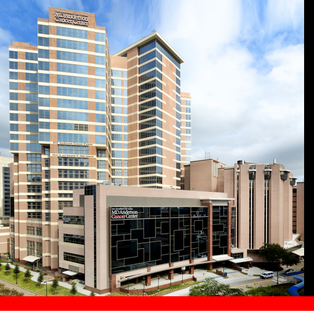

# Investigating Chromatin Organization Around Prominent Oncogenes Through Hi-C Analysis

**Kristy Mendoza Rangel[1], Kadir Caner Akdemir[2]**

**1** PCCSM **; 2** Department of Neurosurgery

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

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## Background

- Three-dimensional-chromatin organization is critical for proper gene expression and communication[1].
- Hi-C allows scientists to investigate chromatin interactions and organization on a genome-wide scale[2].
- Hi-C shows squares displaying interaction frequencies, depicted by color intensity, between pairs of loci.
- TADs are prominent features in Hi-C maps that are high self-interacting regions that are conserved among cell types. Within TADs, other features include loops, stripes, and sub-TADs are observed..
- Our understanding of chromatin organization within non-cancerous cell types is expanding. What remains questionable is how chromatin organization differs in cancer cells from normal cells, especially around the prominent oncogenic regions.
- Studying the chromatin organization in cancer cells could identify potentially important non-coding regulatory regions.

## Methods

- Used two data visualization tools: HiGlass[3] and Juicebox[4] to look at chromatin organization of several oncogenes[5] and compared them to different cell lines.
- Control cell line: normal lymphoblastoid cell line, GM12878.
- Compared each gene's chromatin organization to other non-cancerous cell lines (HMEC, HUVEC, IMR90).
- Compared it to cancerous cell lines (leukemia, adult and child brain tumors, sarcoma, melanoma, lung cancer, esophageal cancer, colon cancer).

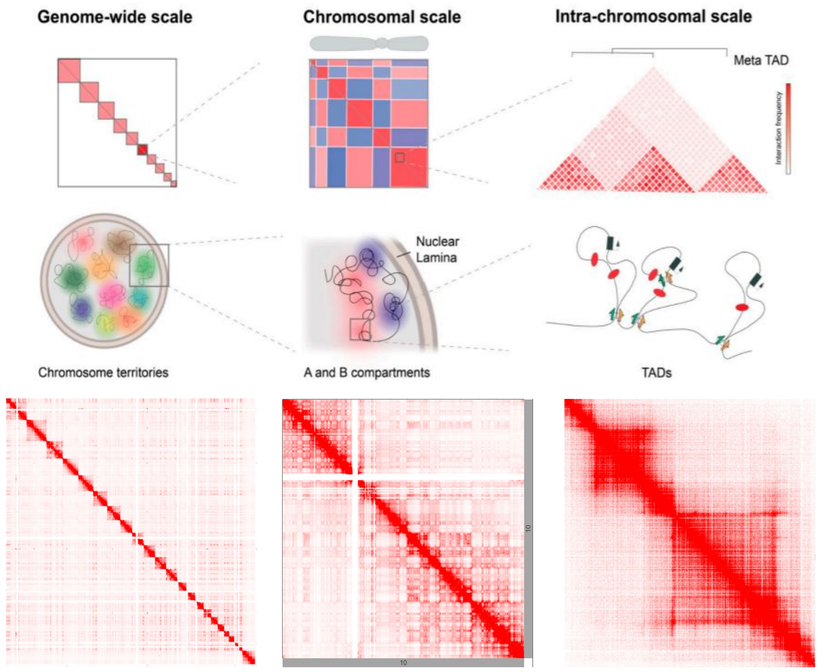


**Fig. 1.** Hi-C contact maps show several prominent features regarding chromatin organization. The genome-wide scale shows each of the 23 pairs of chromosomes. In the chromosomal scale, there are A/B compartments. A compartments have more open chromatin and higher transcription while B compartments have more closed chromatin and lower transcription. Within those compartments, chromatin is organized into TADs. TADs are highly self-interacting regions that are conserved among cell types.
These features allow us to investigate cell-type specific chromatin organization among different cell types and altered oncogene regulation in different cancer types.

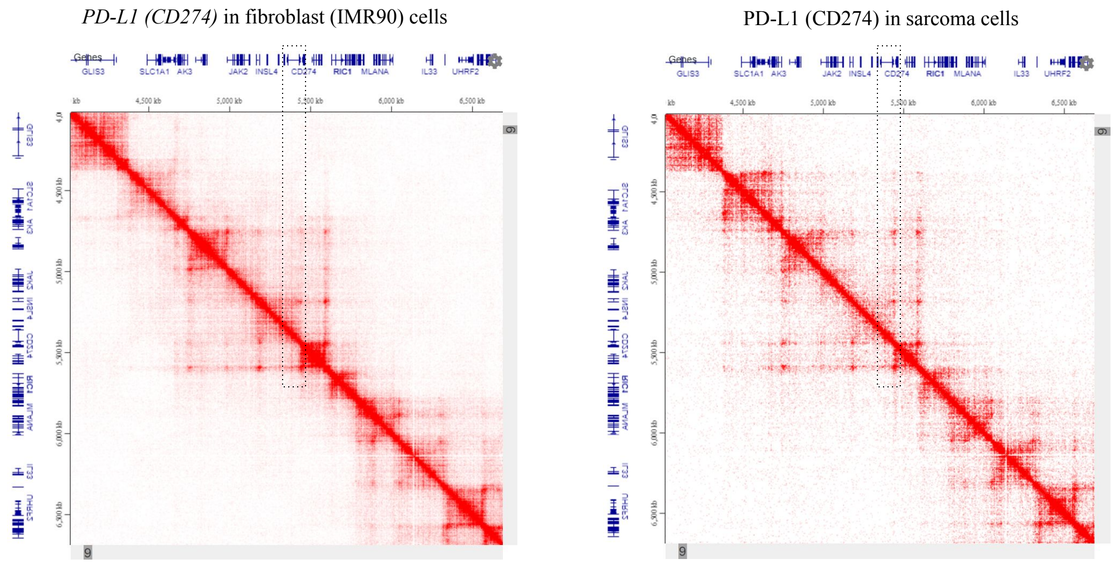


**Fig. 2.** *PD-L1* locus exhibits several distal-loop formations in a sarcoma genome compared to normal epithelial cell.

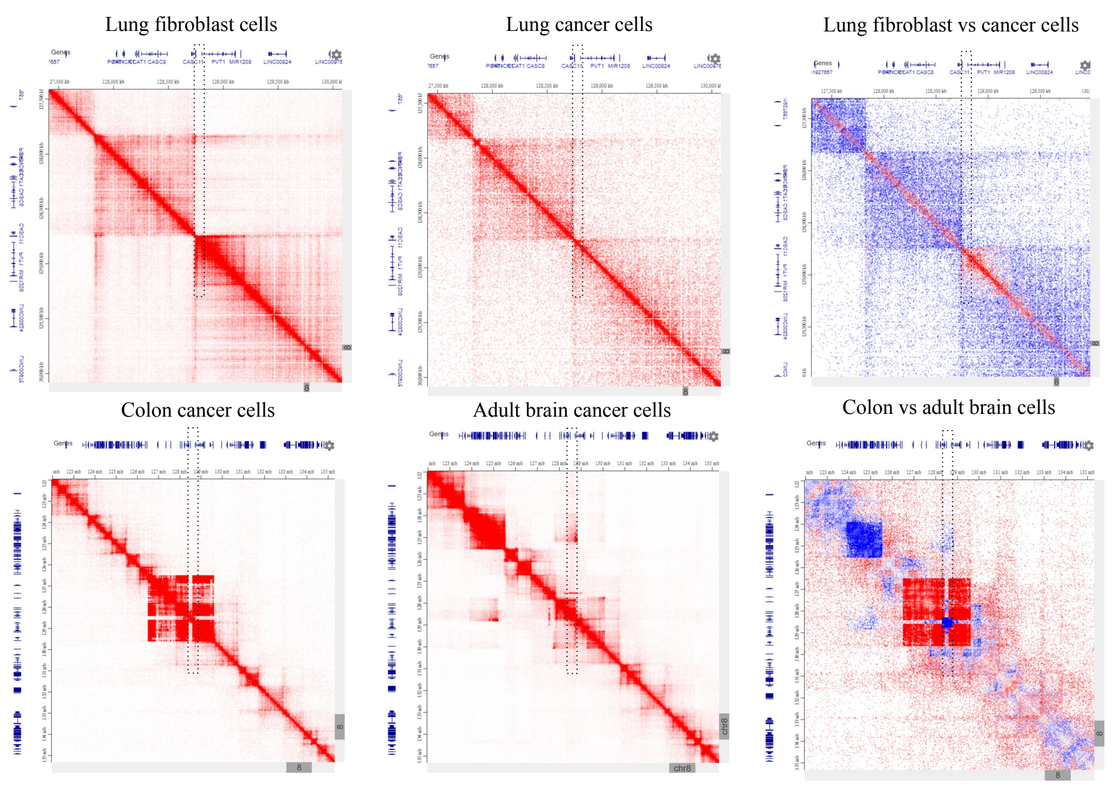


**Fig. 3.** *c-MYC* locus exhibits differential chromatin organization because of differentiation or mutations affecting the locus.

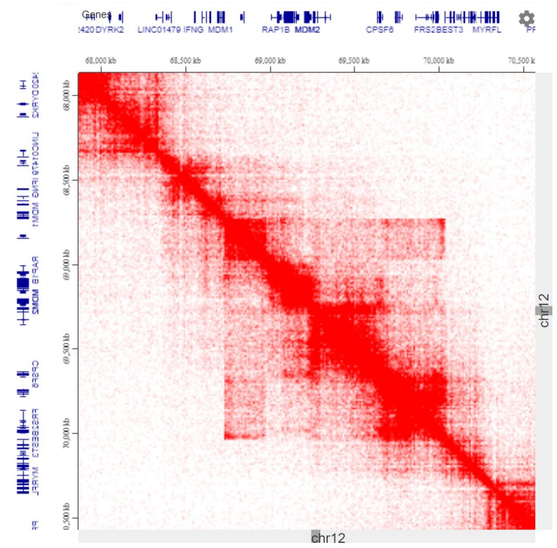


**Fig. 4.** *MDM2* TAD exhibits differential chromatin organization because of extra-chromosomal/double-minute amplifications in an adult brain tumor sample.

| Gene | Lung (A508) | Colon (SW480) | Adult Brain (Tissue) | Child Brain (Tissue) | Sarcoma (Tissue) | Melanoma (H596) | Esophageal (OE33) |
|---|---|---|---|---|---|---|---|
| SOX-9 | | | | | | | |
| ASCL1 | | | | | | | |
| BRD4 | | | | | | | |
| RUNX1 | | | | | | | |
| GLI2 | | | | | | | |
| FOXA1 | | | | | | | |
| SOX8 | | | | | | | |
| STAT3 | | | | | | | |
| MECOM | | | | | | | |
| GATA6 | | | | | | | |

**Table 1.** Summary of distinct chromatin organization features around selected oncogenic regions in various human types. Colors depict different organizational features, i.e. mustard is for mutations in the chromatin organization, purple is for differing TAD/compartment organization, green is for differing loop/stripes organization, black is for no difference shown.

## Conclusions

- Revealed certain oncogenic regions exhibit differential chromatin organization in a cancer specific manner[6].
- Further investigation will reveal potential non-coding elements driving the oncogene expression.

## References

1) Mota-Gómez et al. Genes 2019;10
2) Rao et al. Cell 2014;14
3) Perkepjiev et al. Genome Biology 2018;19
4) Durand et al. Cell Systems 2016;3
5) Futreal et al. Nat Rev Cancer 2004;3
6) Akdemir et al. Nature Genetics 2020;52