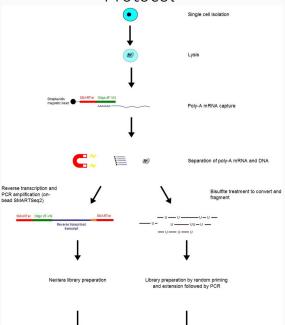
PARALLEL SINGLE-CELL SEQUENCING LINKS TRANSCRIPTIONAL AND EPIGENETIC HETEROGENEITY

Angermueller et al., Nature Methods, January 11, 2016. doi:10.1038/nmeth.3728.

Saket Choudhary February 11, 2016 BISC 542 scM&T-seq: Parallel single-cell genome-wide methylation & transcriptome seq ⇒ Coupled/Uncoupled?

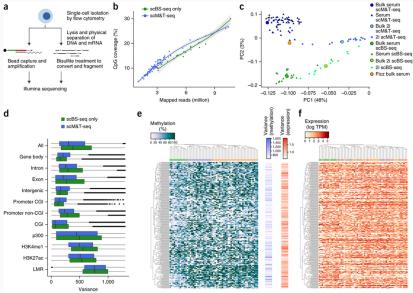
Protocol



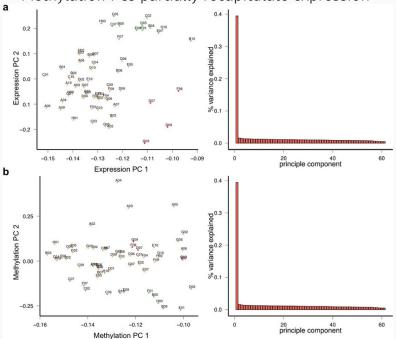
Data:

76 individual serum ESC + 16 ESCc in '2i'[induces hypomethylation]

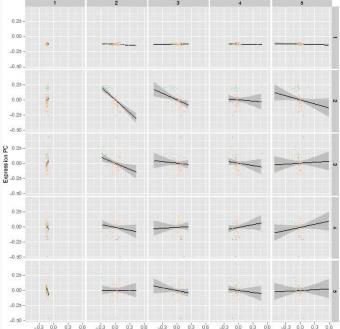
Variation in methylation levels are explained by cell type



Methylation PCs partially recapitulate expression

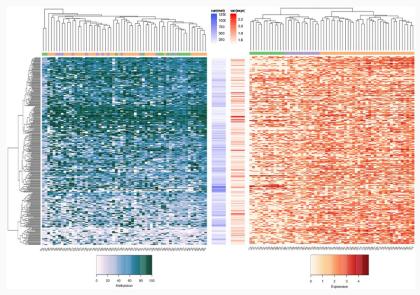


Methylation PCs correlate with Expression PCs



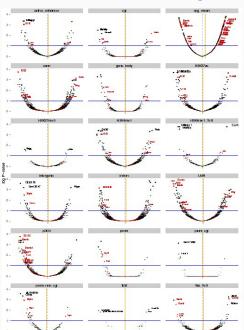
Methylation PC

Global methylome and transcriptome profiles are complementary

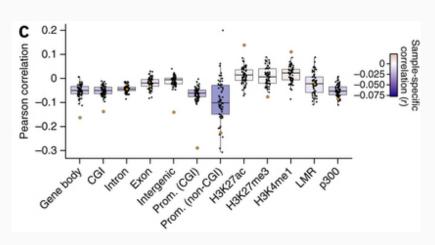


Association between expression levels and methylation : BOTH negative and positive \implies Interactions are Complex!

Correlation coefficients in alternative genomic context:



Validates with bulk RNA-seq and BS-seq[Oranges]



Insights

Transcriptome and Methylome can be uncoupled

Insights

Association with transcription:

- v/s methylation at non-CpG island promoters : negative (known)
- v/s methylation at distal regulatory elements :both

Summary

- Parallel methylome & transcriptome profiling: feasbile
- · Associations can be quantified at single-cell level
- Fluctuating pluripotency in serum ESC ≅
 Epigenetic heterogenity

Ideas/Issues

- Spearman Correlation? for individual CpGs or regions to observe trend
- · Infer cell state from data?[Complementary]
- · CA instead of PCA to reveal transcriptome-methylome clusters. See Fellenberg et al.
- $(-)log_{10}(q-val)$ and Pearson (r^2) ?

Academic Valentine

http://tinyurl.com/acadvalentines

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