



# Simultaneous methylation and chromatin accessibility profiling on breast cancer cells

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#### Epigenome

**Epigenome :** Multitude of chemical compounds that tell the genome what to do







#### **NOMe-seq**

NOMe-seq : Nucleosome Occupancy and Methylome sequencing (Kelly et. al. Genome Res. 2012)

• Simultaneously measures DNA methylation (CpG) and chromatin accessibility (GpC)



#### nanoNOMe

**NOMe-seq :** Nucleosome Occupancy and Methylome sequencing (Kelly et. al. *Genome Res.* 2012)

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# **DNA methylation detection using nanopolish**



Nanopolish : post-alignment methylation caller using a hidden Markov model

(Simpson, et. al. Nat. Method 2017)

• Uses the raw current signal and alignment information to determine methylation status



# Nanopore sequencing can distinguish DNA modifications







# NanoNOMe

Detecting DNA methylation and chromatin accessibility

# NanoNOMe captures chromatin states at CTCF sites



Anticorrelation of DNA methylation and open chromatin Chromatin states around CTCF agrees with NOMe-seq



# NanoNOMe captures chromatin states on single reads

Methylati

GpC

#### **Chromatin Protection (1-GpC)**



**Endogenous Methylation (CpG)** 





#### NanoNOMe shows read-level nucleosome variation

#### **Chromatin Protection (1-GpC)**



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# NanoNOMe in cancer

DNA methylation and chromatin accessibility in breast cancer cell lines

#### **NanoNOMe on Breast Cancer Cell Lines**

#### MCF-10A vs MCF-7

**MALAT1 :** downregulated in breast cancer



#### **MALAT1 is downregulated in MCF-7**



Promoter region is **methylated** Promoter is **inaccessible** 

#### **MALAT1 is expressed in MCF-10A**



Promoter region is **unmethylated** 

Promoter is accessible in a subset of reads - allele-specific or heterogeneous

## NanoNOMe profiles are different at MALAT1

#### MCF-10A vs MCF-7

**MALAT1 :** downregulated in breast cancer

#### **Expression in MCF-10A :**

Unmethylated promotor accessible promoter in a subset **Silencing in MCF-7 :** 

Methylated promoter Inaccessible promoter



# **Conclusion and Future Work**

#### Using nanoNOMe, we can observe :

- CpG methylation and chromatin accessibility simultaneously on long reads
- Heterogeneity of chromatin states
- Allele-specific chromatin states

#### **Future Work**

- Haplotype chromatin states based on SNPs
- Different methylation motifs
  - Dam (GATC)
  - EcoGII (A)
- Other exogenous labeling techniques
  - damID



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# **Extra Slides**