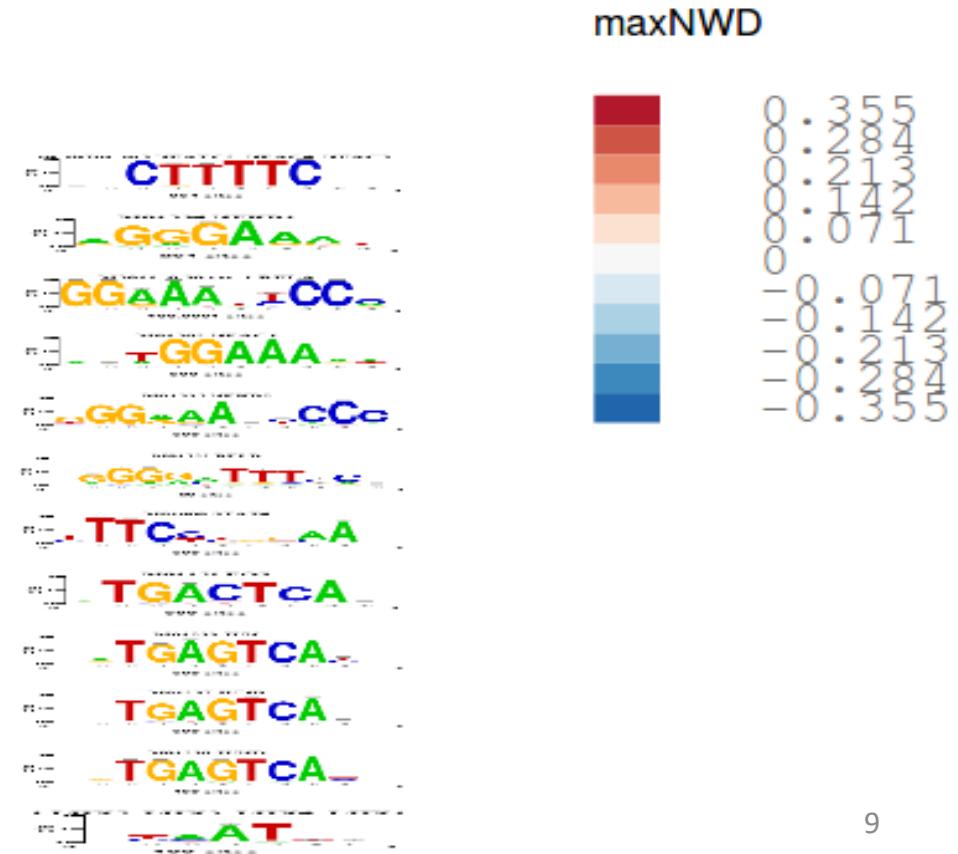
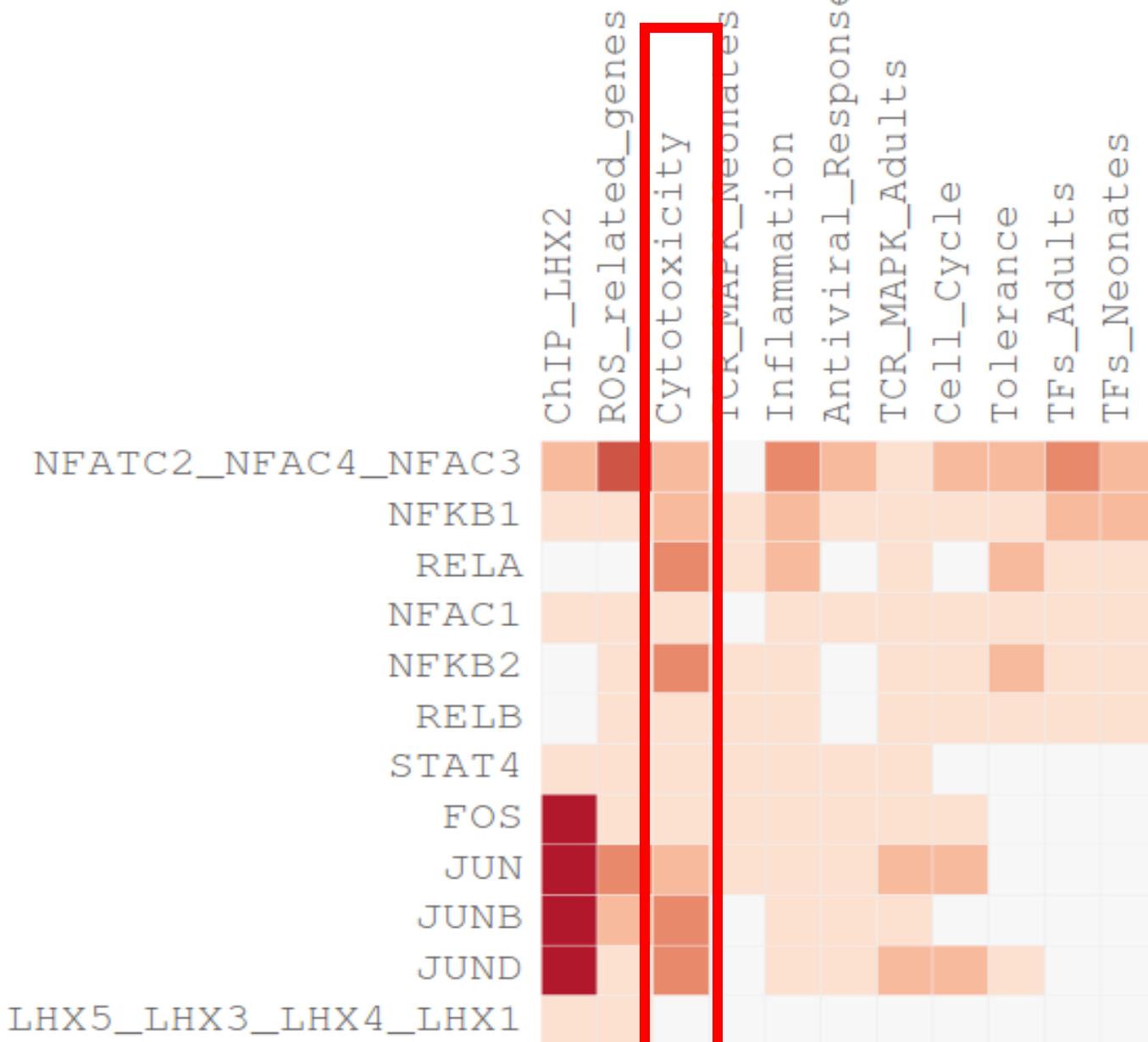
Promotor ACTB



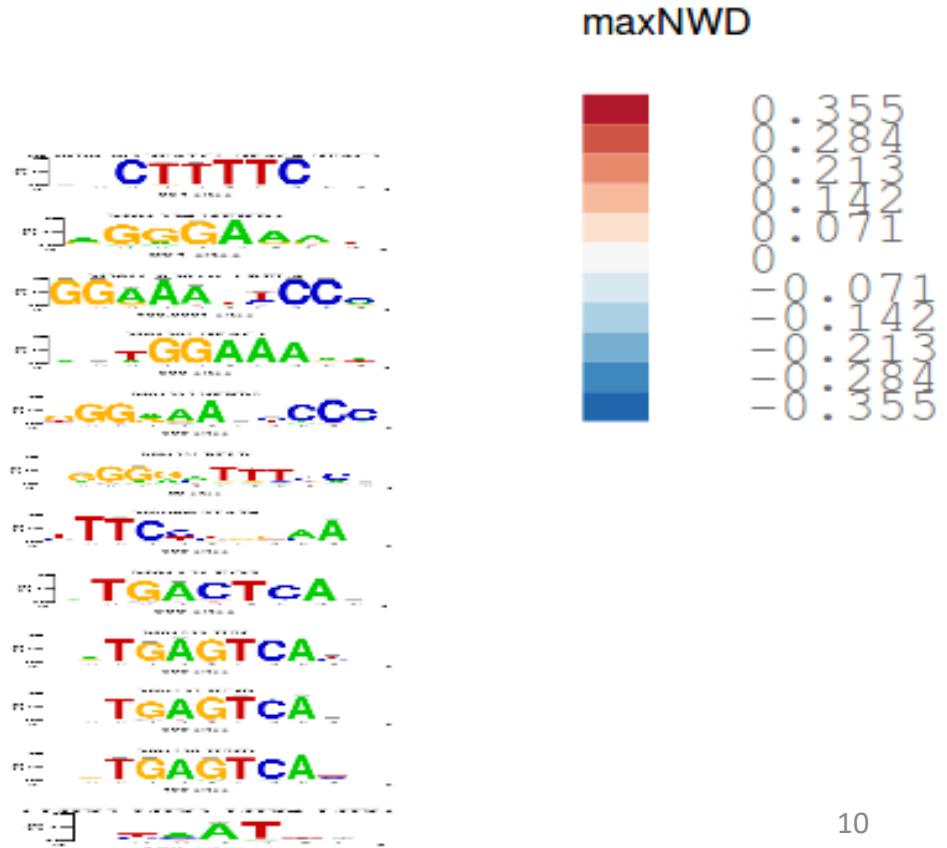
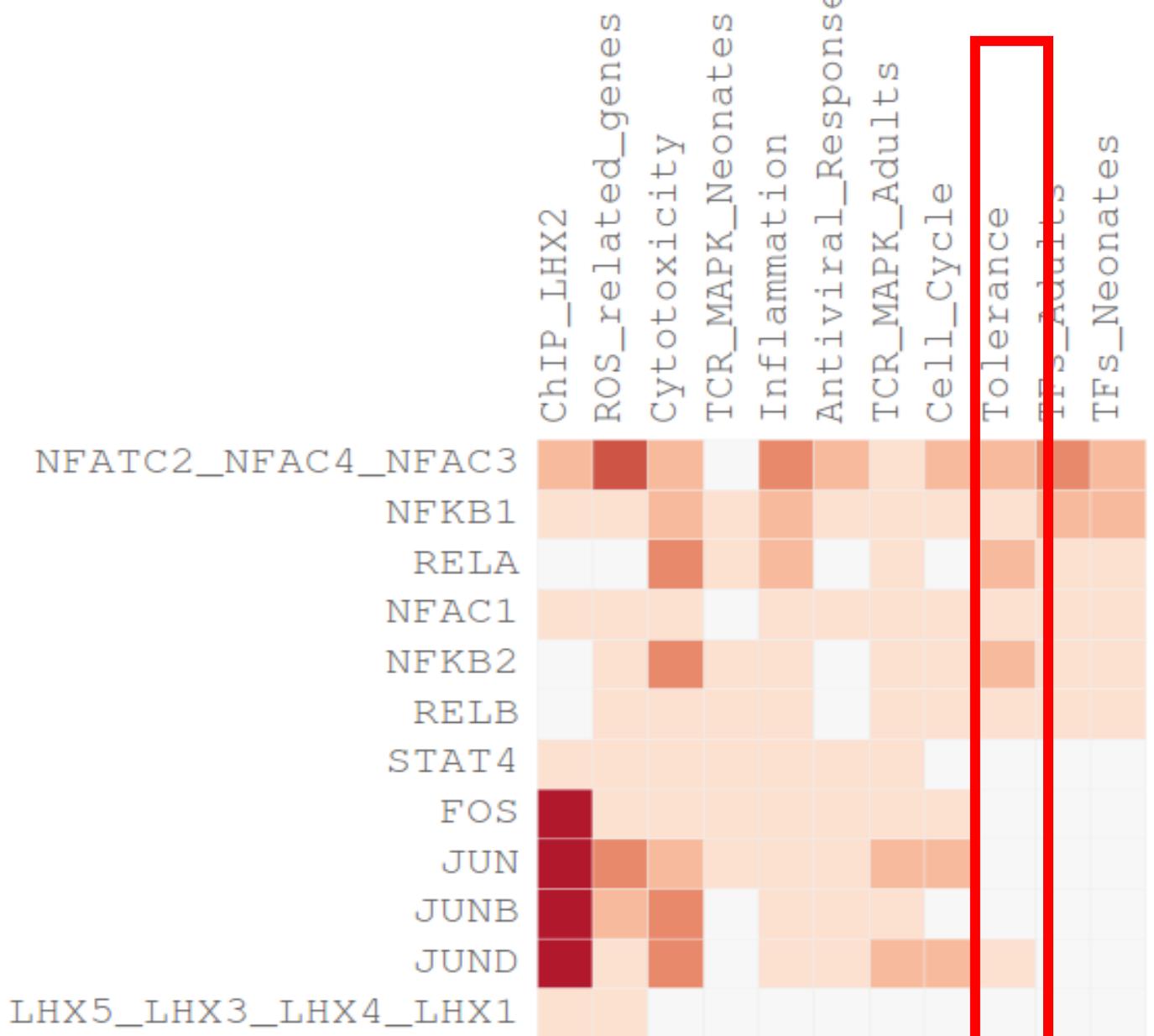
Promotor EBF1



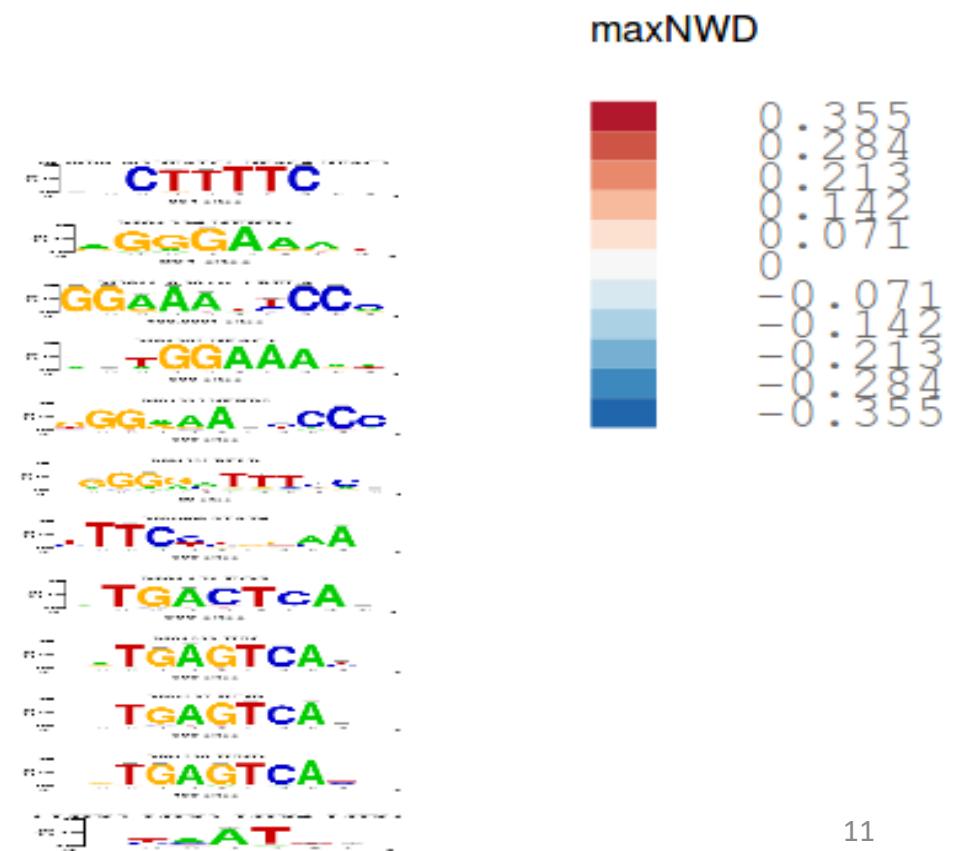
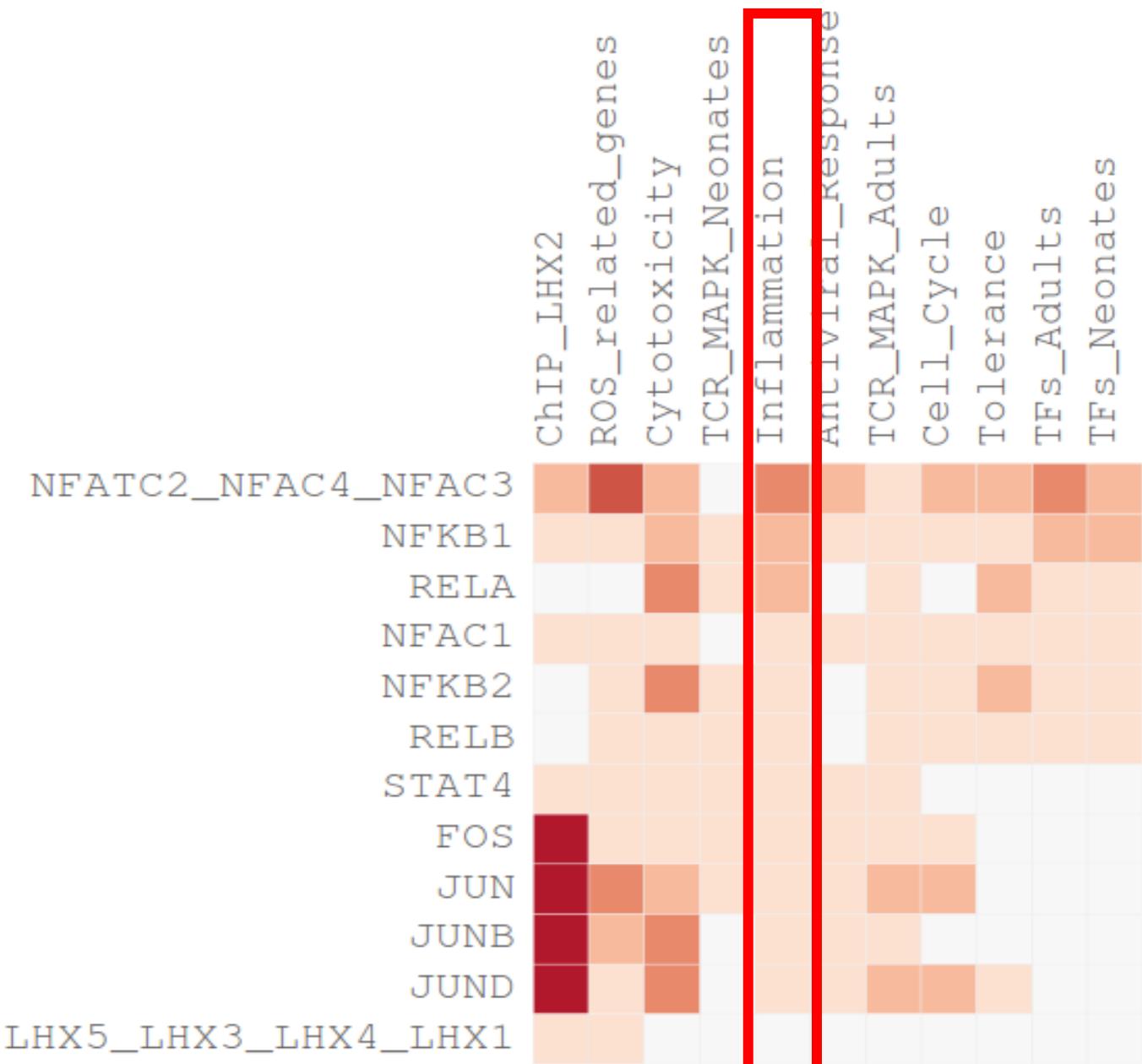
MATRIX_ENRICHMENT: Clusters



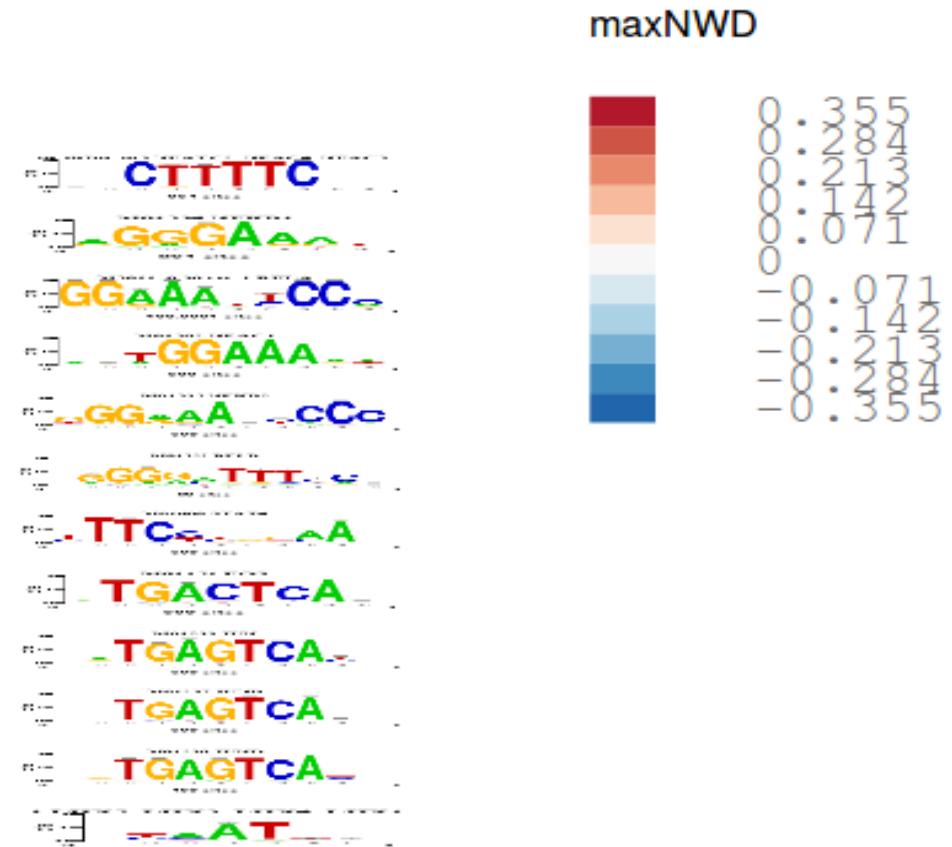
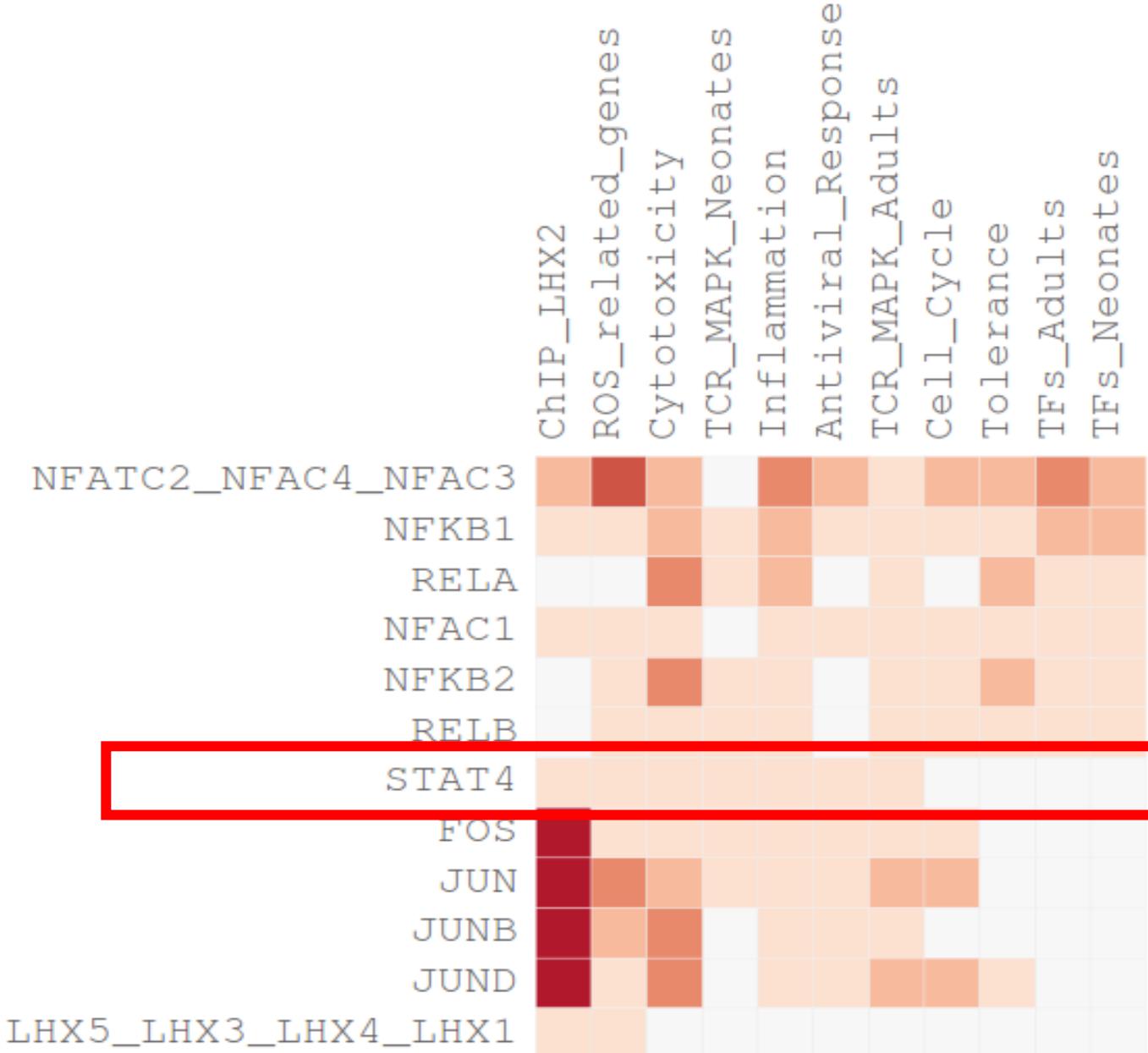
MATRIX_ENRICHMENT: Clusters



MATRIX_ENRICHMENT: Clusters



MATRIX_ENRICHMENT: Clusters

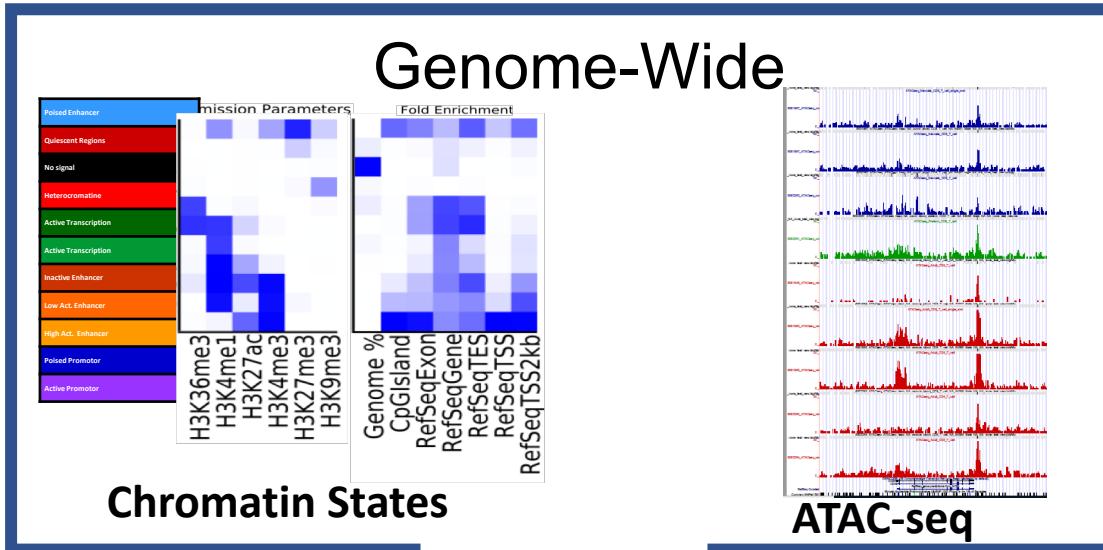


Perspectives

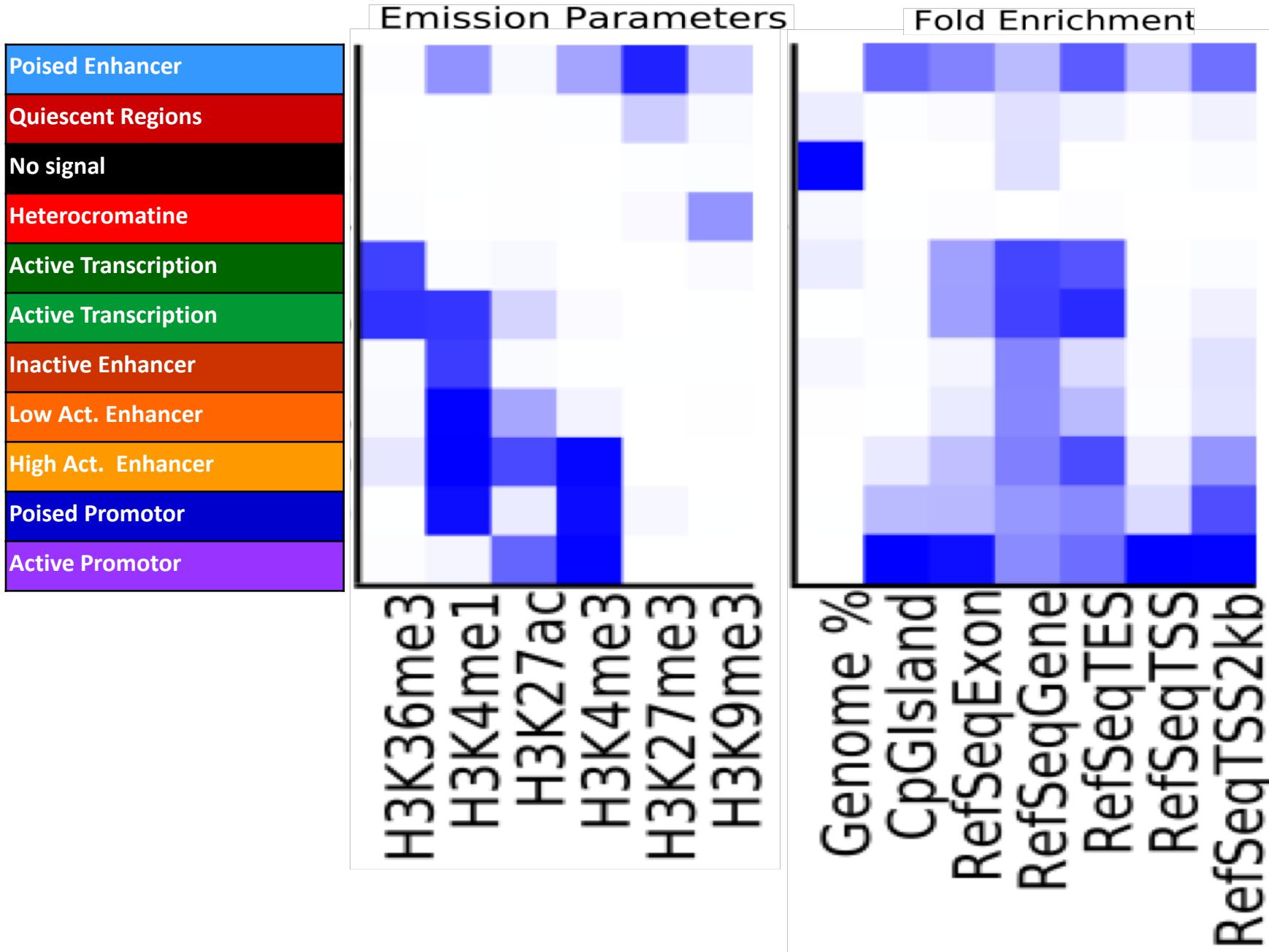
Transcriptome of UNSTIMULATED AND CD3/CD28/IL-12 stimulated cells from neonates and adults.

ChIP-seq histone modifications in UNSTIMULATED AND CD3/CD28/IL-12 stimulated cells from neonates and adults.

Genome-wide Analysis



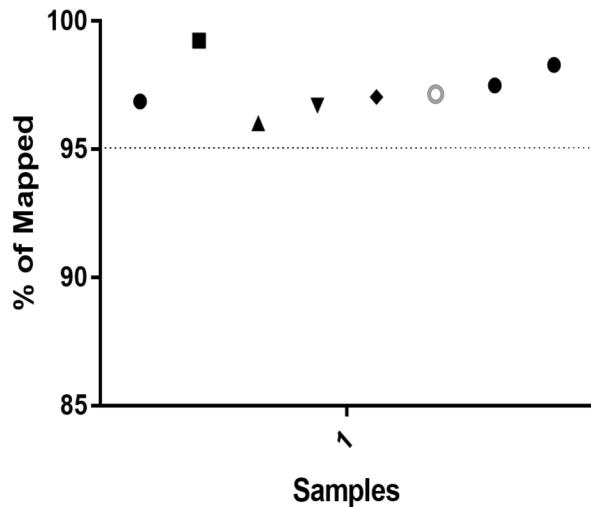
Chromatin States



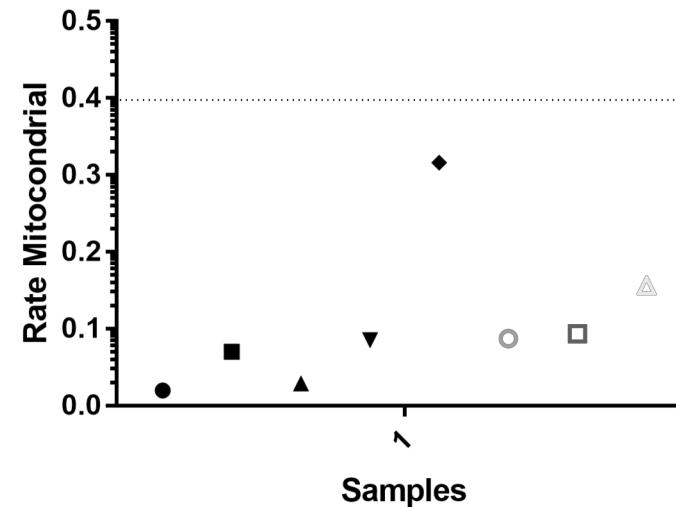
Quality Metrics

ATAC-seq

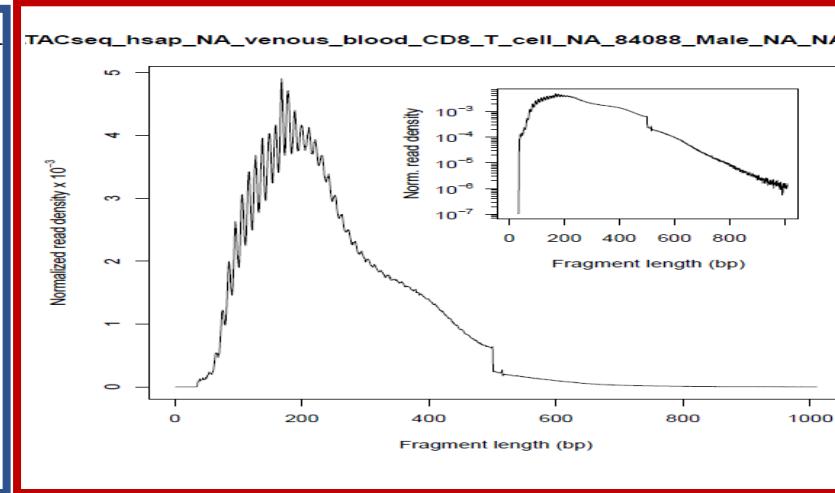
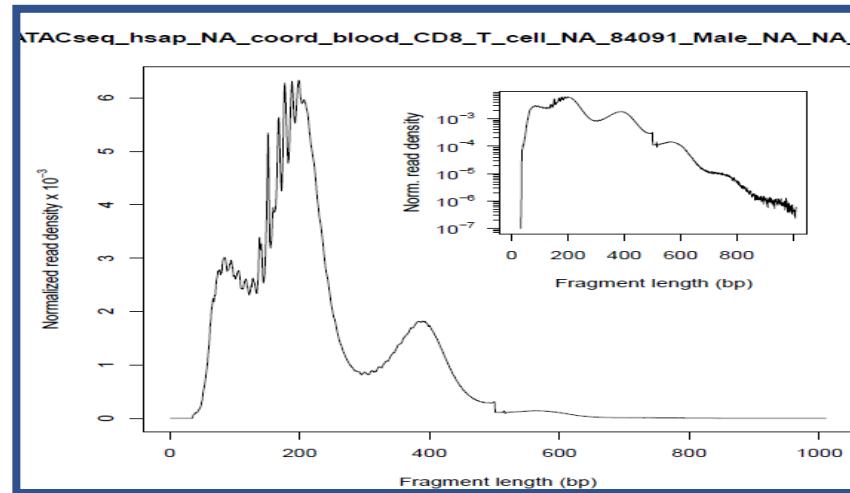
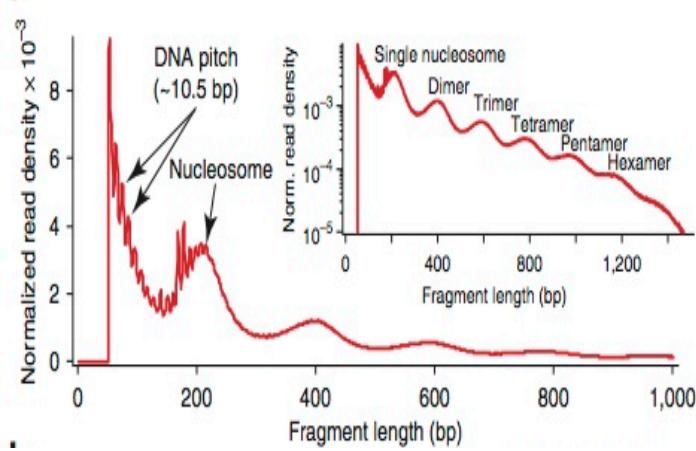
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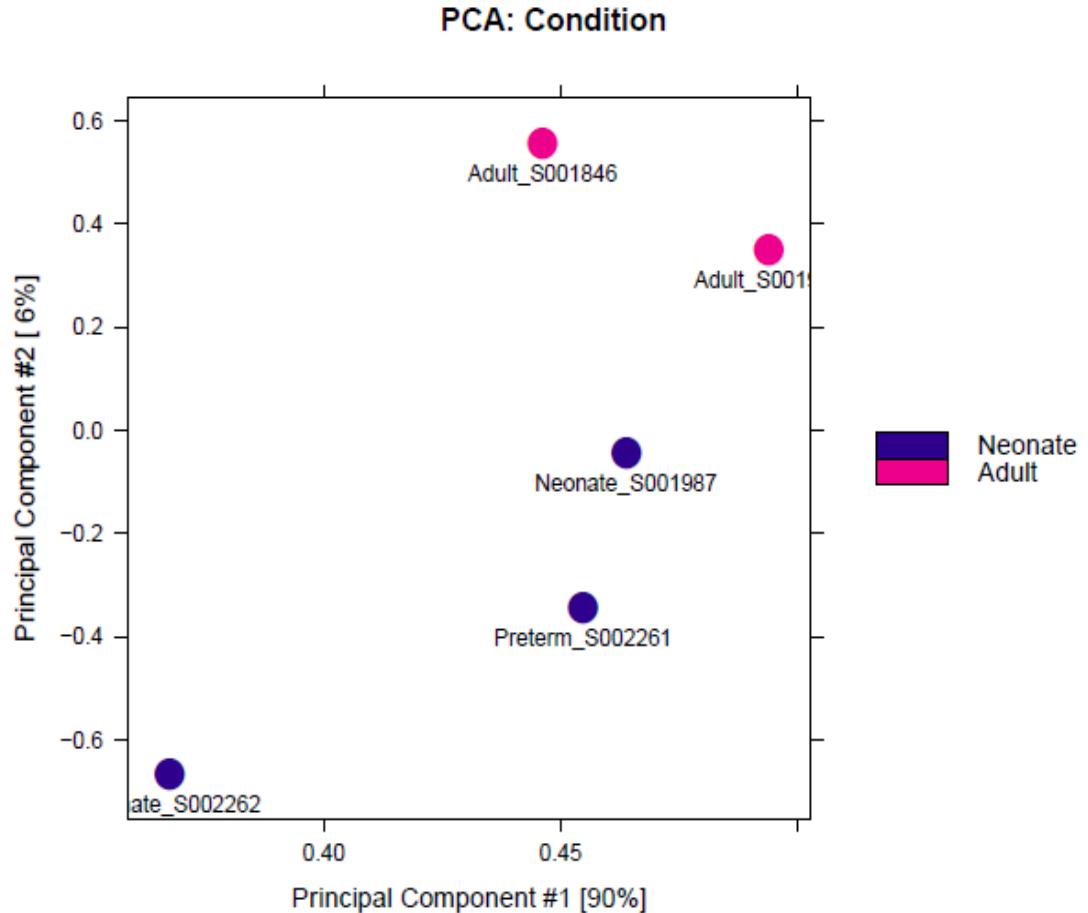
Rate Mitocondrial



a



ATAC-seq :PCA and VISUALIZATION

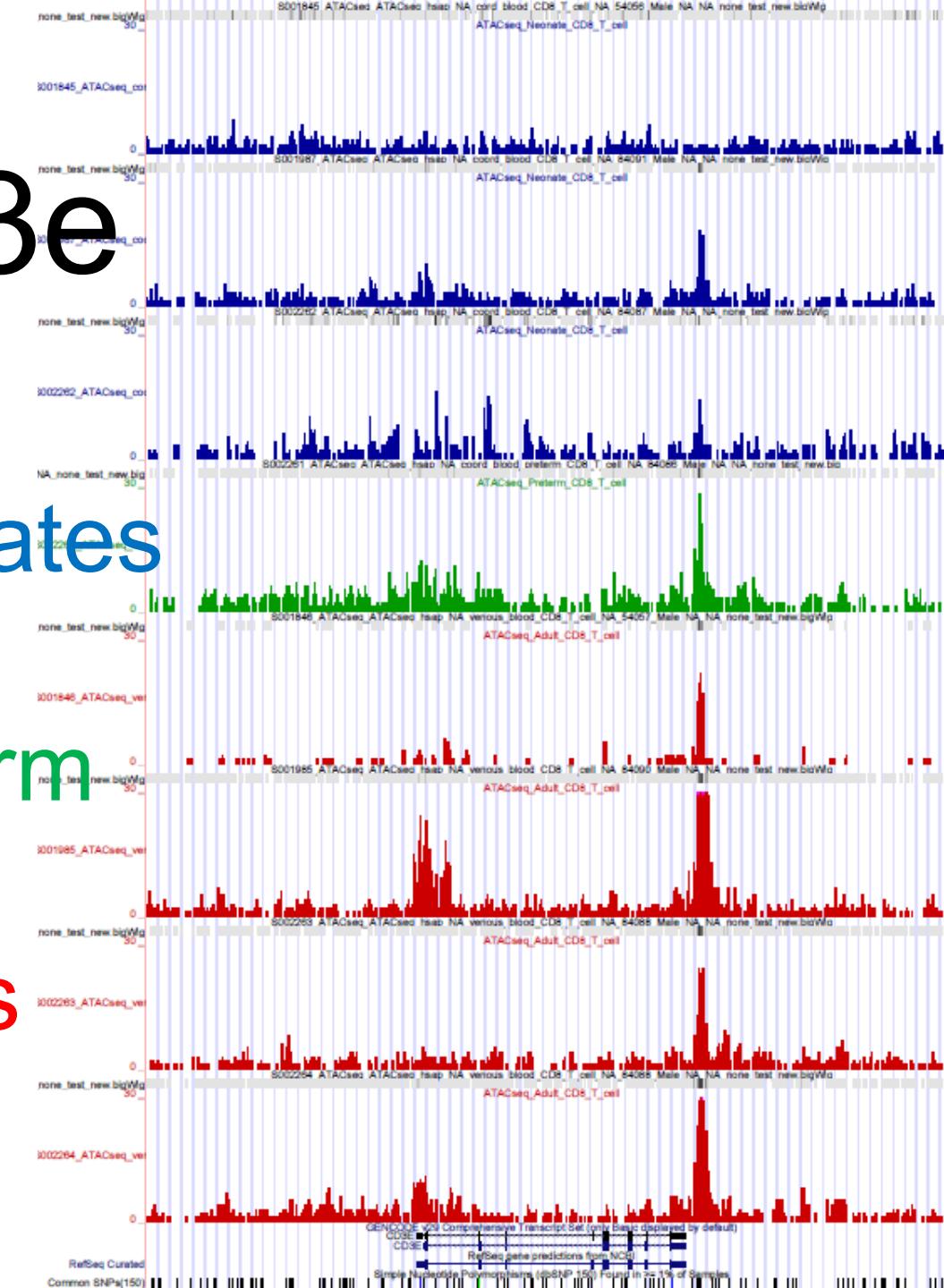


CD3e

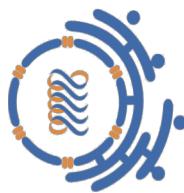
Neonates

Preterm

Adults



ACKNOWLEDGEMENT



Centro de
Investigación en
Dinámica Celular

Dra. Angelica Sanatana Calderón
Biol. Oscar Ramirez Pliego
Linda Aimara Kempis Calanis
Ximena Pacheco
Carlos Ventura



LIIGH-UNAM
INTERNATIONAL LABORATORY FOR
HUMAN GENOME RESEARCH

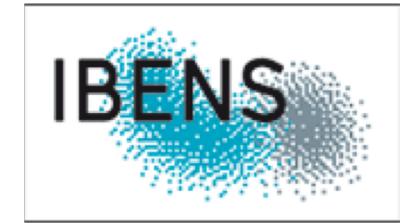
Dra. Alejandra Eugenia Medina
Karen Nuñez



LAVIS
Luis Aguilar
Jair Garcia

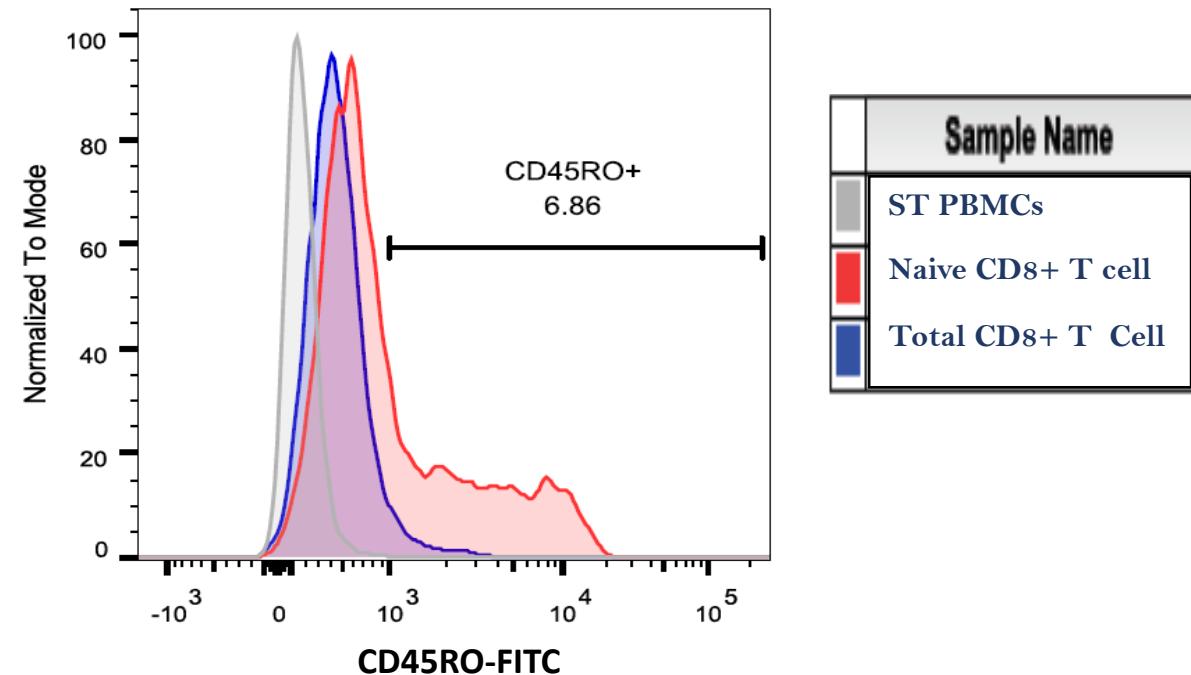
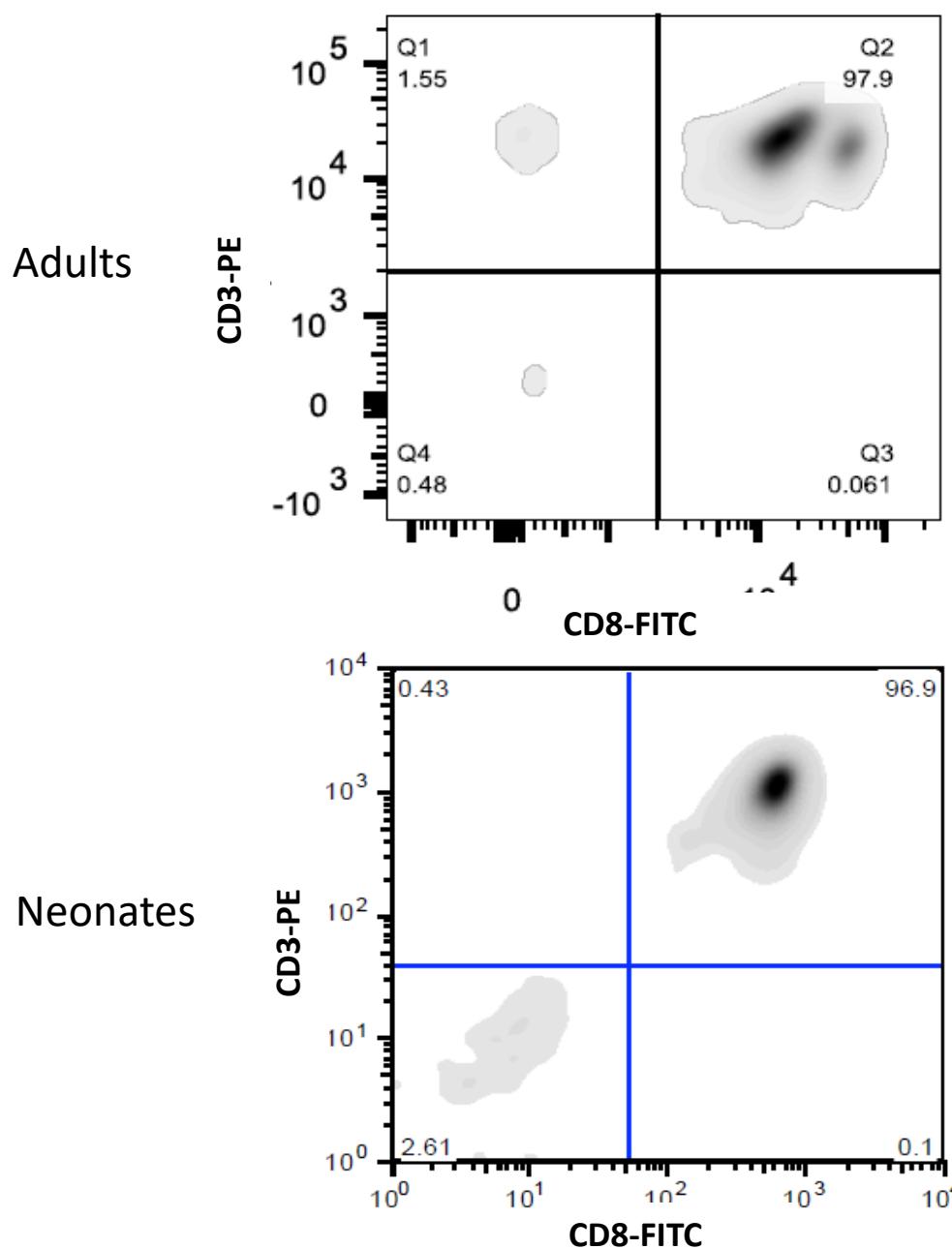


Dra. Morgane Thomas-Chollier
Dr. Denis Thieffry

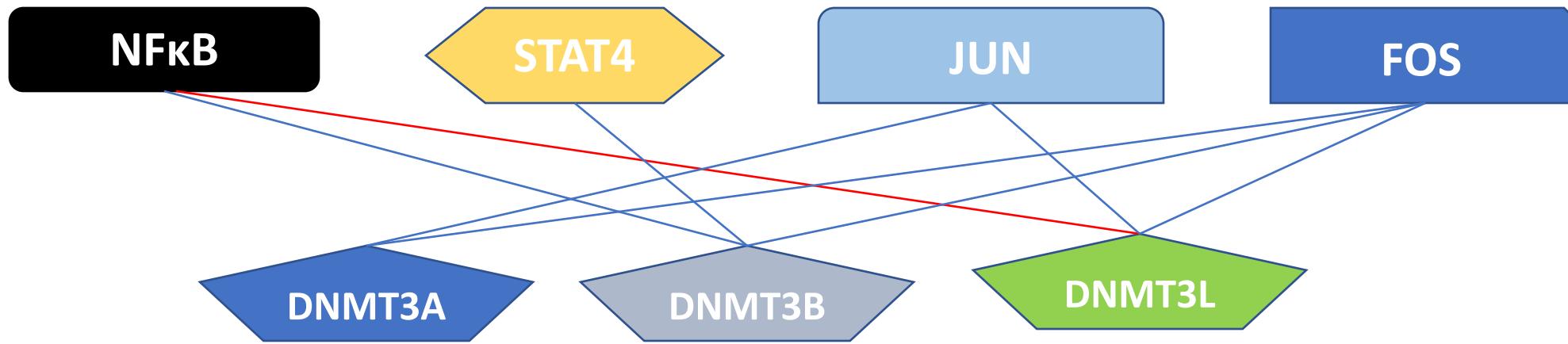


Dr. Salvatore Spicuglia

Figure. Cell purification

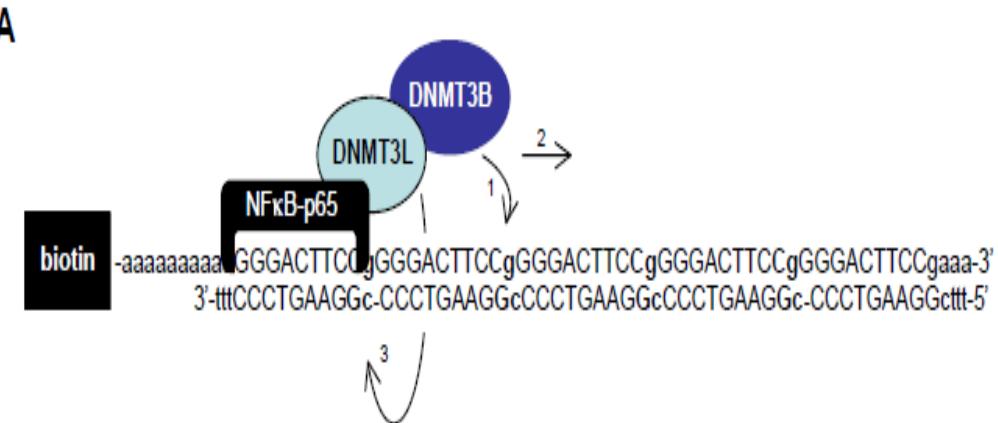


Factores Transcripcionales inducidos por la IL-12 y el TCR interactúan con DNMTs

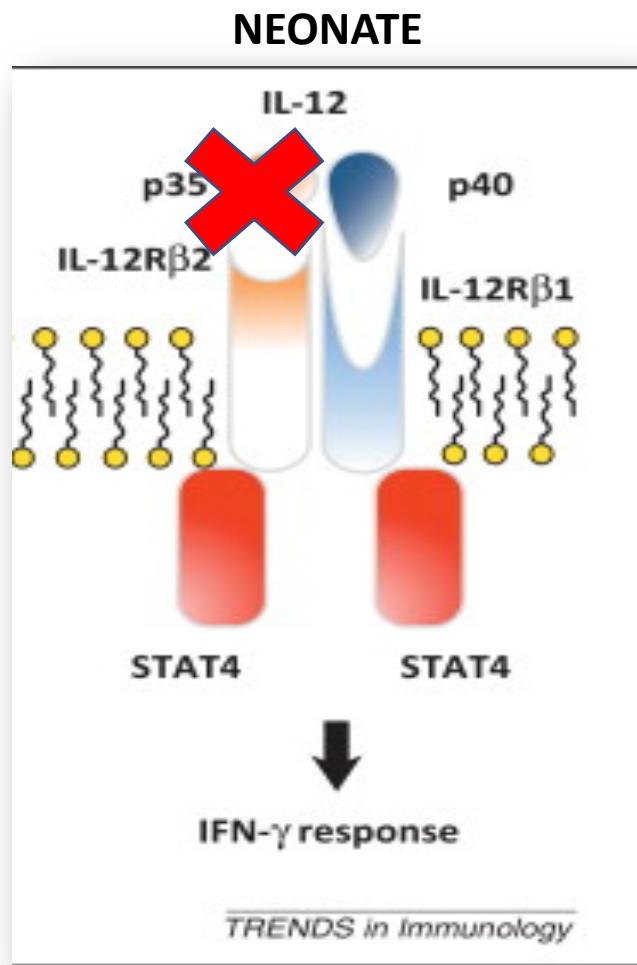


DNMT3L participa en la metilación de *novo*

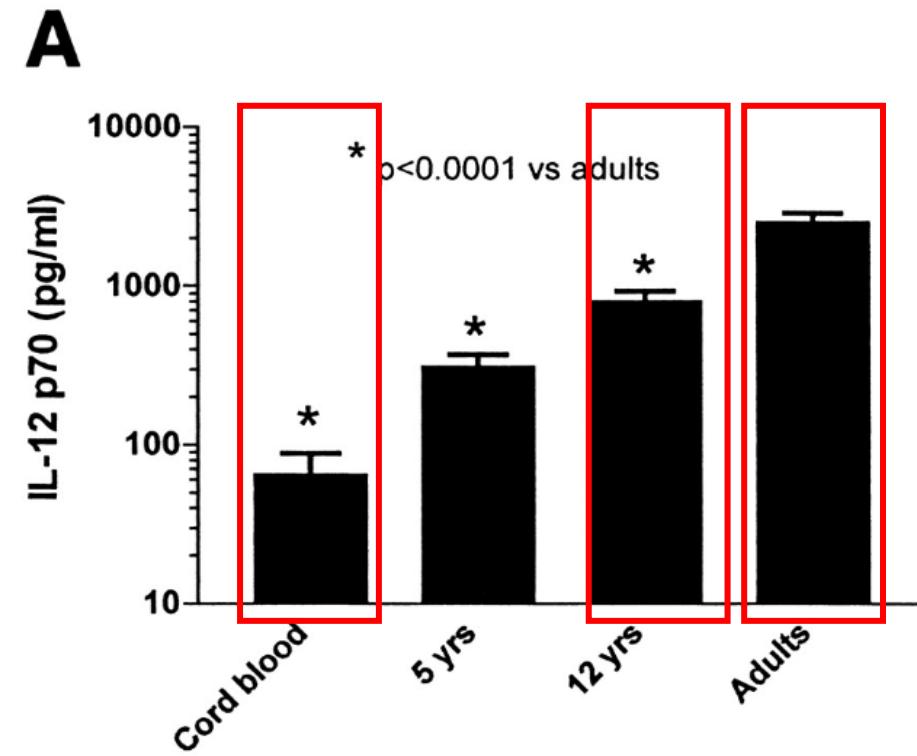
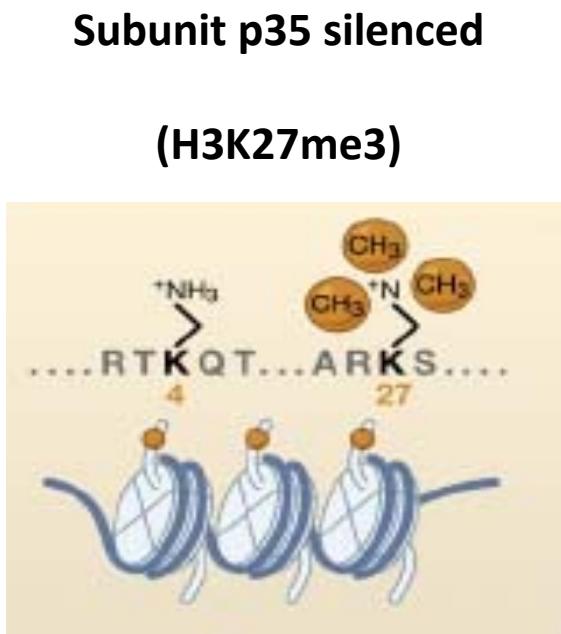
TRAF1 metilación



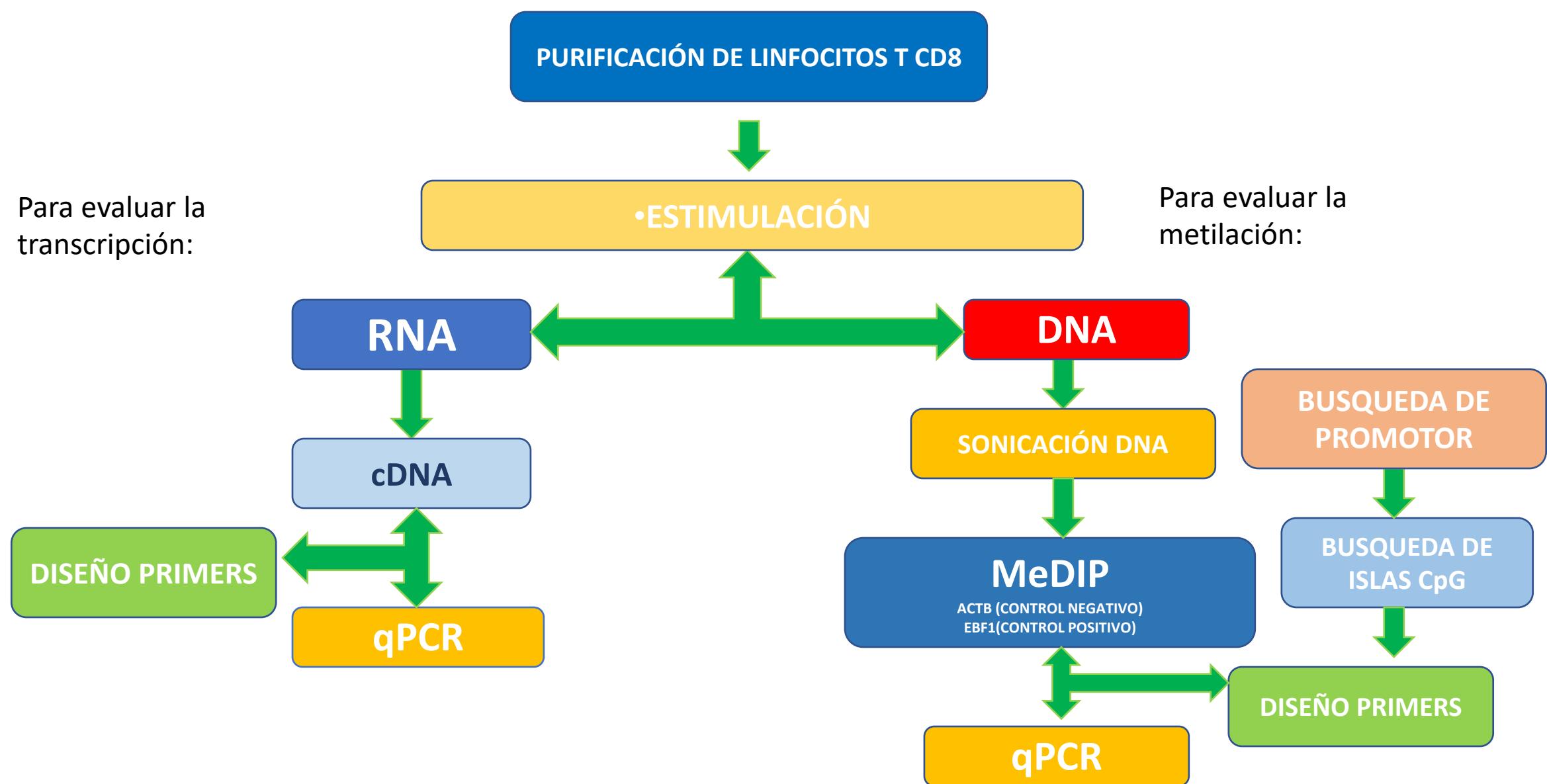
Background



Low production of IL-12 in Neonates

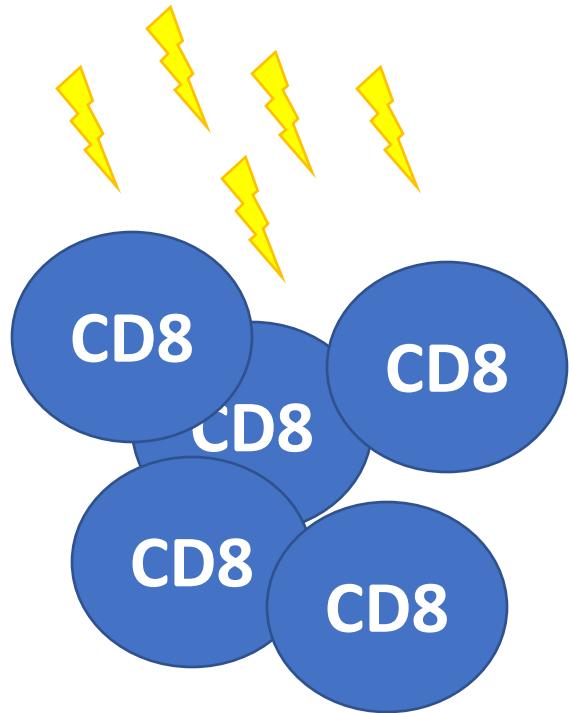


METODOLOGÍA

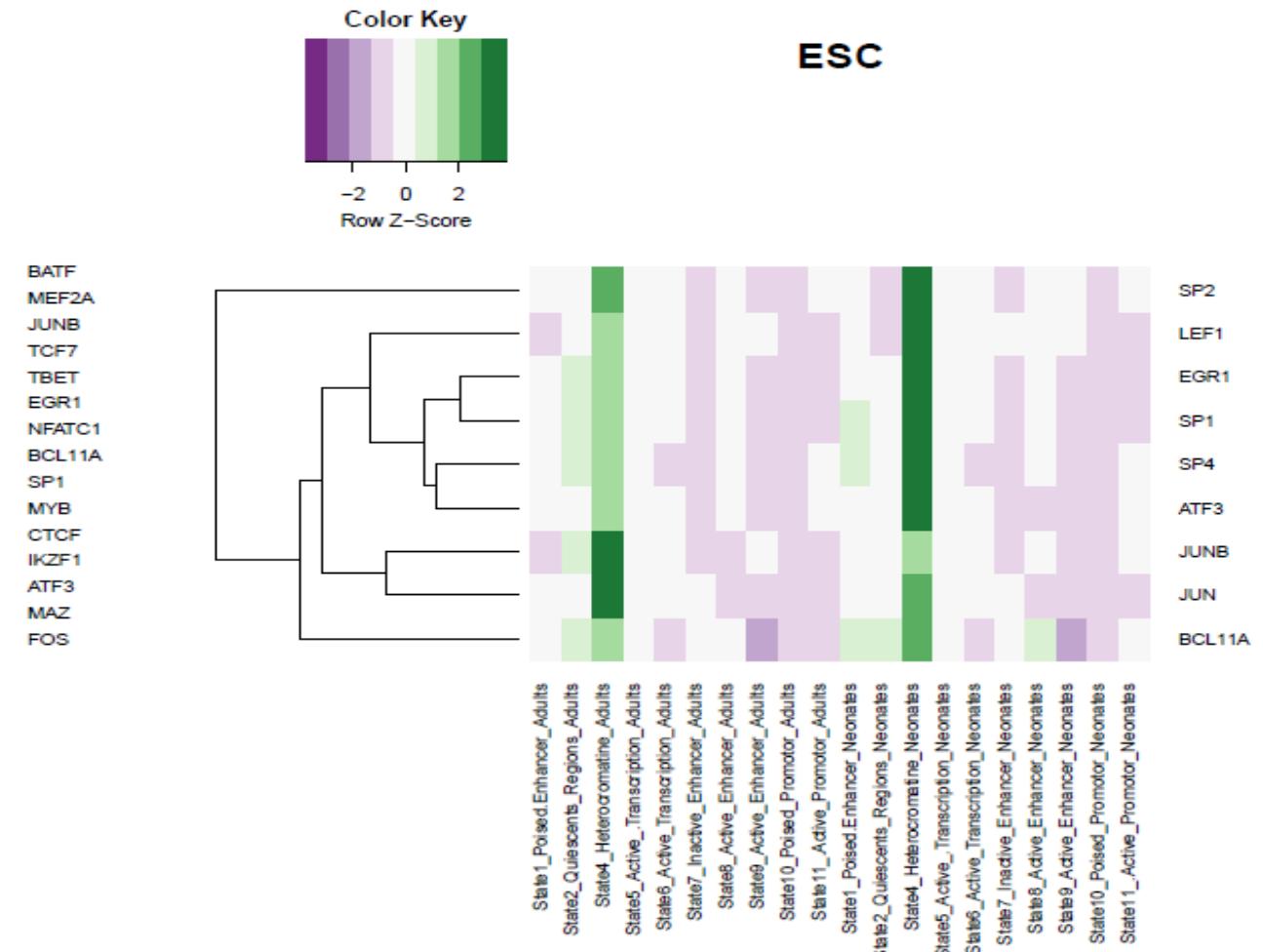
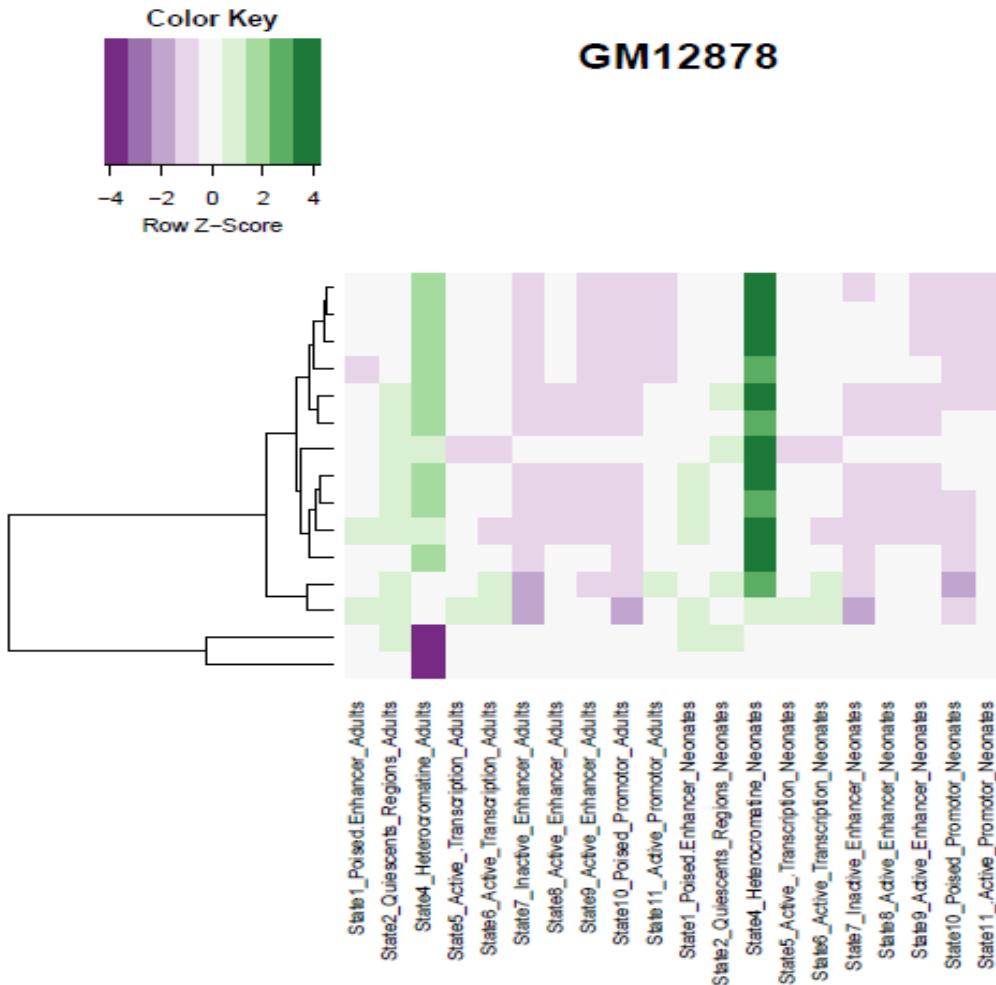


ESTIMULACIONES

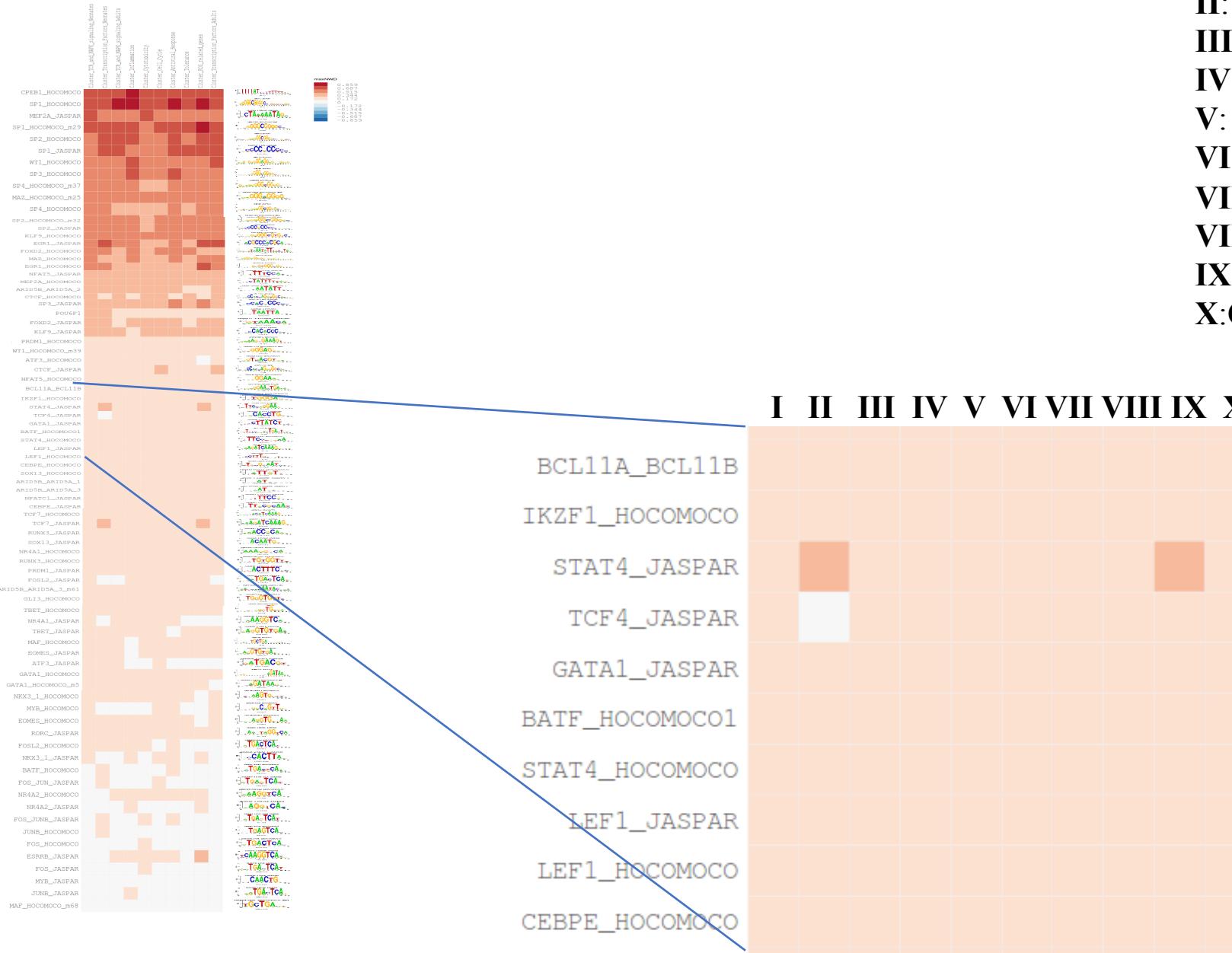
36 Horas



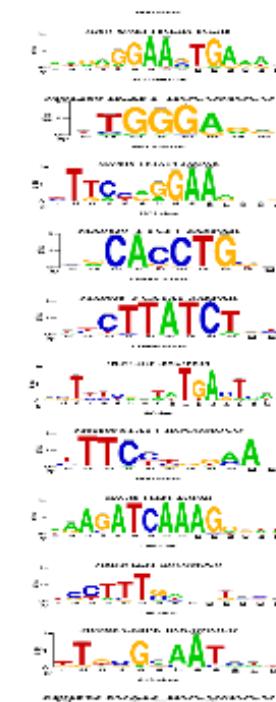
GAT:Overlap ChIP-seq and Chromatin States/ATAC-seq



RSAT:Matrix-enrichment



- I: Cluster TCR and MAPK signaling Neonates
- III: Cluster Transcription Factors Neonates
- III: Cluster TCR and MAPK signaling Adults
- IV: Cluster Inflammation
- V: Cluster Cytotoxicity
- VI: Cluster Cell Cycle
- VII: Cluster Antiviral Response
- VIII: Cluster Tolerance
- IX: Cluster ROS related genes
- X: Cluster Transcription Factors Adults



MATRIX_ENRICHMENT: SEQUENCE NEGATIVE CONTROL

