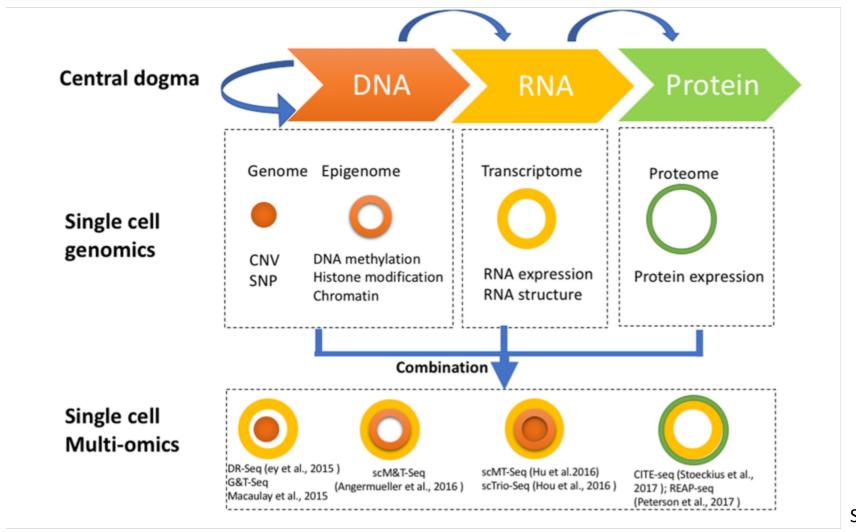
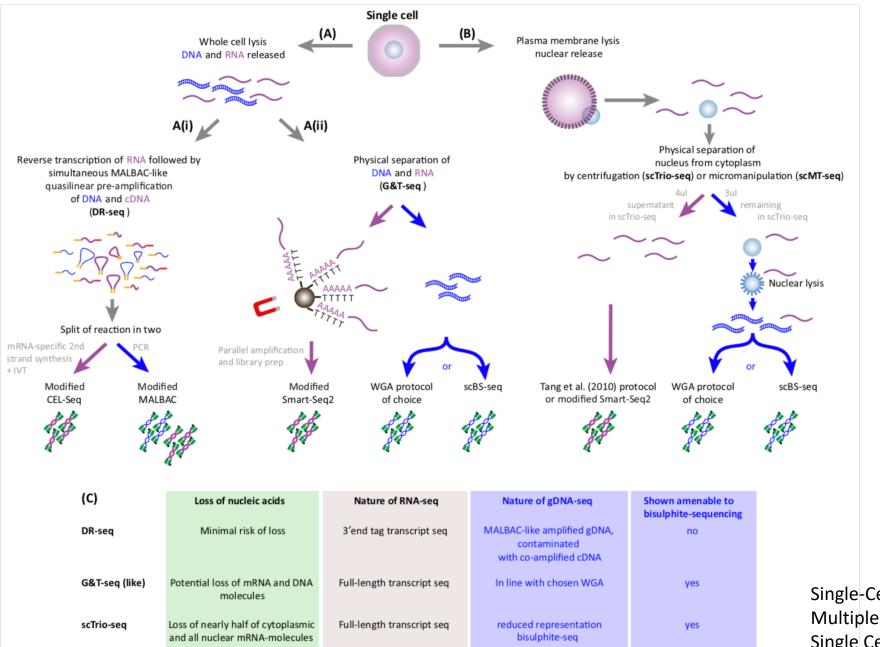
Single-cell multiomics sequencing and analyses of human colorectal cancer
Science Nov 2018
Shuhui Bian et. al.

Presented by Shayan Tabe Bordbar

Single cell Multi-omics



Single Cell Multi-Omics Technology: Methodology and Application. Hu et al. Front Cell Dev Bipl. 2018



Full-length transcript seq

scMT-seq

Loss of some cytoplasmic

and all nuclear mRNA-molecules

during micromanipulation

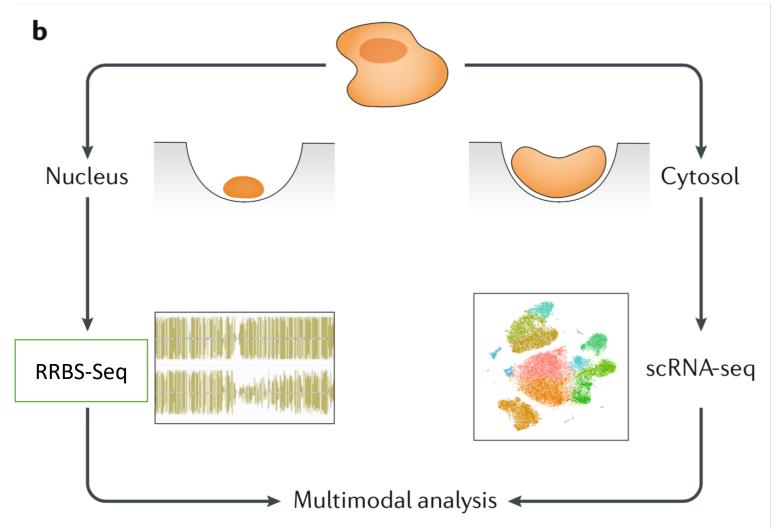
reduced representation

bisulphite-seq

yes

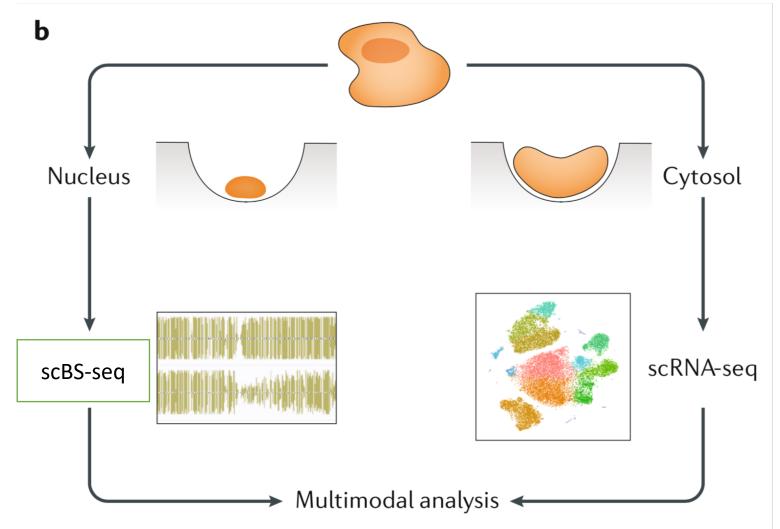
Single-Cell Multiomics:
Multiple Measurements from
Single Cells.
Macaulay et al. Cell Trends in
Genetics 2017

scTrio-seq



Integrative single-cell analysis. Stuart et al. Nature Reviews 2019

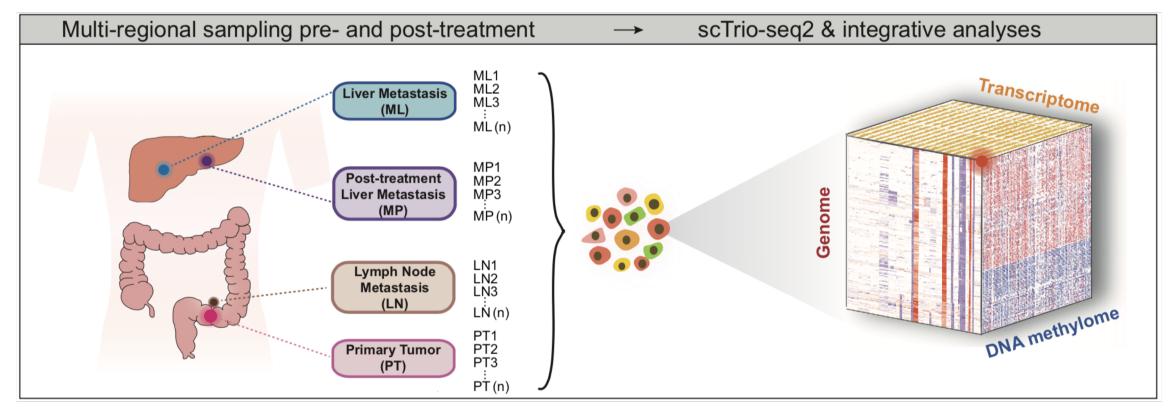
scTrio-seq2



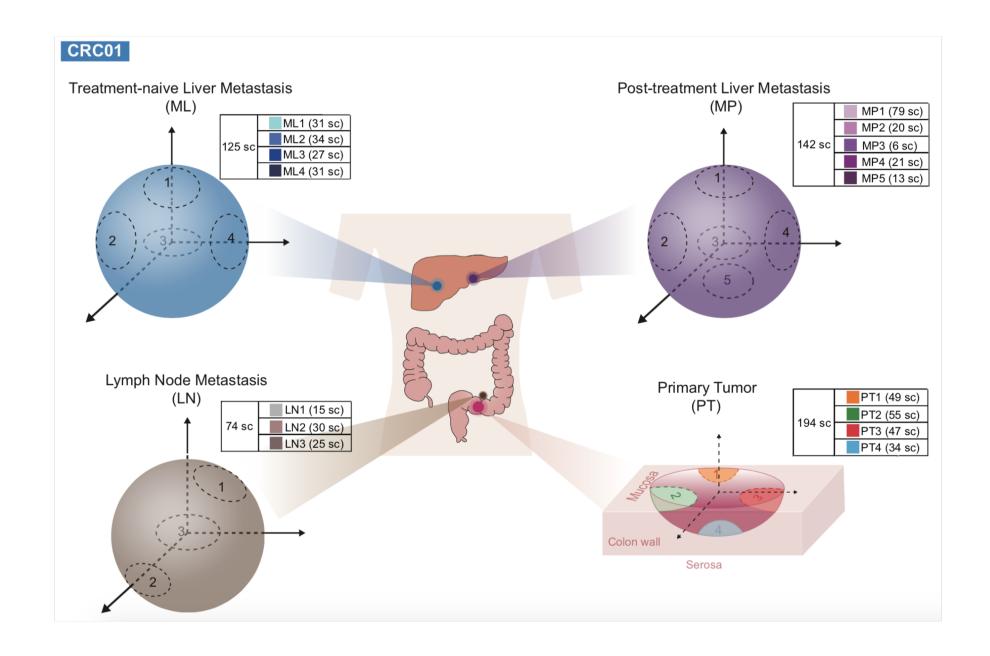
Integrative single-cell analysis. Stuart et al. Nature Reviews 2019

DNA methylation

- Addition of a methyl group to the cytosine residues of the dinucleotide CpG.
- 80-90% of CpG sites in Human genome are methylated.
- DNA methyltransferase is the enzyme responsible for this.
- CpG islands 300-3000 bp long found near ~ 40% of promoters.
- Unlike other CpG sites, the islands in promoters are normally unmethylated if the genes are expressed.
- Treatment of DNA with bisulfite converts cytosine residues to uracil, but leaves 5-methylcytosine residues unaffected.

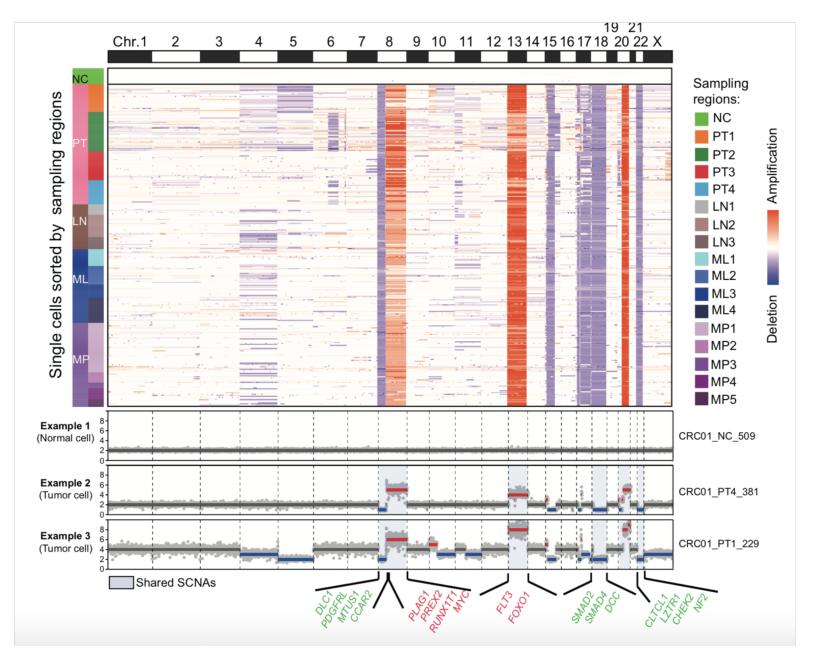


12 patients ~1900 cells

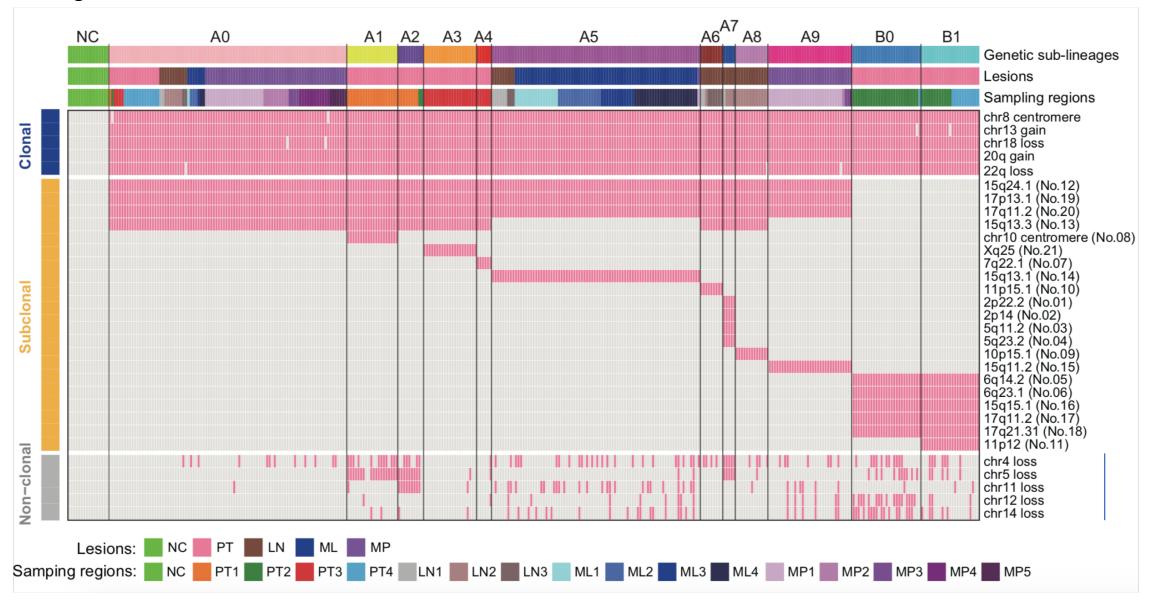


Genome wide Somatic Copy Number Aberration Inference.

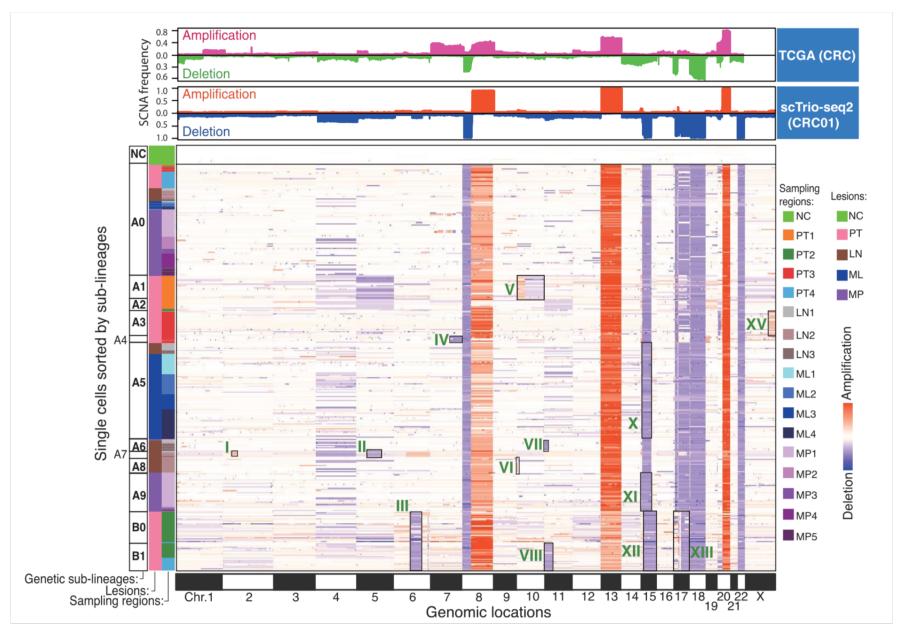
- Resolution 250-kb
- Used Ginkgo algorithm



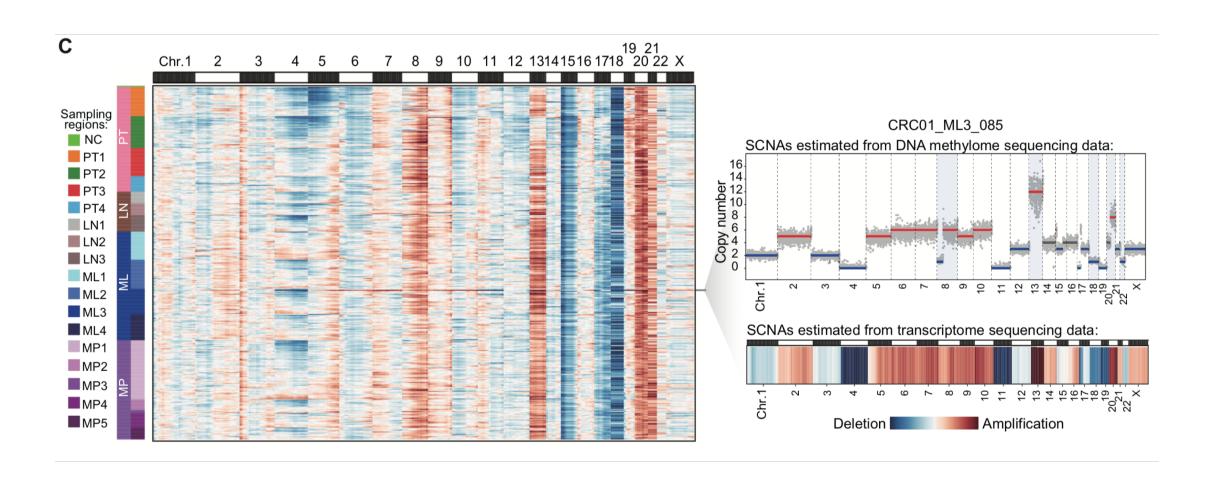
Genetic lineage classification



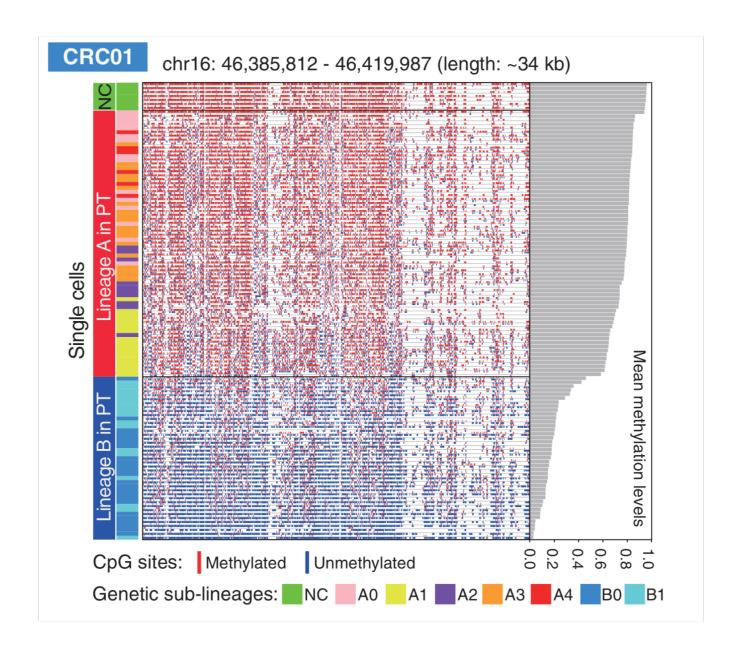
Global SCNA patterns (250-kb resolution) of CRC01.

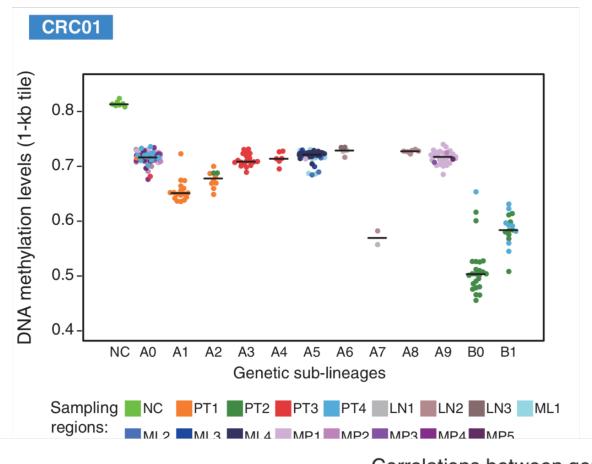


The SCNA profiles inferred from single-cell transcriptome data



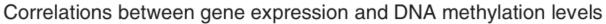
Representative DMR

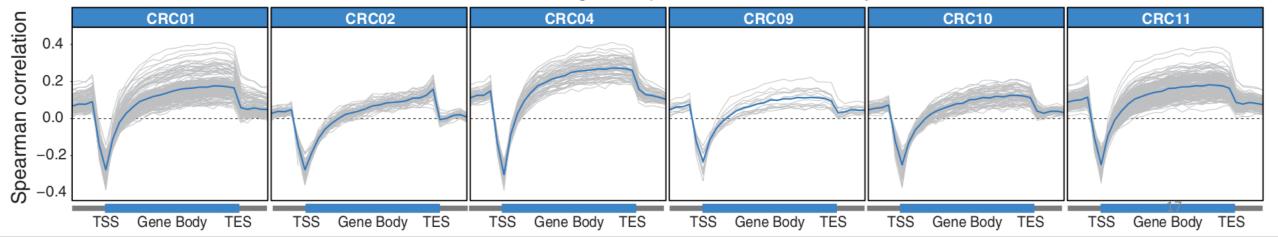


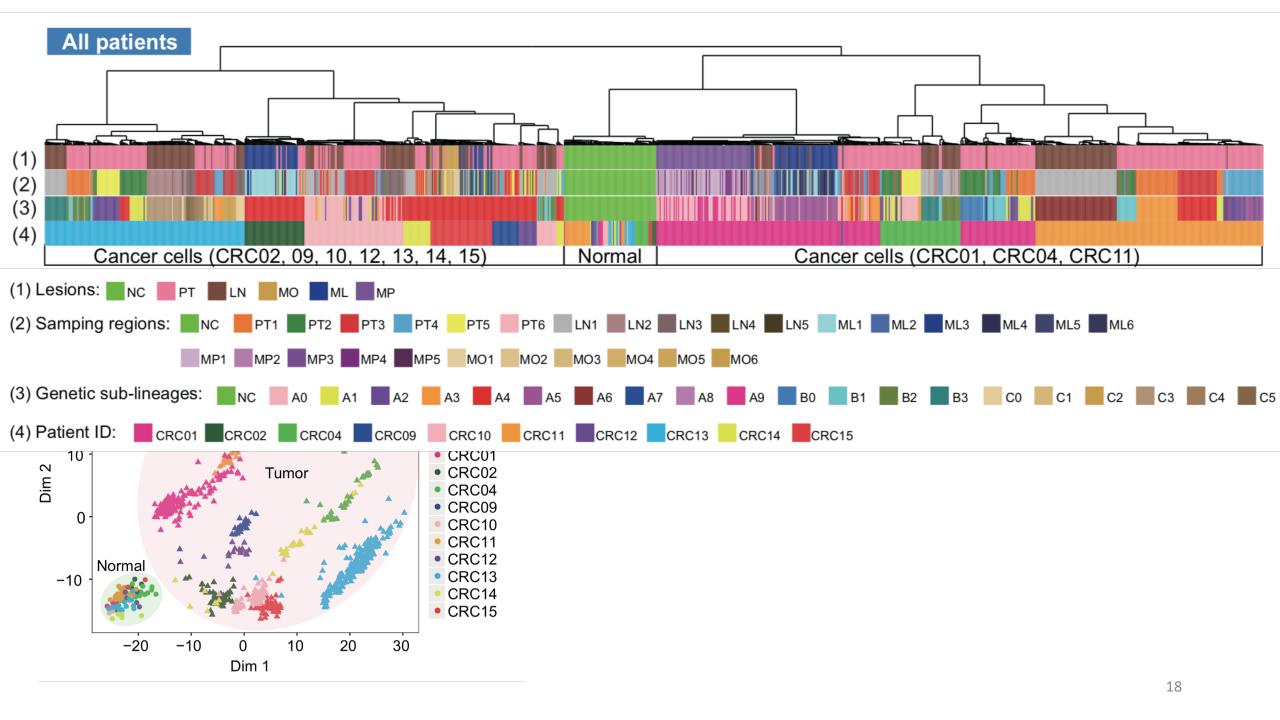


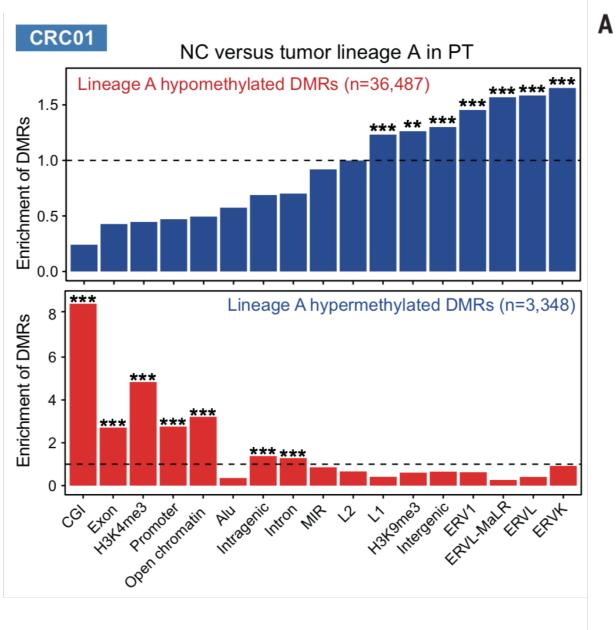
Methylation levels

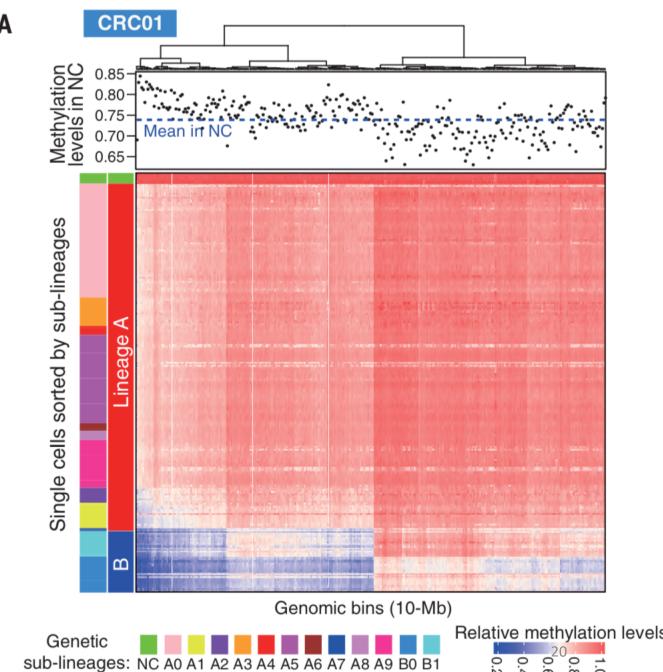
Genome-wide hypomethylation in cancer cells compared with normal cells



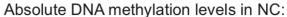


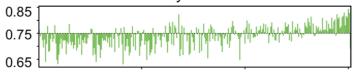




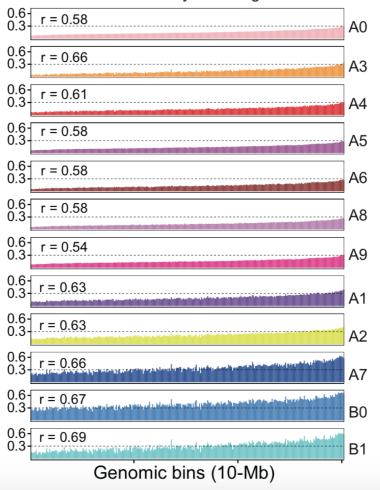


CRC01

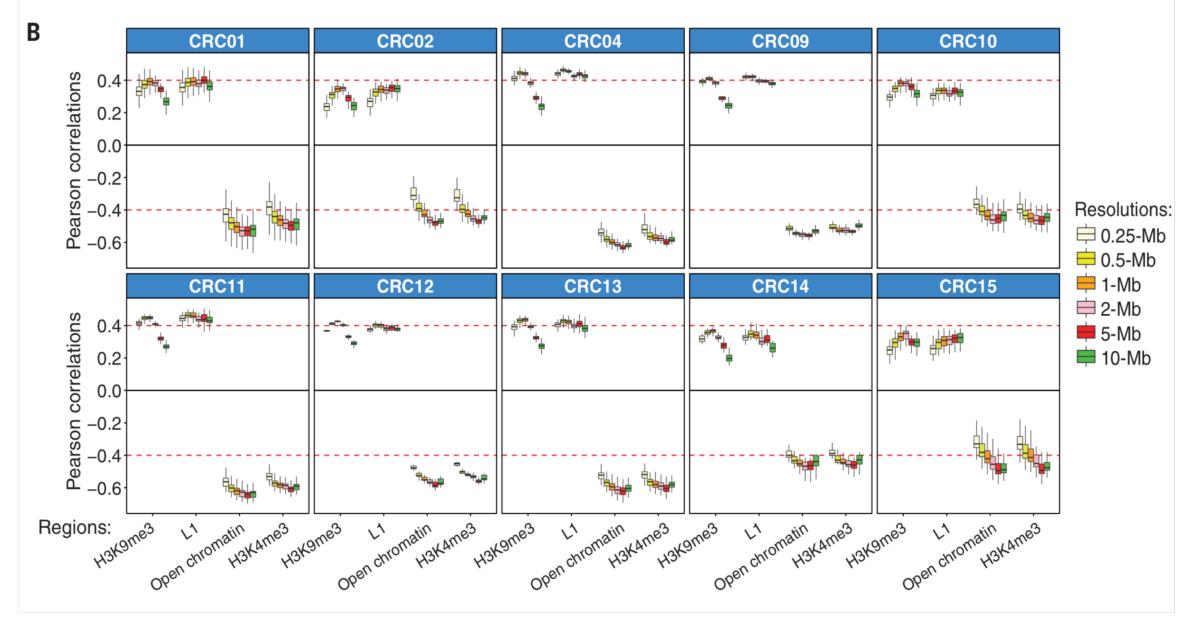




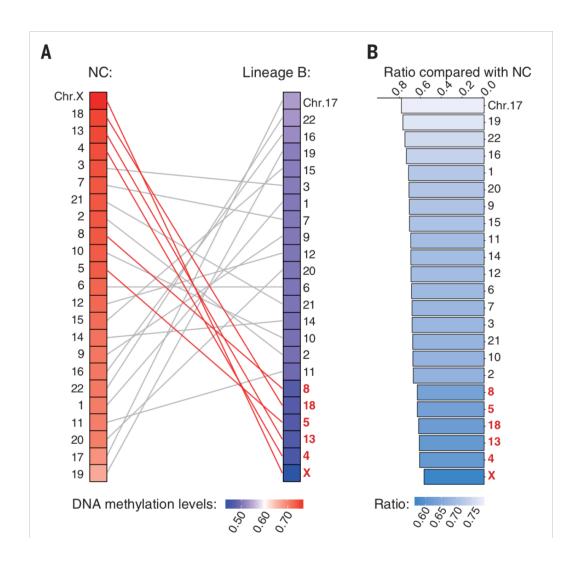
Relative DNA demethylation degree in cancer cells:

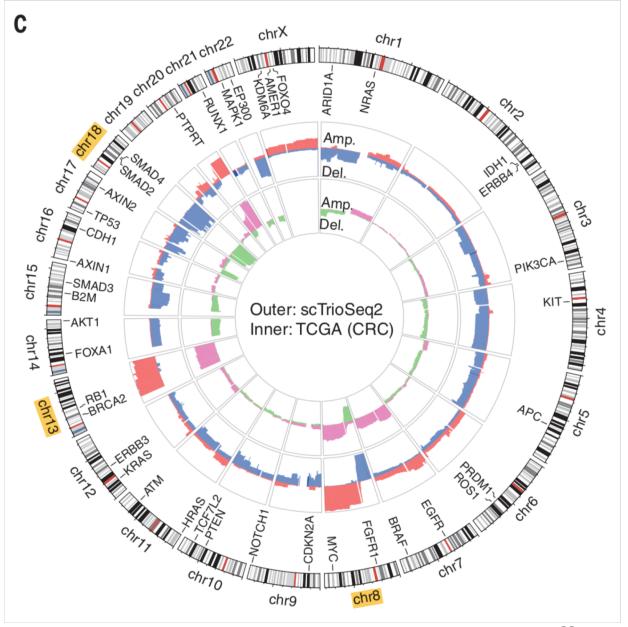


The relative demethylation degrees of cancer cells were correlated with the absolute DNA methylation levels of NC cells across the genome



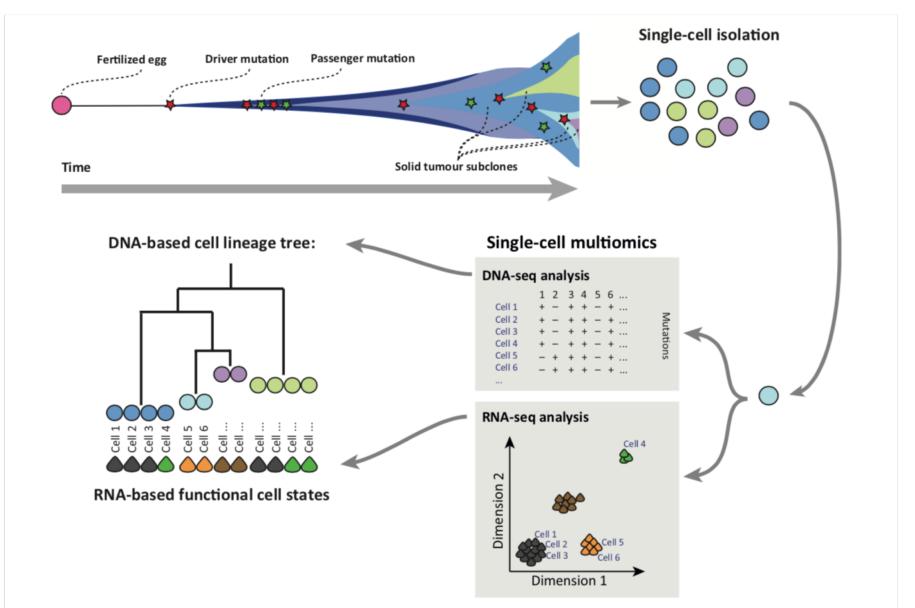
Pearson correlations between the **DNA demethylation levels** of genomic bins in individual cancer cells and the **densities of genomic features**





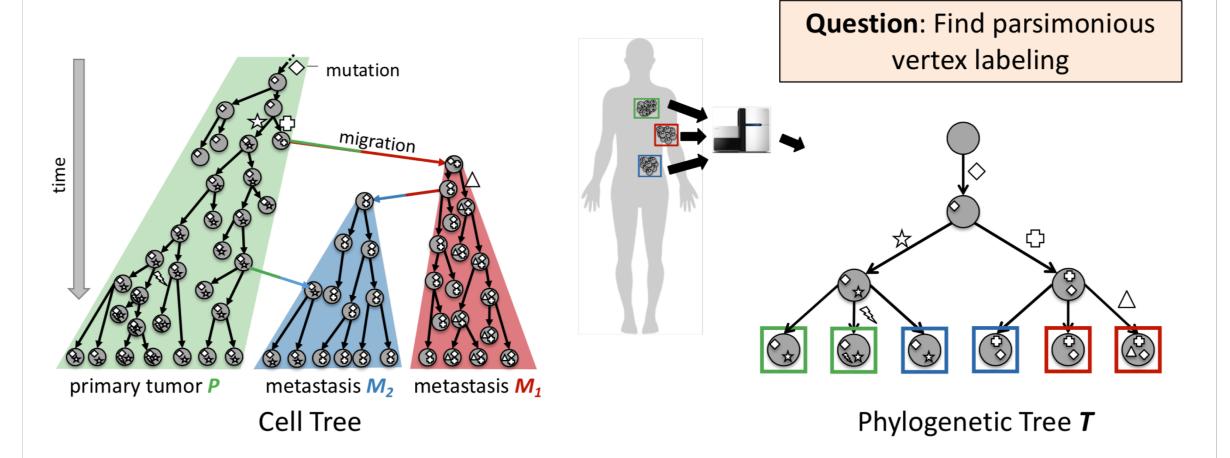
Paper Conclusion

- Simultaneous measurement of SCNA, methylation and transcriptome of single cells.
- Reconstruction of genetic lineages using multi-omics sequencing.
- Genome-wide DNA methylation levels were relatively consistent within a single genetic sublineage.
- Demethylation degrees of cancer cells were correlated with the absolute DNA methylation levels of NC cells.



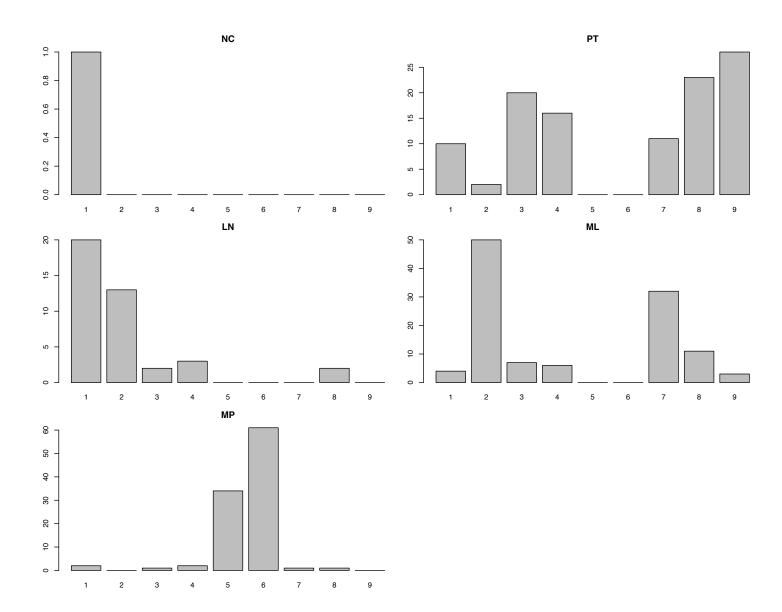
Single-Cell Multiomics:
Multiple Measurements from
Single Cells.
Macaulay et al. Cell Trends in
Genetics 2017

Tumorigenesis: (i) Cell Division, (ii) Mutation & (iii) Migration



Goal: Given phylogenetic tree *T*, find *parsimonious* vertex labeling *ℓ* with fewest migrations

Expression matrix clustering Patient CRC01



Genetic lineage classification

