

## **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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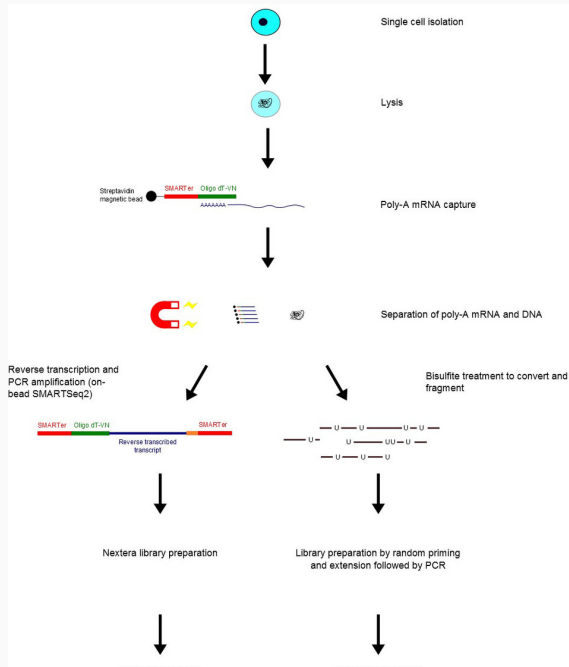
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BISC 542

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

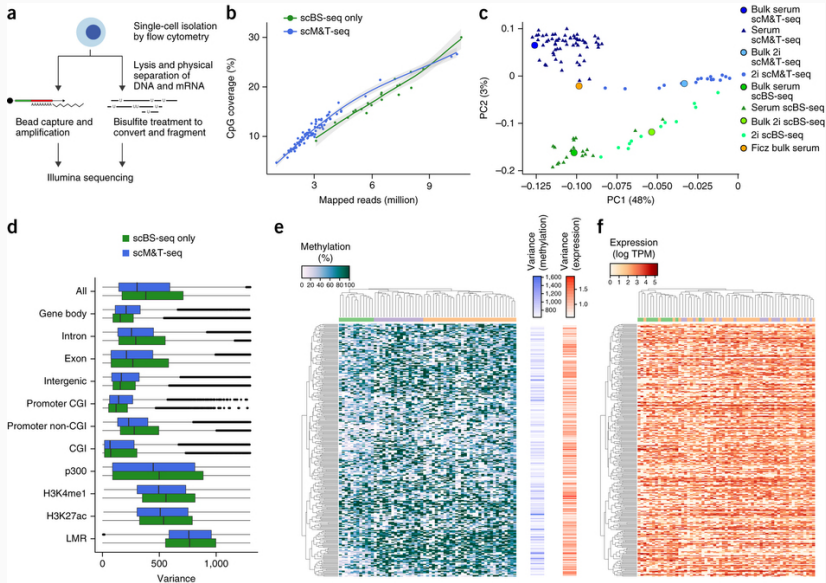
# Protocol



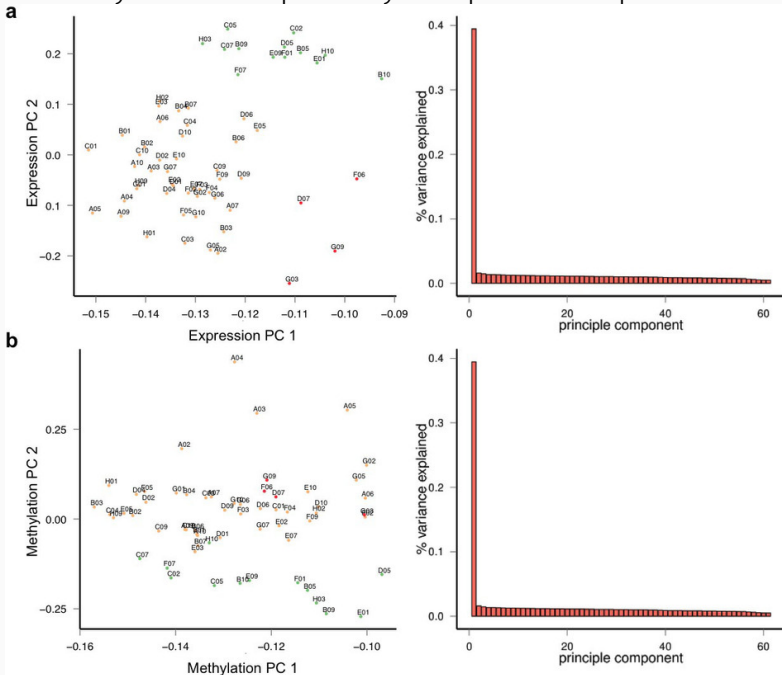
Data:

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

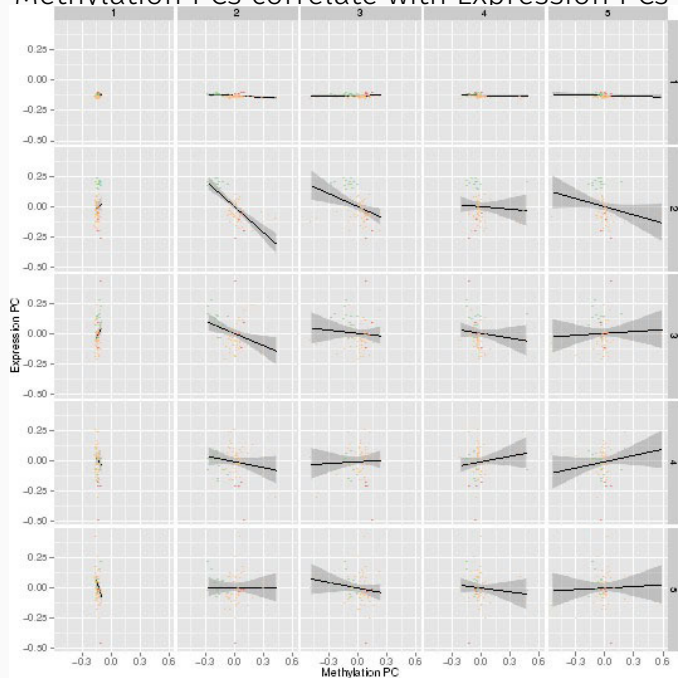
# Variation in methylation levels are explained by cell type



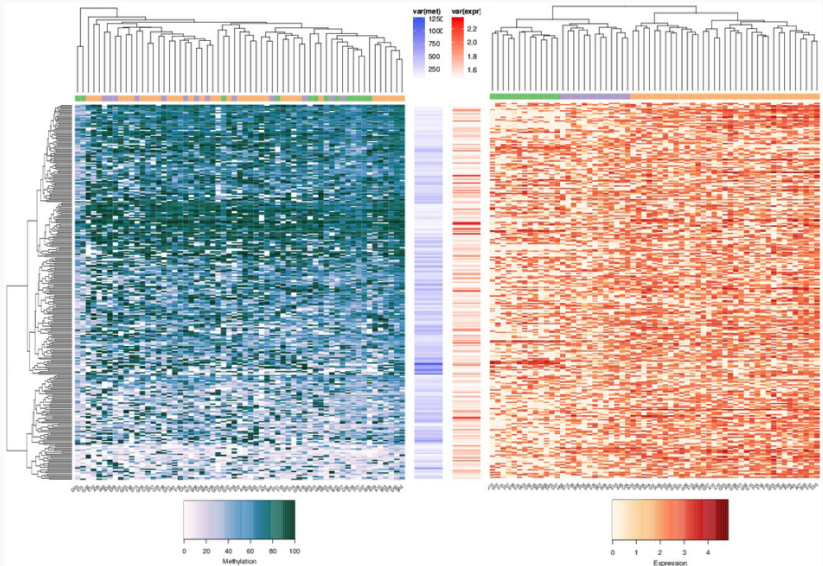
# Methylation PCs partially recapitulate expression



# Methylation PCs correlate with Expression PCs



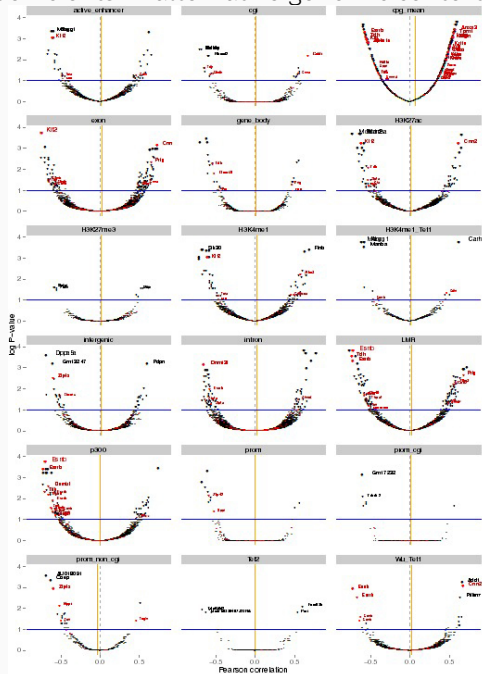
# Global methylome and transcriptome profiles are complementary



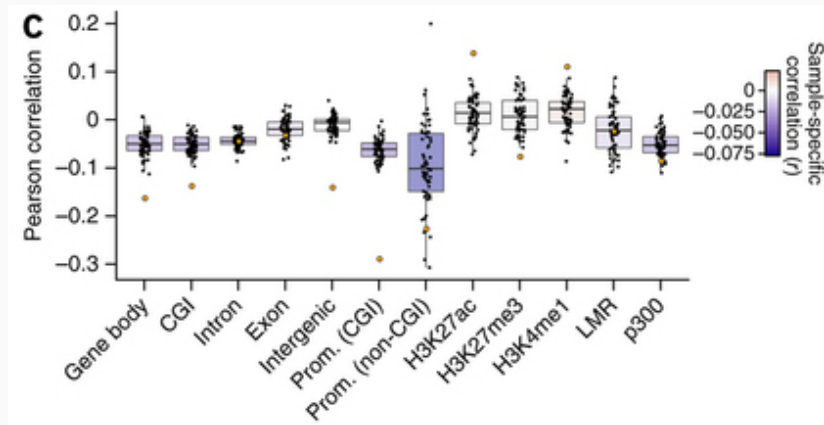


Association between expression levels and methylation : BOTH negative and positive  $\Rightarrow$  Interactions are Complex!

# Correlation coefficients in alternative genomic context:



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



## 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: feasible
- Associations can be quantified at single-cell level
- Fluctuating pluripotency in serum ESC  $\cong$  Epigenetic heterogeneity

# References

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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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