

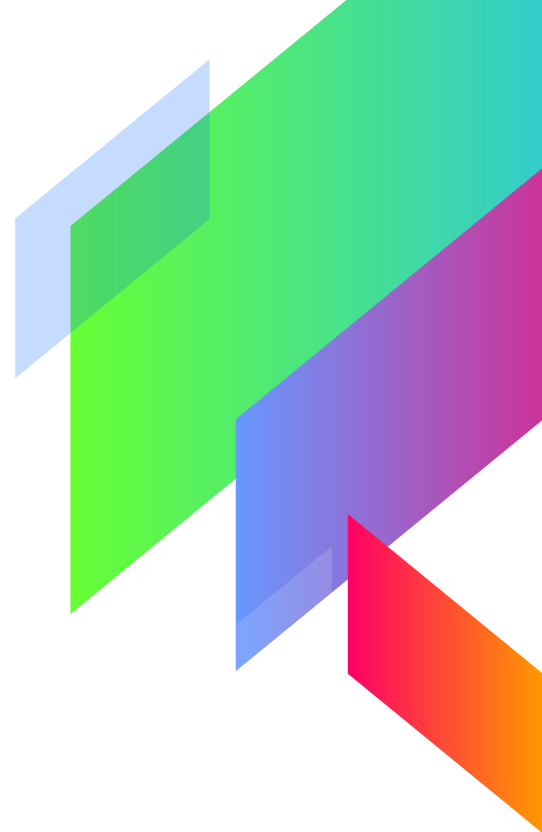
Exploring the Blueprint data

Luigi Grassi

Cambridge 02/06/2017

Abstract geometric shapes in the top-left corner, including a green parallelogram, a light blue parallelogram, a brown parallelogram, and a large purple parallelogram.

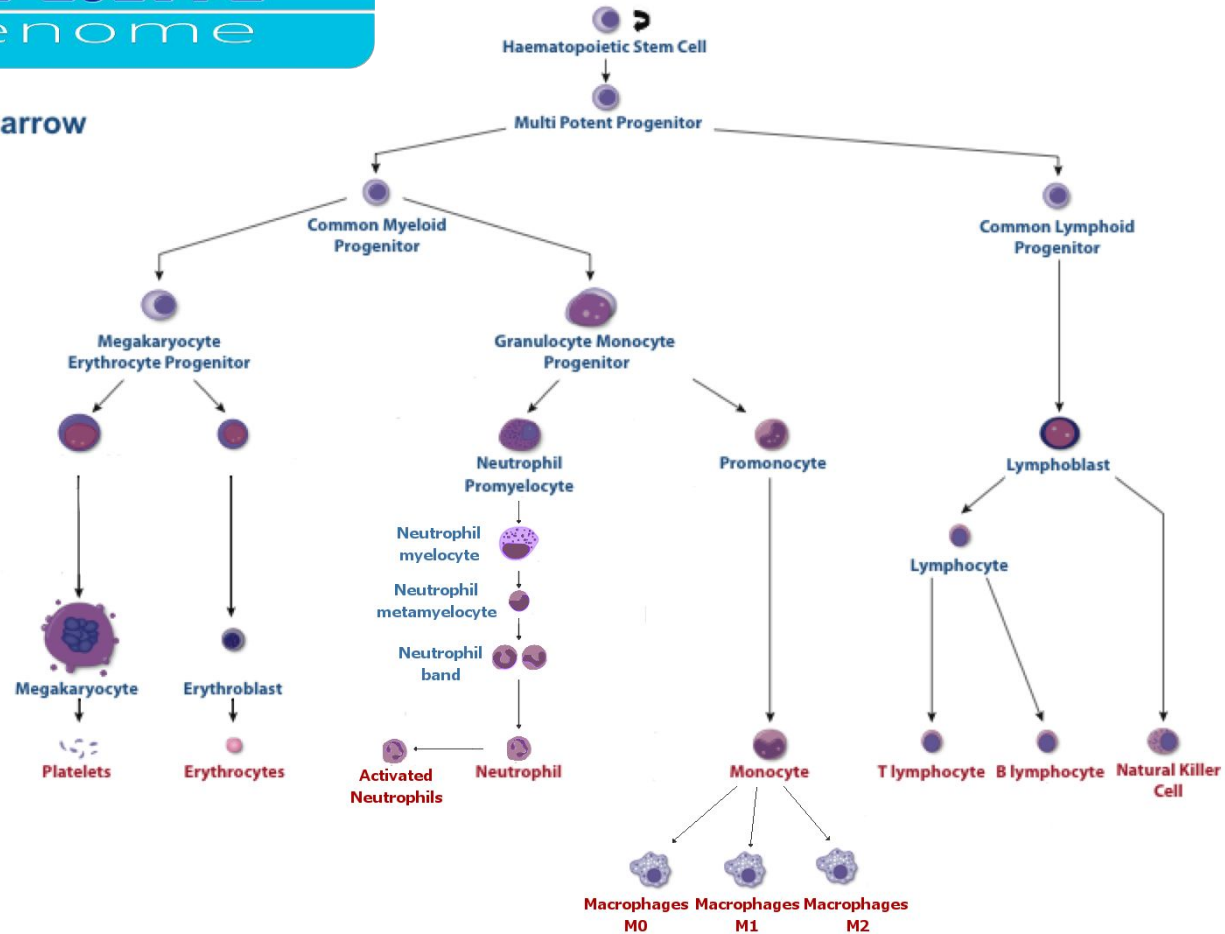
The RNA Blood Atlas



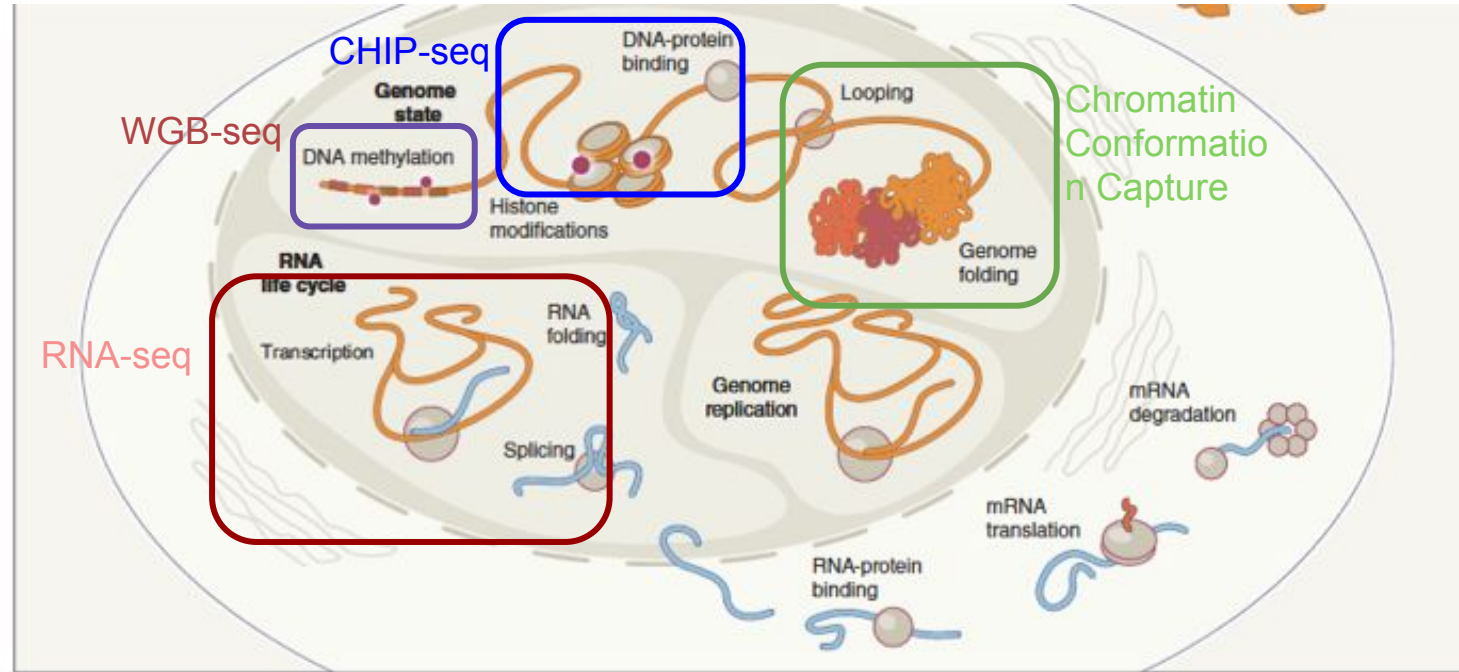
Bone marrow

Blood

Tissue



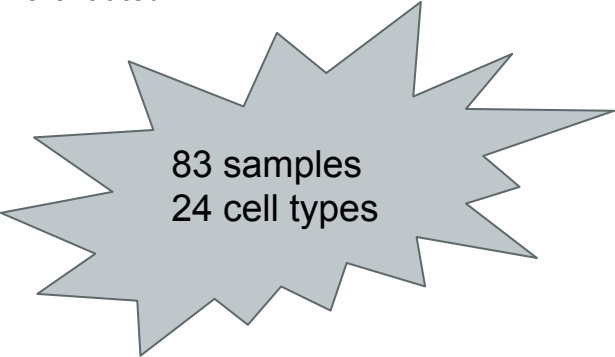
The Strategy



Shendure J. et al., Nat Biotechnol. 2012 Nov;30(11):1084-94

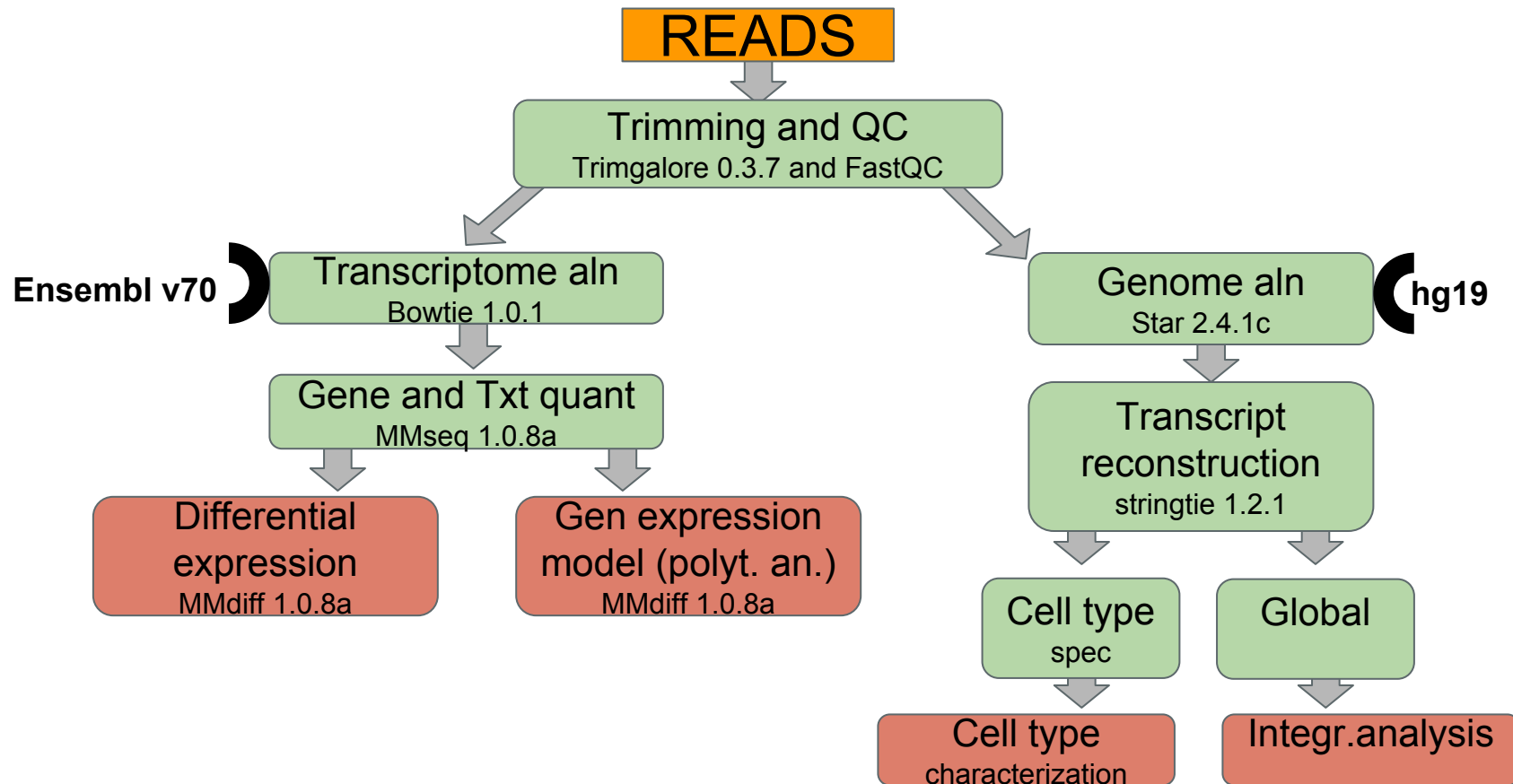
The dataset

Adult endothelial progenitor cell 2
Alternatively activated macrophage 7
CD14-positive, CD16-negative classical monocyte 8
CD34-negative, CD41-positive, CD42-positive megakaryocyte cell 3
CD38-negative naive B cell 3
CD4-positive, alpha-beta T cell 10
CD8-positive, alpha-beta T cell 2
central memory CD4-positive, alpha-beta T cell 2
central memory CD8-positive, alpha-beta T cell 1
class switched memory B cell 1
conventional dendritic cell 2
cytotoxic CD56-dim natural killer cell 4
effector memory CD4-positive, alpha-beta T cell 2
effector memory CD8-positive, alpha-beta T cell 2
effector memory CD8-positive, alpha-beta T cell, terminally differentiated 1
endothelial cell of umbilical vein (proliferating) 2
endothelial cell of umbilical vein (resting) 2
Erythroblast 2
inflammatory macrophage 6
Macrophage 6
Mature neutrophil 11
Memory B cell 1
Mesenchymal stem cell of the bone marrow 2



83 samples
24 cell types

The pipeline



Heatmap visualization showing gene expression profiles across various cell lines and tissues. The color scale ranges from 0.0 (blue) to 1.0 (red). The x-axis is labeled 'Tissue Type' and the y-axis is labeled 'Cell Line'. The heatmap shows a clear pattern of high expression (red) for certain cell lines and tissues, particularly in the top-left and bottom-right corners. The color scale is indicated by a vertical bar on the right side of the heatmap.

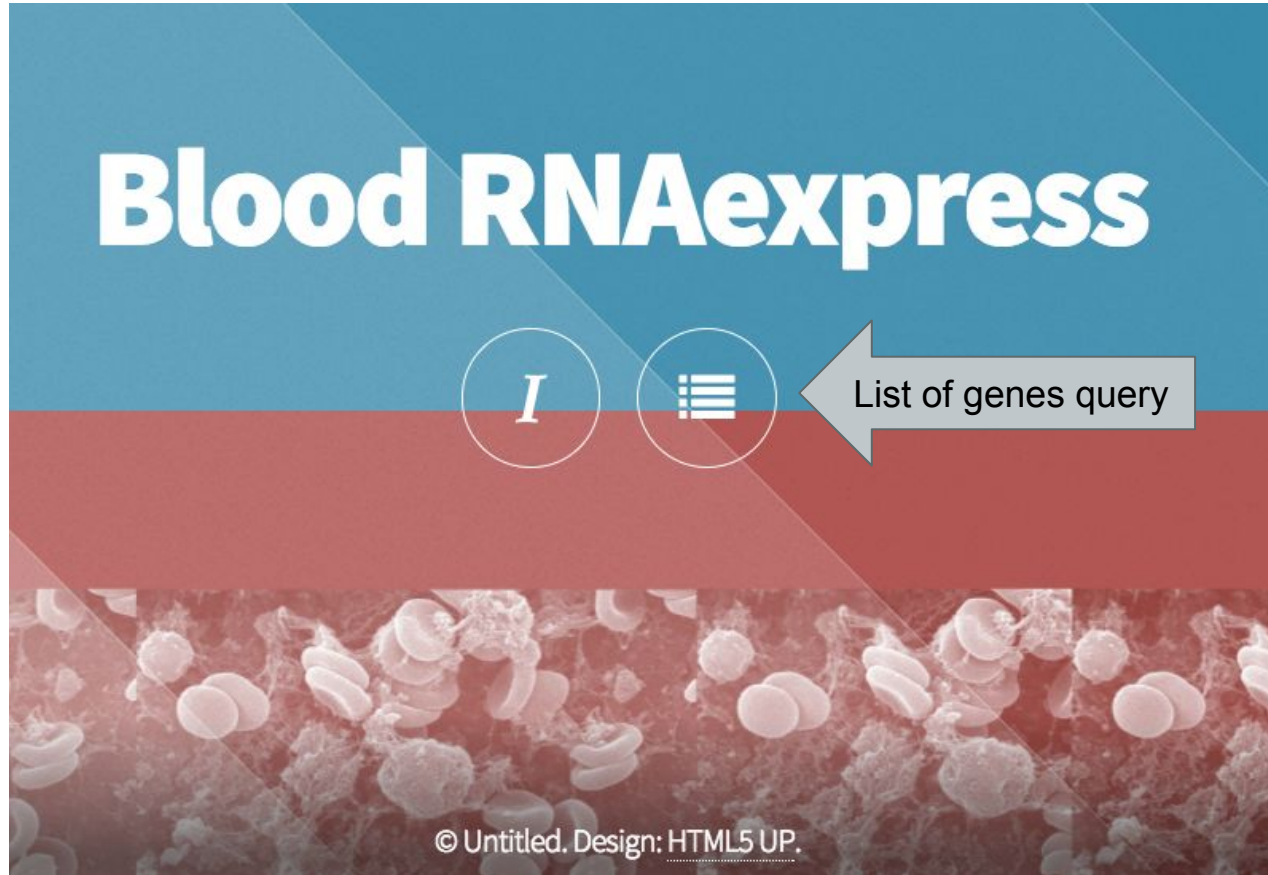
Exploring the RNA-Seq results



Exploring the RNA-Seq results



Exploring the RNA-Seq results



RNA-Seq results (next step)

Integration of

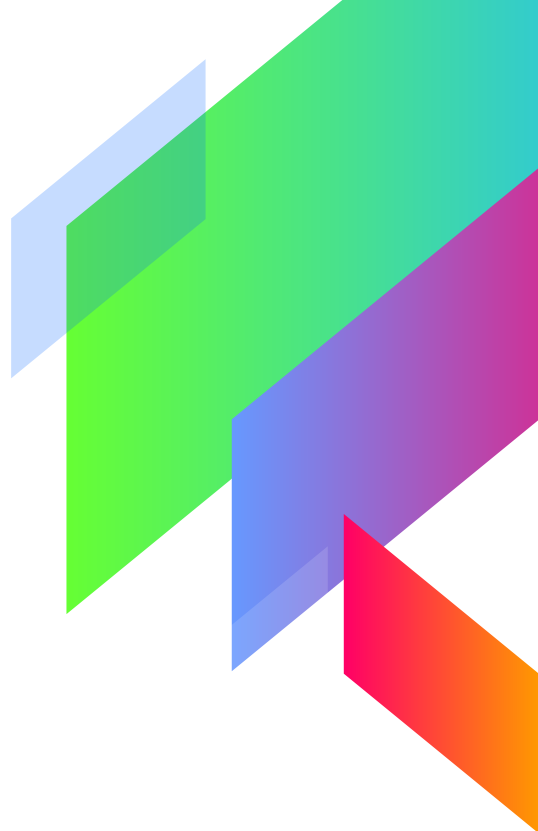
- 1) microRNA expression results;
- 2) polytomous analysis and expression models;
- 3) expression similarity.

Exploring the RNA-Seq results

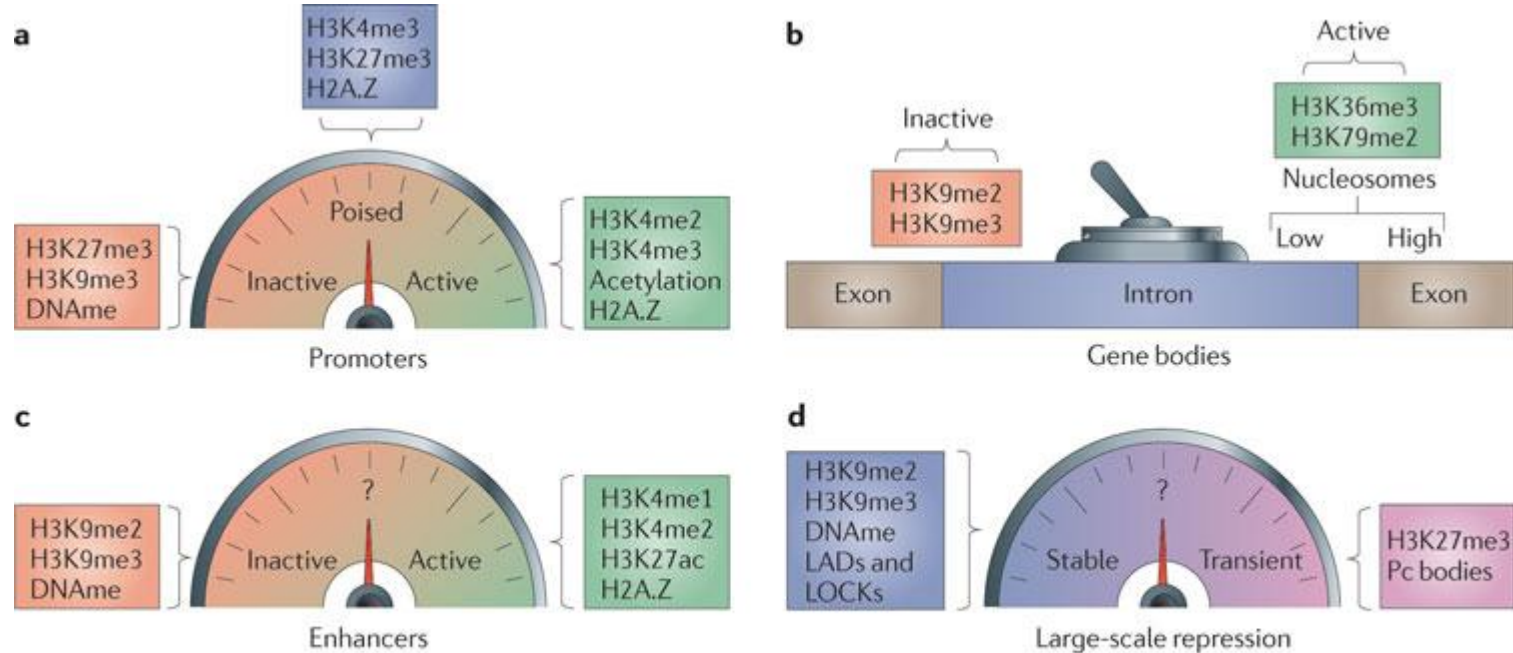
<https://blueprint.haem.cam.ac.uk/bloodatlas>

Abstract geometric shapes in the bottom left corner, including a green triangle, a blue parallelogram, a brown trapezoid, a red parallelogram, and a purple parallelogram.

Epigenomic landscapes

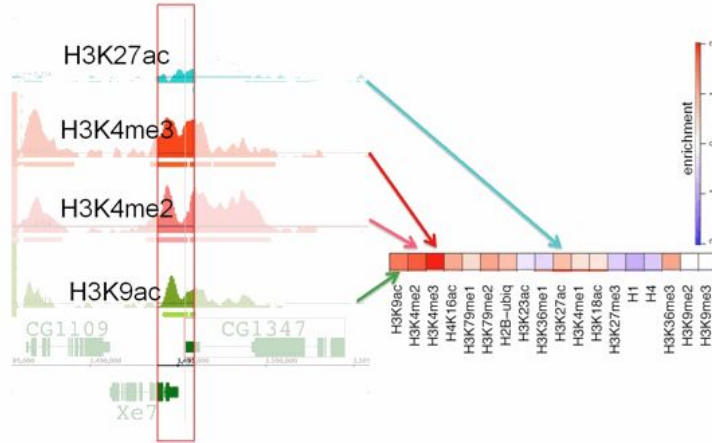
Abstract geometric shapes in the bottom right corner, including a green parallelogram, a blue parallelogram, a purple parallelogram, and a red parallelogram.

Chromatin states of MKs and EBs

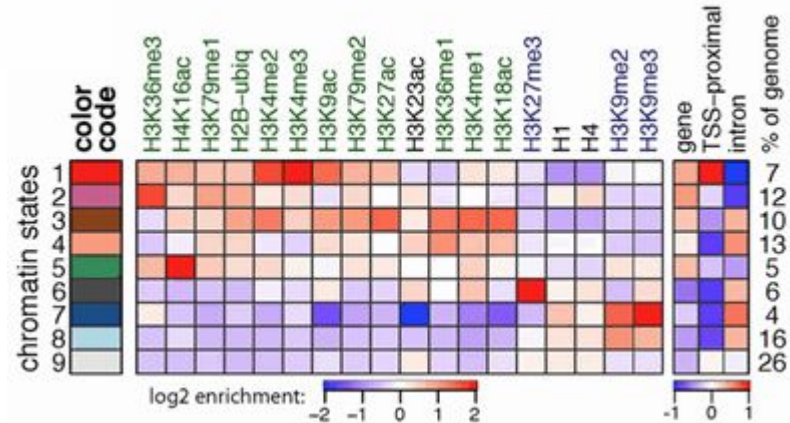


Vicky W. Zhou, Alon Goren & Bradley E. Bernstein
Nature Reviews Genetics **12**, 7-18 (January 2011)

Chromatin states of MKs and EBs



<http://modencode.sciencemag.org/>



Chromatin states

Epigenome/Erythroblasts/EB_IDEAS_genome_segmentation.bed

Epigenome/Megakaryocytes/MK_IDEAS_genome_segmentation.bed

Epigenome/endothelial_cell_proliferating_S00DCSH1/S00DCSH1_12_Blueprint_release_012015_dense.bed

Epigenome/mature_neutrophil_C004GDH1/C004GDH1_12_Blueprint_release_012015_dense.bed

Epigenome/alternatively_activated_macrophage_S00622H1/S00622H1_12_Blueprint_release_012015_dense.bed

Epigenome/CD4_Tcell_S007DDH2/S007DDH2_12_Blueprint_release_012015_dense.bed

Epigenome/CD8_Tcell_C002YMH1/C002YMH1_12_Blueprint_release_012015_dense.bed

Chromatin states

State1 - Repressed Polycomb High signal H3K27me3

State2 - Repressed Polycomb Low signal H3K27me3

State3 - Low signal

State4 - Heterochromatin High Signal H3K9me3

State5 - Transcription High signal H3K36me3

State6 - Transcription Low signal H3K36me3

State7 - Genic Enhancer High Signal H3K4me1 & H3K36me3

State8 - Enhancer High Signal H3K4me1

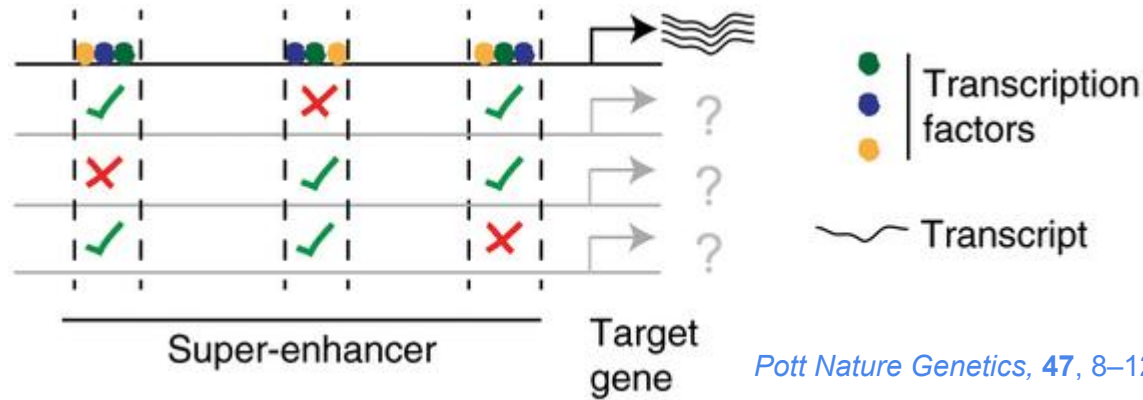
State9 - Active Enhancer High Signal H3K4me1 & H3K27Ac

State10 - Distal Active Promoter (2Kb) High Signal H3K4me3 & H3K27Ac & H3K4me1

State11 - Active TSS High Signal H3K4me3 & H3K4me1

State12 - Active TSS High Signal H3K4me3 & H3K27Ac

Enhancer and SUPER enhancer

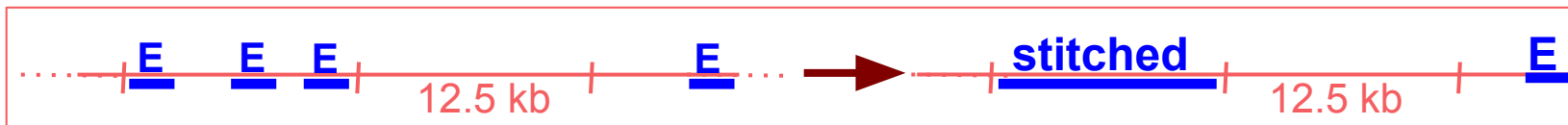


Pott Nature Genetics, 47, 8–12 (2015)

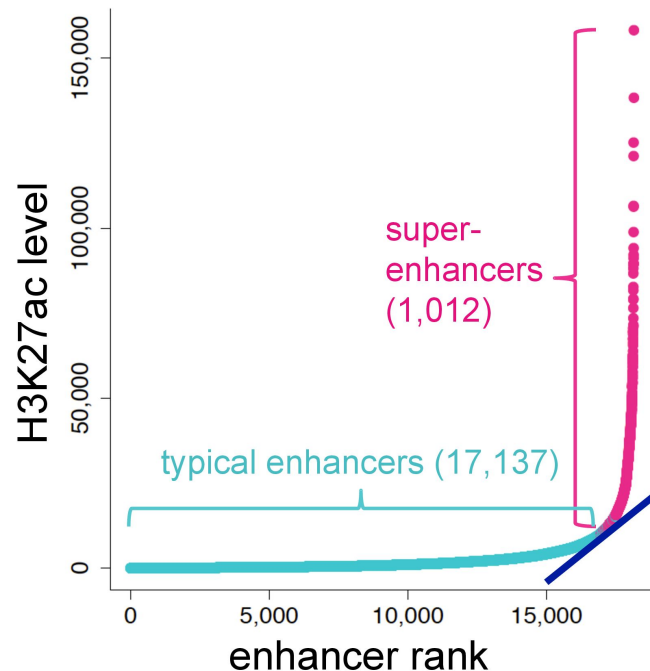
Play an important role for cell identity specification:

- 1) a high density of enhancers (high number/small distance)
- 2) high levels of H3K27ac (active promoters/enhancers)
- 3) extensive binding of Mediator
- 4) high transcription factor occupancy

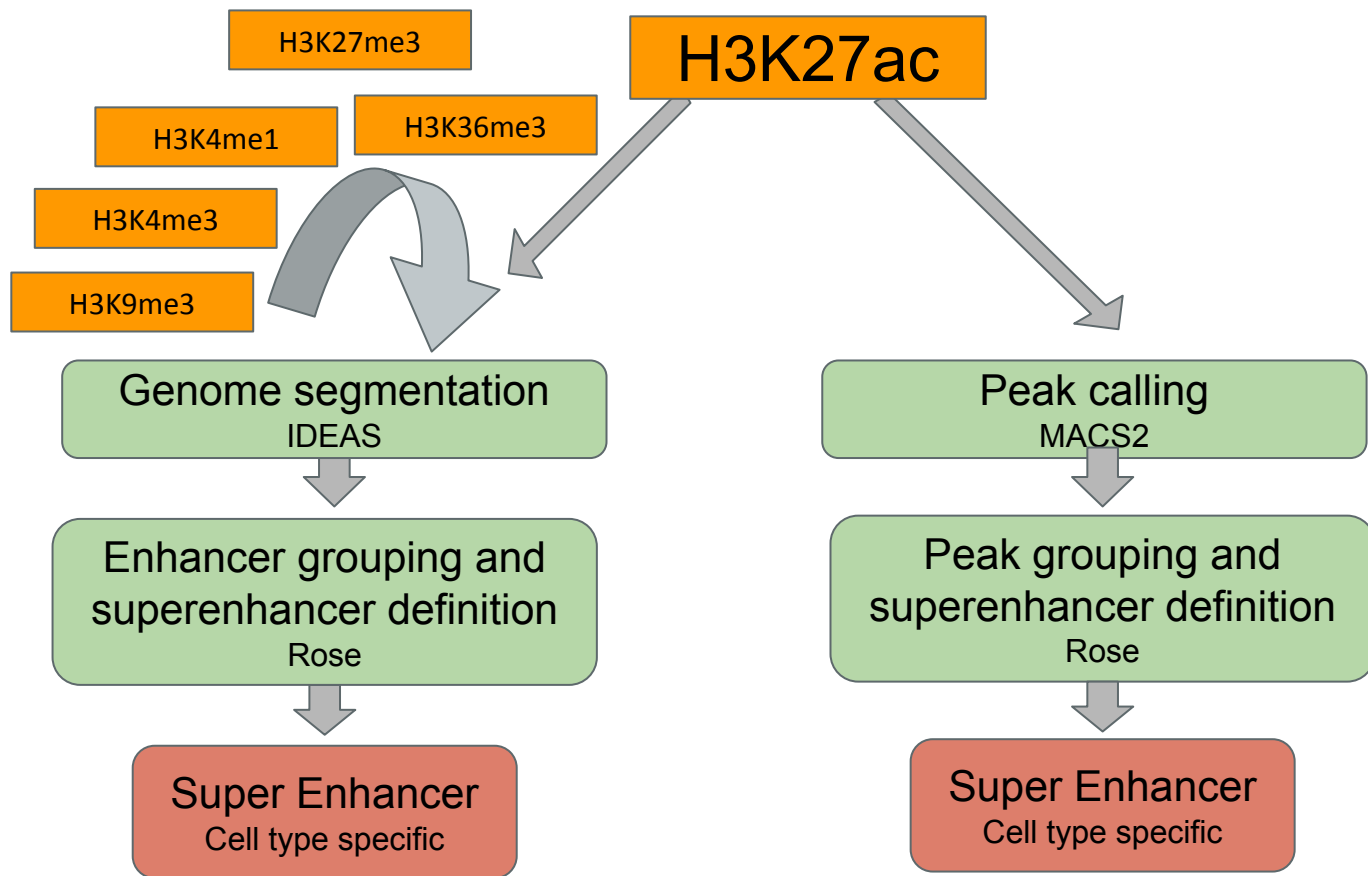
Defining SUPERenhancers



- 1) stitch enhancer distant less than 12.5 kb
- 2) Count H3K27ac signal in the stitched and unstitched regions
- 3) rank regions by H3K27ac signal
- 4) fit tangent with slope 1
- 5) ROSE algorithm (Whyte et al 2013)



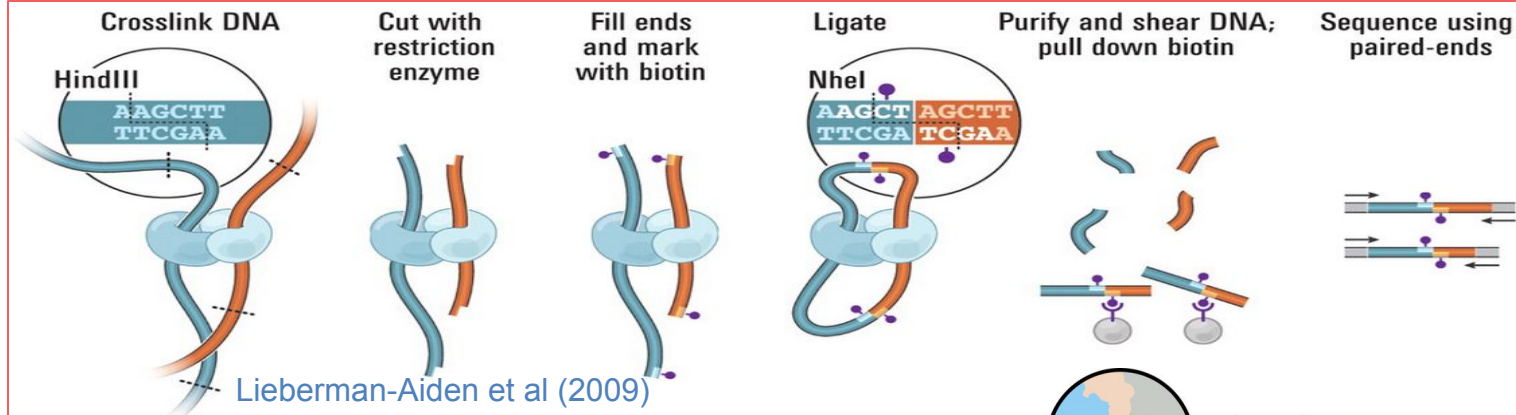
The pipeline



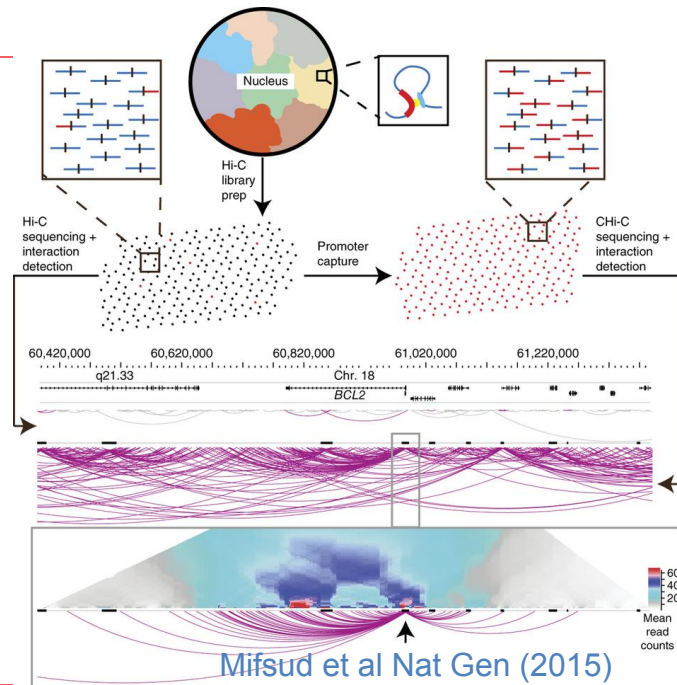
Superenhancers of MKs and EBs

Epigenome/Erythroblasts/2016-01-08-unstitched_EBs_strong_enhancers_IDEAS_minusP1000_collapsed_2_Gateway_SuperEnhancers.bed

Epigenome/Megakaryocytes/2016-01-08-unstitched_MKs_strong_enhancers_IDEAS__minusP1000_collapsed_2_Gateway_SuperEnhancers.bed



Promoter capture Hi-C



Genomic interactions

Cell



Volume 167, Issue 5, 17 November 2016, Pages 1369–1384.e19

Resource

Lineage-Specific Genome Architecture Links Enhancers and Non-coding Disease Variants to Target Gene Promoters

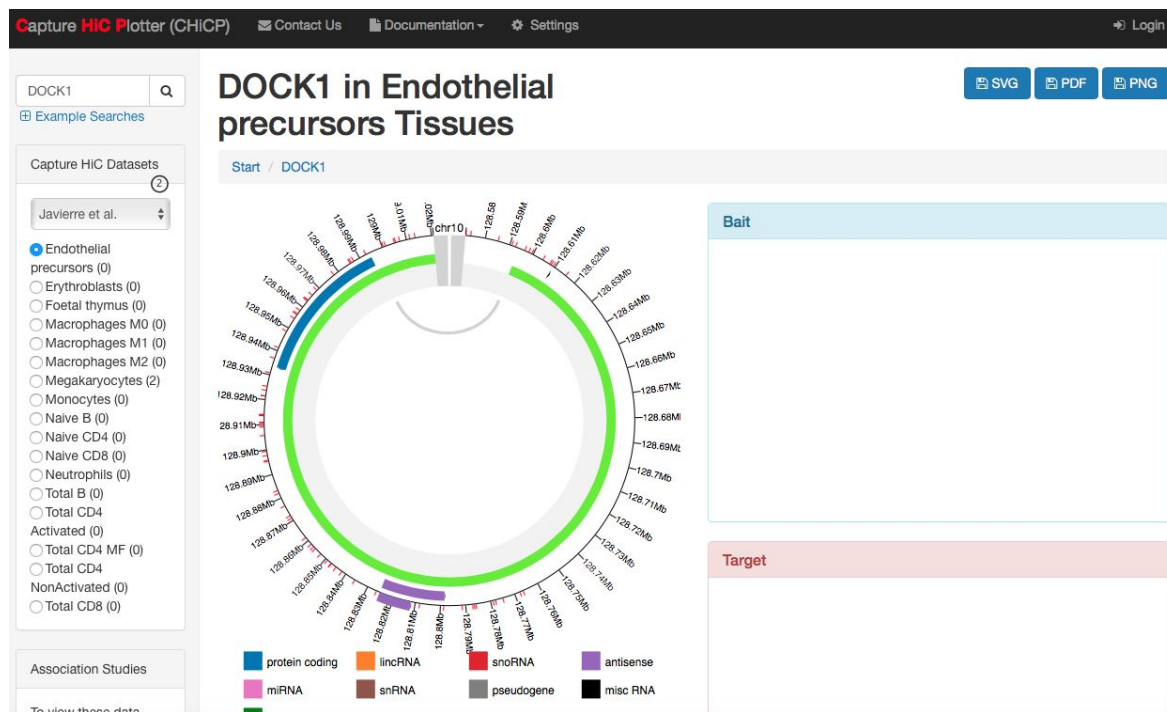
Biola M. Javierre^{1, 11}, Oliver S. Burren^{2, 11}, Steven P. Wilder^{3, 11}, Roman Kreuzhuber^{3, 4, 5, 11}, Steven M. Hill^{6, 11}, Sven Sewitz¹, Jonathan Cairns¹, Steven W. Wingett¹, Csilla Várnai¹, Michiel J. Thiecke¹, Frances Burden^{4, 5}, Samantha Farrow^{4, 5}, Antony J. Cutler², Karola Rehnström^{4, 5}, Kate Downes^{4, 5}, Luigi Grassi^{4, 5}, Myrto Kostadima^{3, 4, 5}, Paula Freire-Pritchett¹, Fan Wang⁶,

▢ [The BLUEPRINT Consortium](#)

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Genomic interactions



<https://www.chicp.org>