

H3K27M, a new kid in the block

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Diffuse Midline Glioma (DMG) a.k.a DIPG





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Diffuse Midline Glioma (DMG) Derived from patients H3-K27 mutated to M H3.3 variant of 20 variants The genome compartmentalize in space (cell type specific)





1Mb

H3K27ac H3K27me3

Figure adapted from Mirny et al. 2019 COCB

Voters are compartmentalized in space Local Moran's I



Experiments: Hi-C & ChIP-seq



Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311. Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.



Solomon, M. J., Larsen, P. L. & Varshavsky, A. (1988) Cell 53, 937–947. Park, P.J. (2009) Nature Reviews Genetics 10, 669–680.



Does H3K27M spatially correlate?

chr1:224,061,851-228,061,851



H3-3A is a H3K27M spatial hub

chr1:224,061,851-228,061,851

2

1





H3-3A is a H3K27M spatial hub

chr1:224,061,851-228,061,851



19,948 protein-coding genes

Do other H3 marks spatially correlate?

19,948 protein-coding genes in the mouse genome



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H3-3A trip in the LMI quadrants chr1:224,061,851-228,061,851













H3-3A trip in the LMI quadrants chr1:224,061,851-228,061,851



LMIs

6

Δ

8

H3-3A most "up-regulated" of all H3 variants



There is an increase H3K27ac/H3K27me3 ratio for H3.3A mutated gene



Some take home messages...

- 1. H3K27M signal is NOT distributed randomly in the spatial genome and H3.3A gene is a hotspot for localization of H3K27M mutant histore 3.
- 2. The presence of H3K27M signal reduces the compartmentalization of the genome due to decrease of spatially distributed H3K27me3
- 3. There is an increase H3K27ac/H3K27me3 ratio for H3.3A gene, which is not observed inmost of the other H3 variants (positive feed-back?)



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