

PARALLEL SINGLE-CELL SEQUENCING LINKS TRANSCRIPTIONAL AND EPIGENETIC HETEROGENEITY

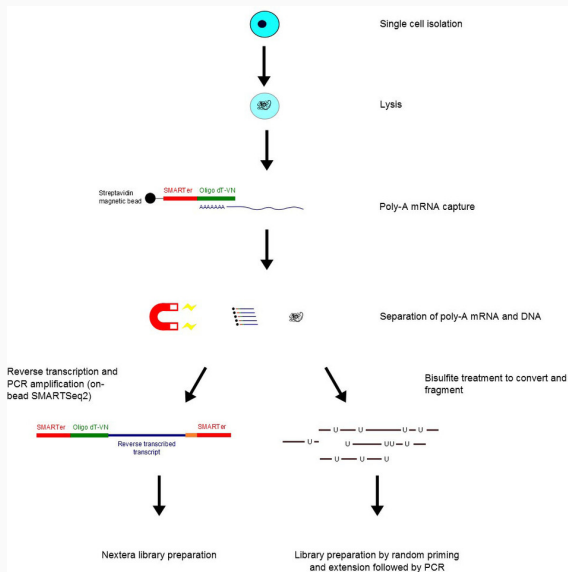
Angermueller et al., Nature Methods, January 11, 2016.
doi:10.1038/nmeth.3728.

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February 8, 2016

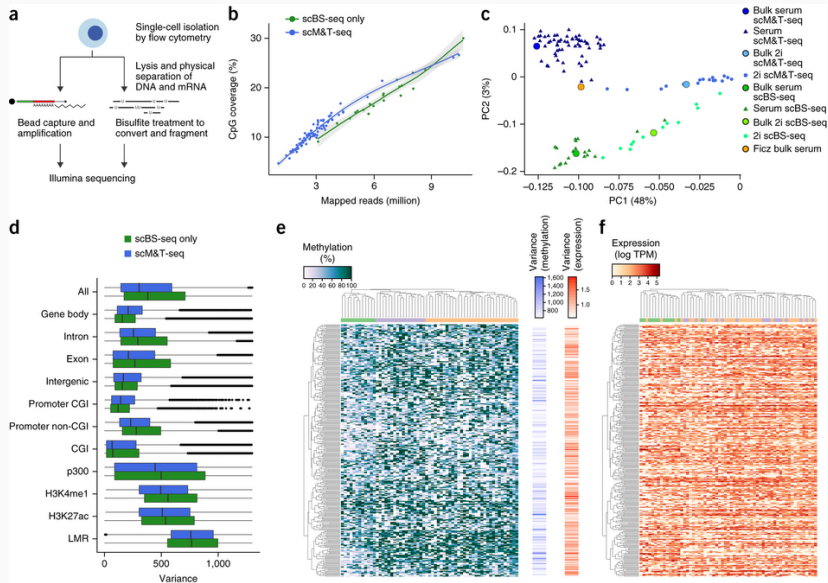
BISC 542

scM&T-seq: Parallel single-cell genome-wide
methylation & transcriptome seq
⇒ Coupled/Uncoupled?

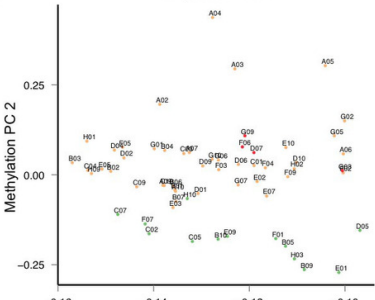
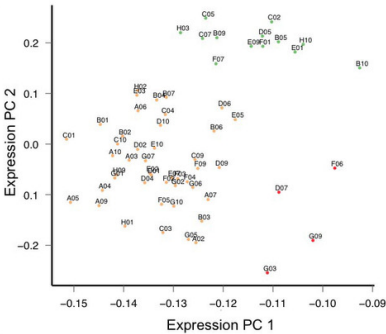


76 individual serum ESC + 16 ESCc in '2i'[induces hypomethylation]

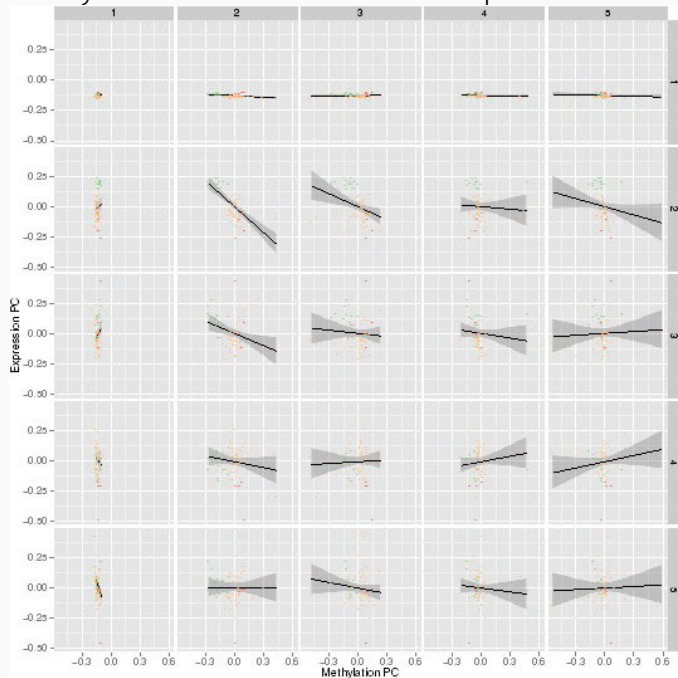
VARIATION IN METHYLATION LEVELS ARE EXPLAINED BY CELL TYPE



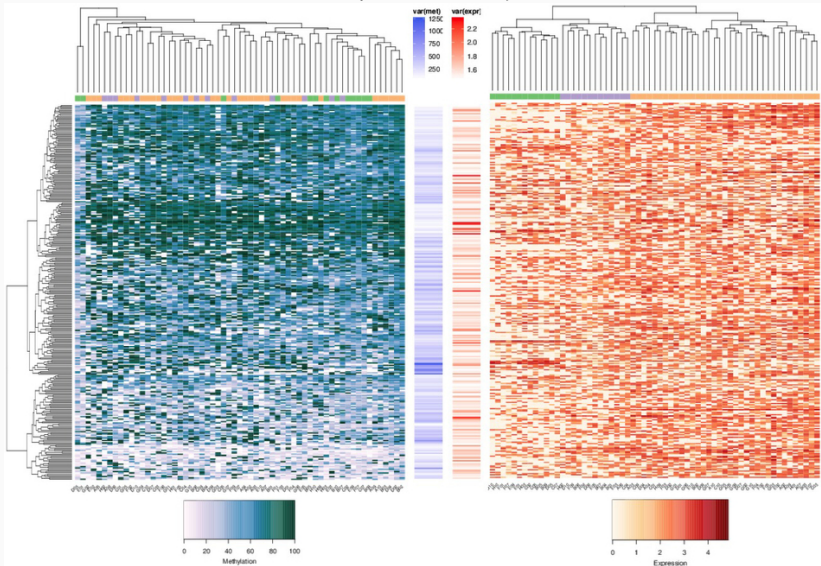
structure



Methylation PCs correlate with Expression PCs

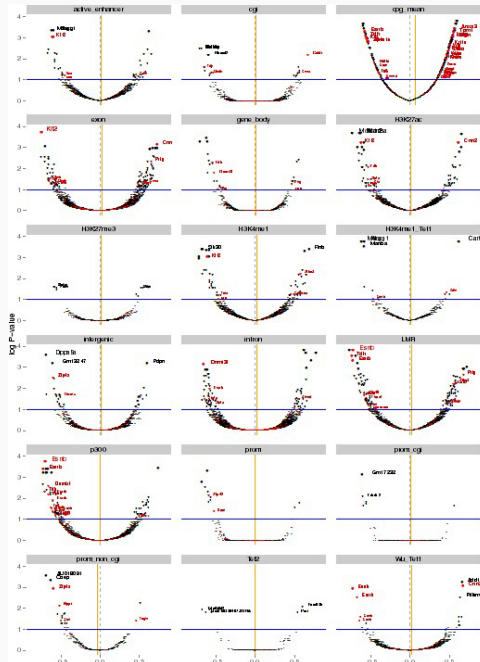


Global methylome and transcriptome profiles are complementary

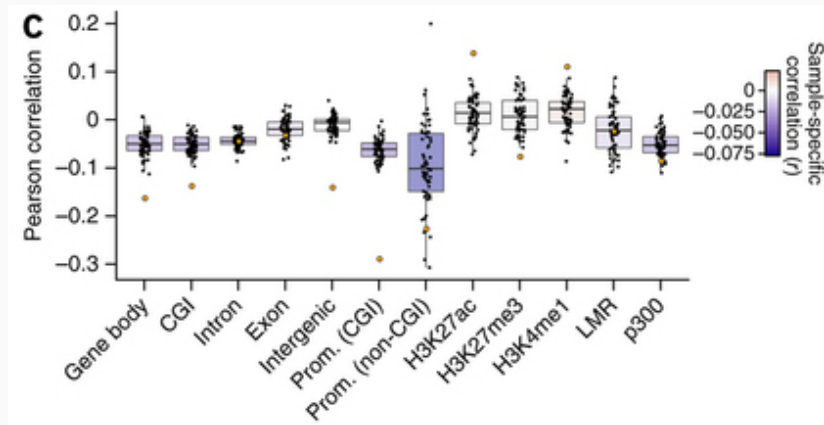


Association between expression levels and methylation : BOTH negative and positive \Rightarrow Interactions are Complex!

Correlation coefficients in alternative genomic context:



Validates with bulk RNA-seq and BS-seq[Orange dots]



Transcriptome and Methylome can be uncoupled

Association with transcription:

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

- Parallel methylome & transcriptome profiling: feasible
- Associations can be quantified at single-cell level
- Fluctuating pluripotency in serum ESC \cong Epigenetic heterogeneity

- Seisenberger, Stefanie, et al. "The dynamics of genome-wide DNA methylation reprogramming in mouse primordial germ cells." *Molecular cell* 48.6 (2012): 849-862.
- Han, Han, et al. "DNA methylation directly silences genes with non-CpG island promoters and establishes a nucleosome occupied promoter." *Human molecular genetics* (2011): ddr356.
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- Smallwood, Sébastien A., et al. "Single-cell genome-wide bisulfite sequencing for assessing epigenetic heterogeneity." *Nature methods* 11.8 (2014): 817-820.
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