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# The utility of epigenetic analysis of cfDNA in treating cancer patients

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# Thank you

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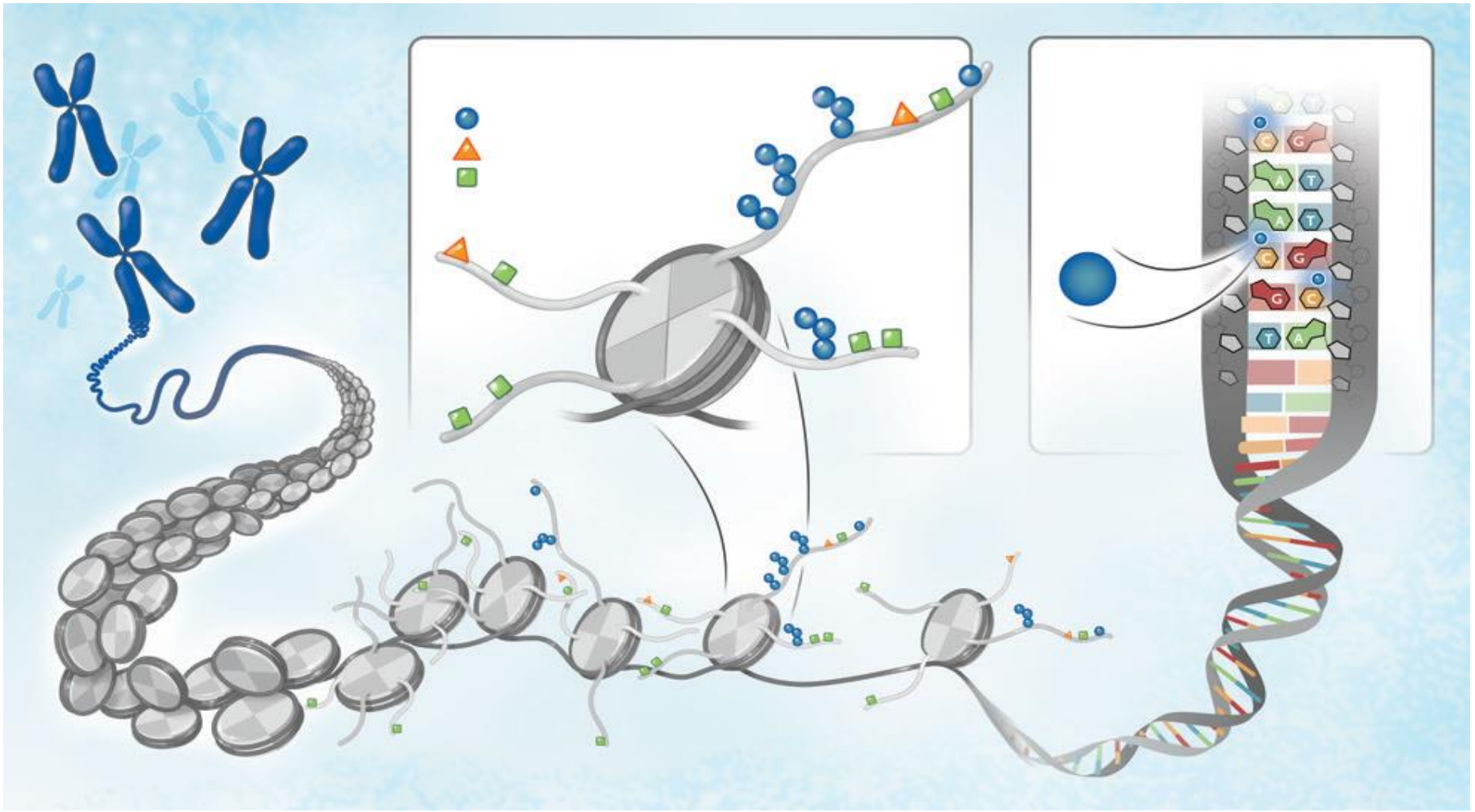
# Topics

- cfDNA
- Breast methylation patterns in cfDNA
- Inferring expression pattern in cfDNA using cfChIP seq
- Measuring copy number alterations in cfDNA using NANO seq

Overview

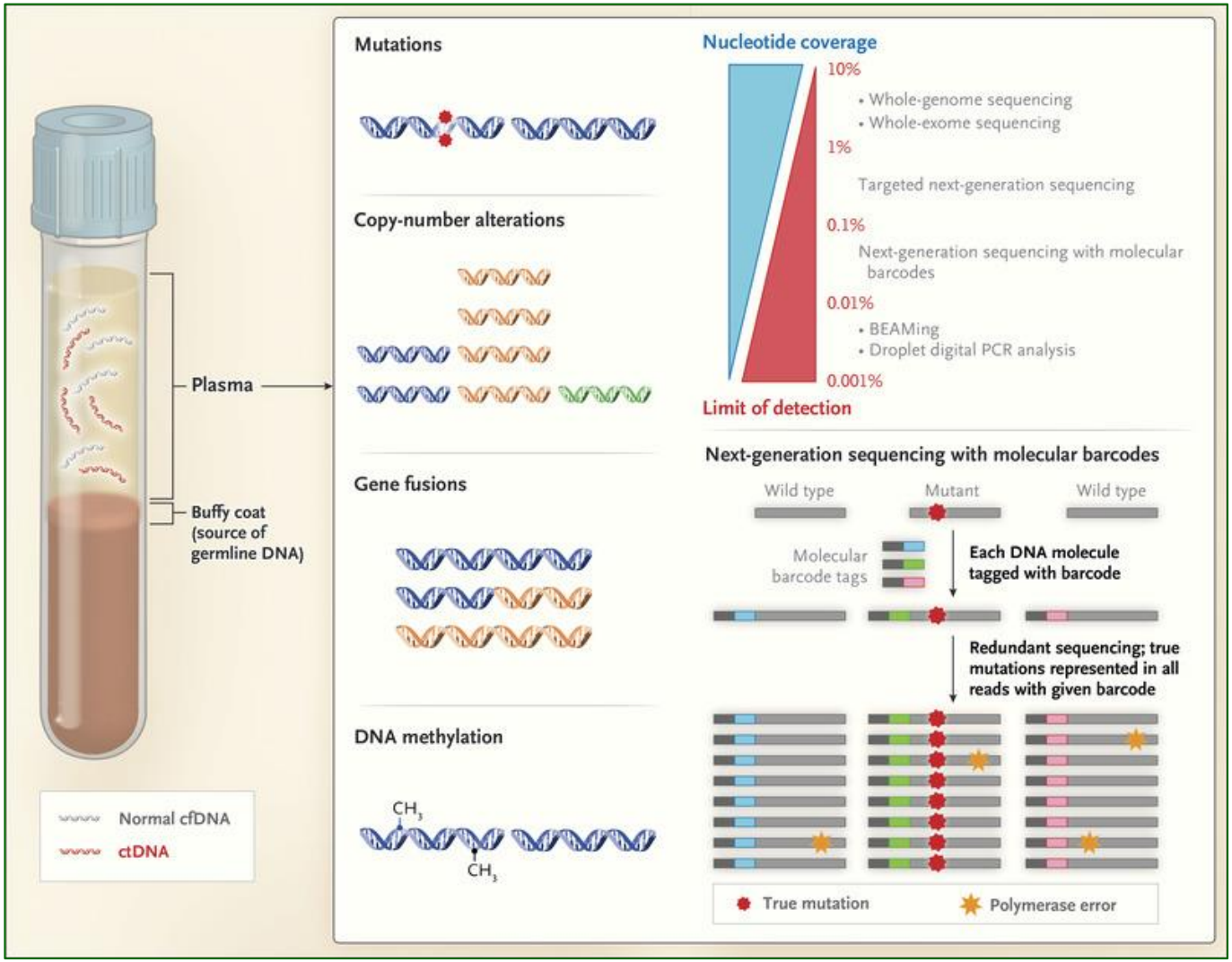
- Utilizing cfDNA epigenetic markers to identify different cell types and expression patterns is feasible in an oncological clinical setting.

# Chromatin



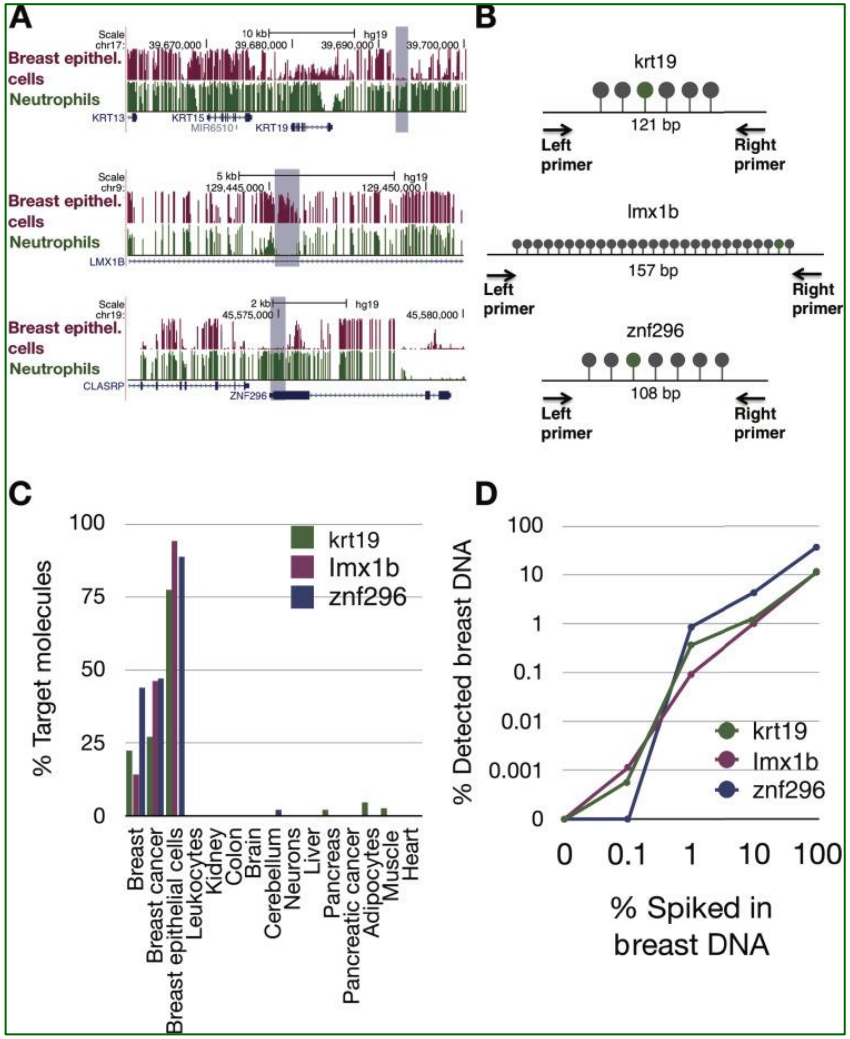
Bates, NEJM, 2020

# Cell free DNA (cfDNA)

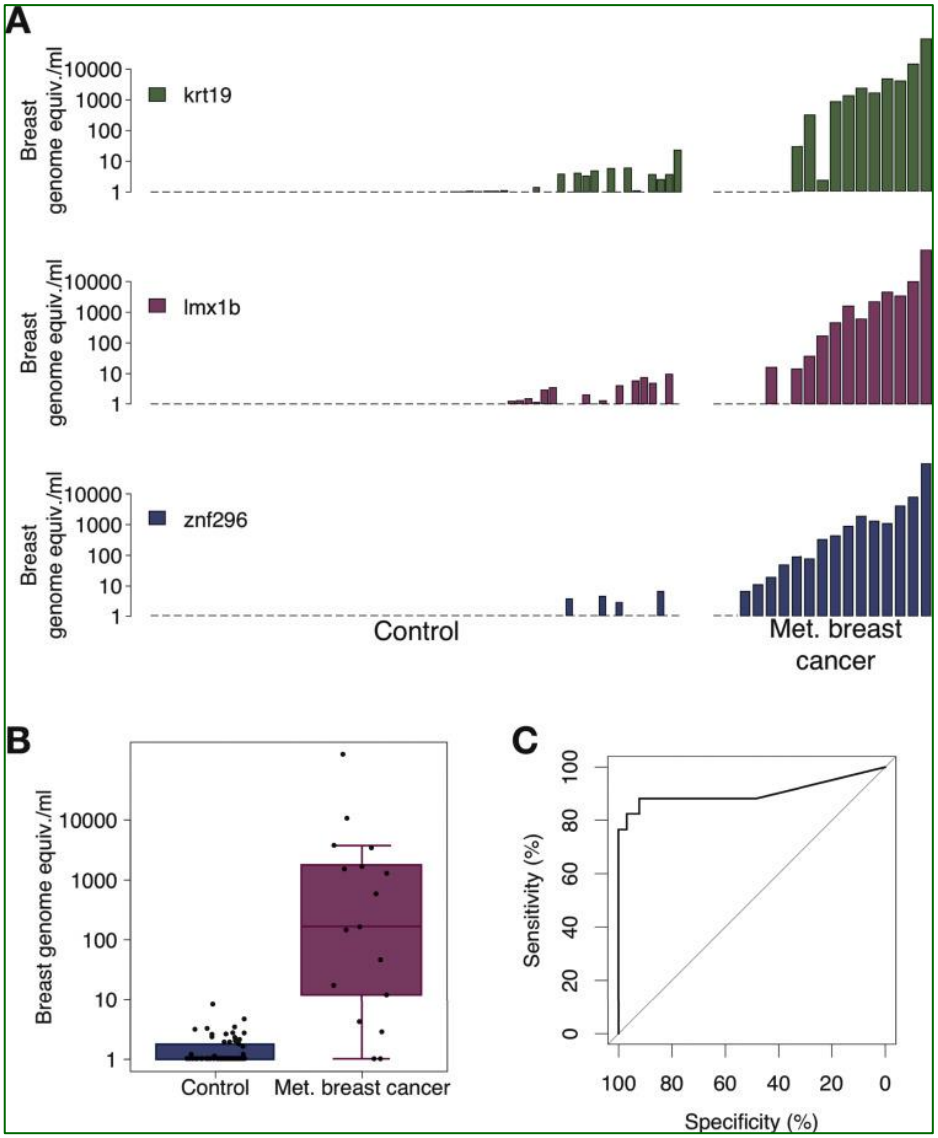



Corcoran *et al,* 2018, *NEJM* 379:1754-1765.

# Breast Specific Methylation Pattern




Moss *et al,* 2020, *Ann Oncol.* Mar;31(3):395-403

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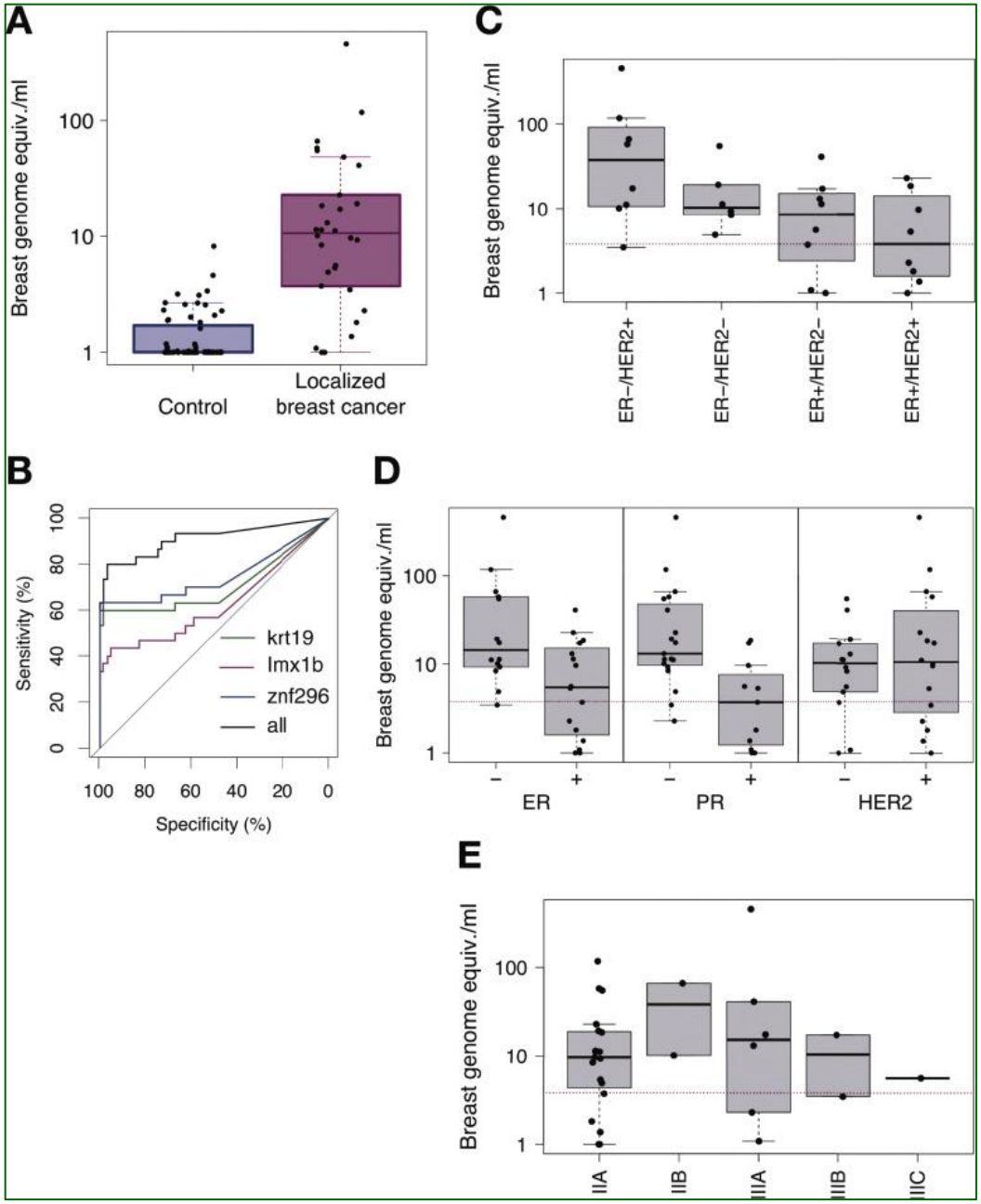


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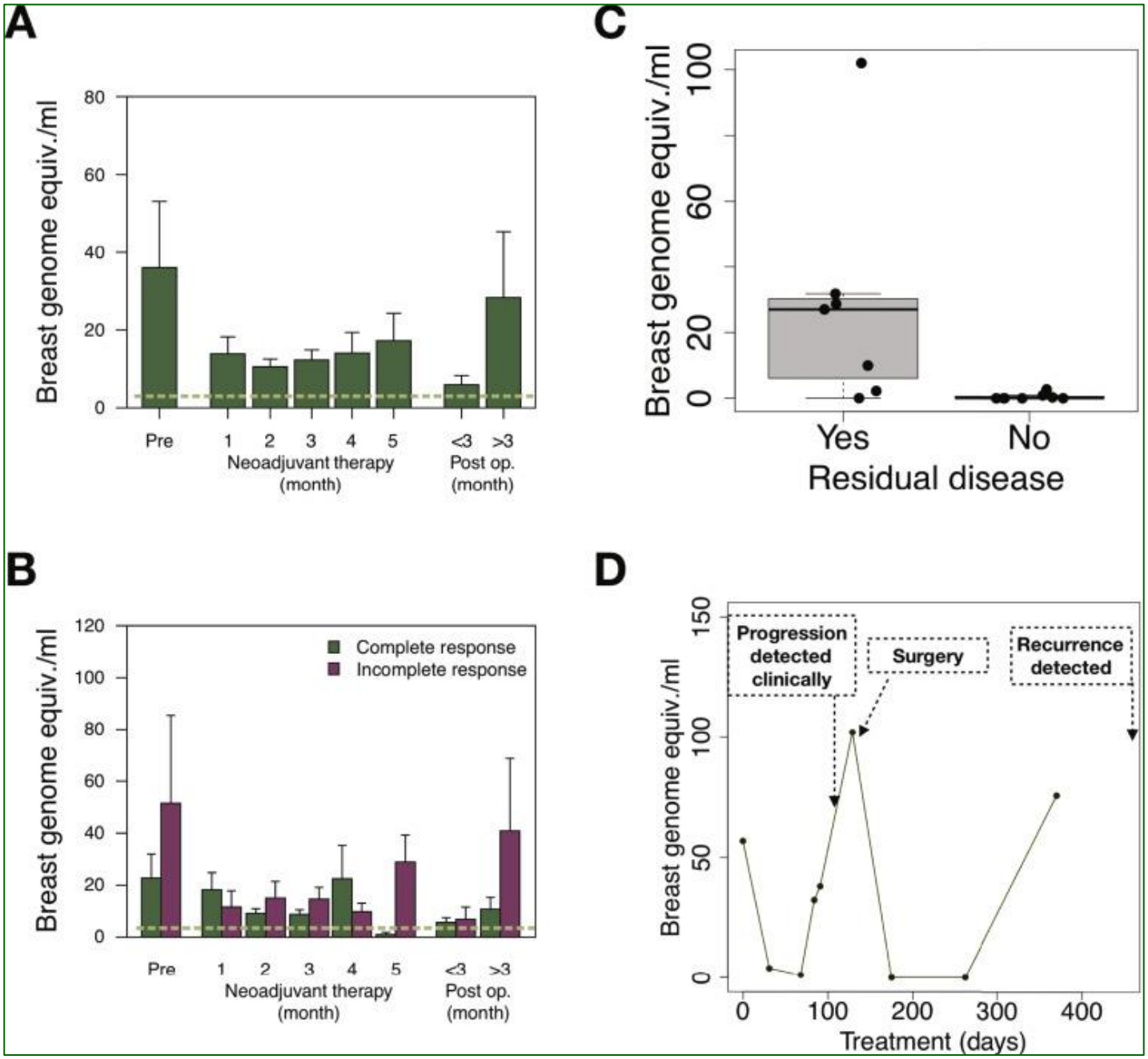
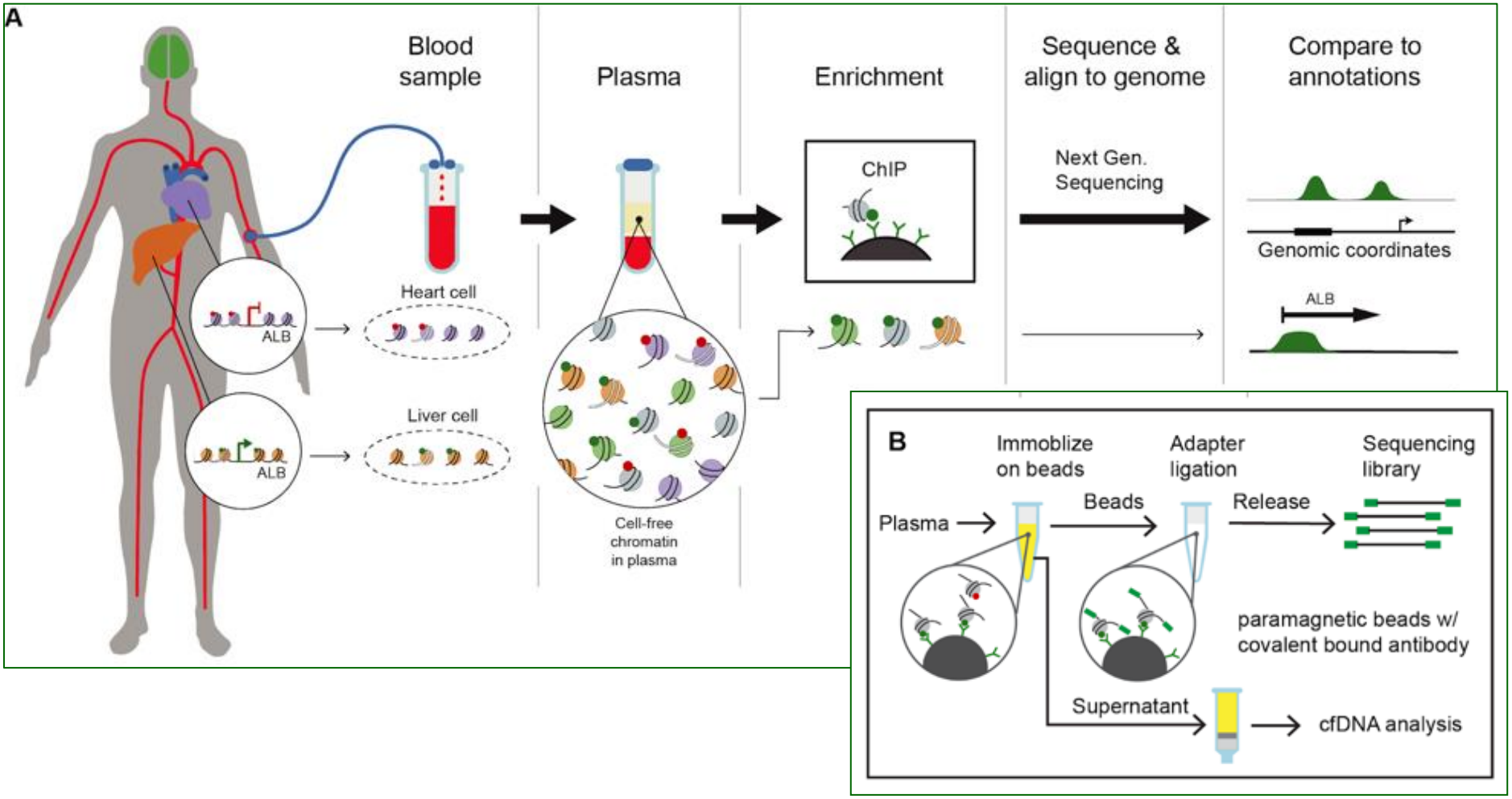


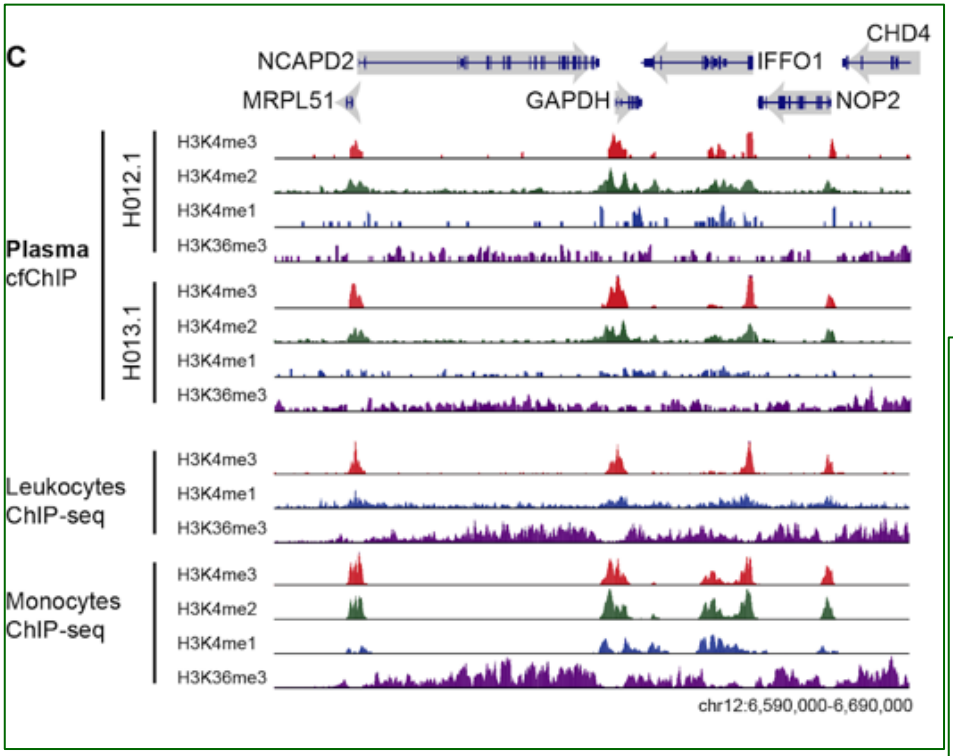

Moss *et al,* 2020, *Ann Oncol.* Mar;31(3):395-403

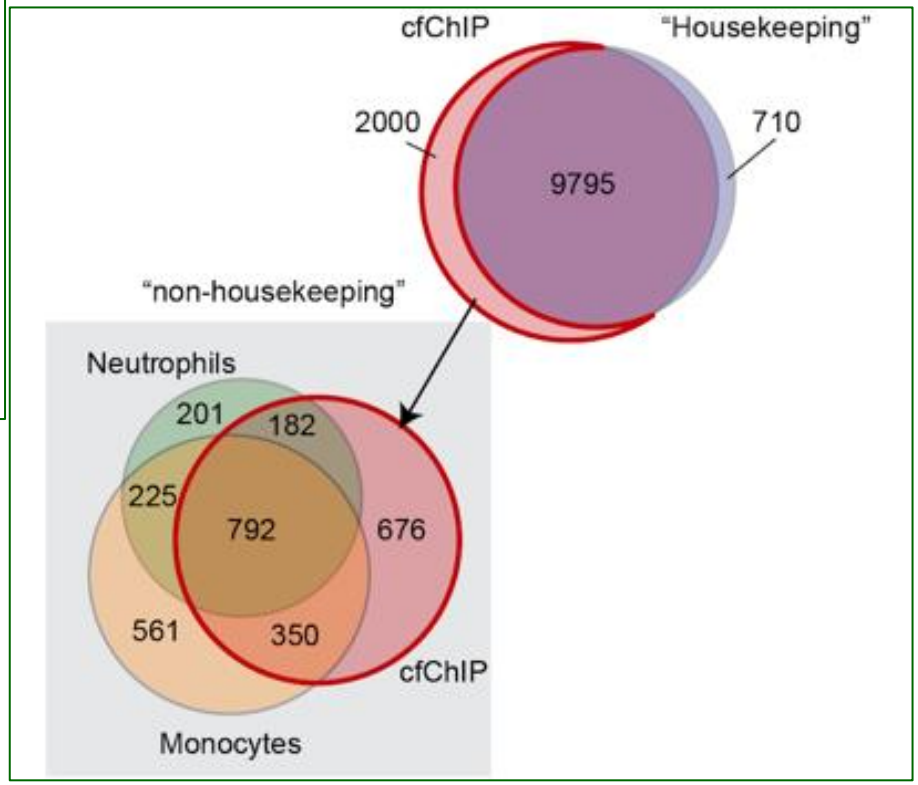
# Immunoprecipitation of chromatin from plasma




Sadeh *et al,* 2021, *Nat Biotechnol.* May;39(5):642.

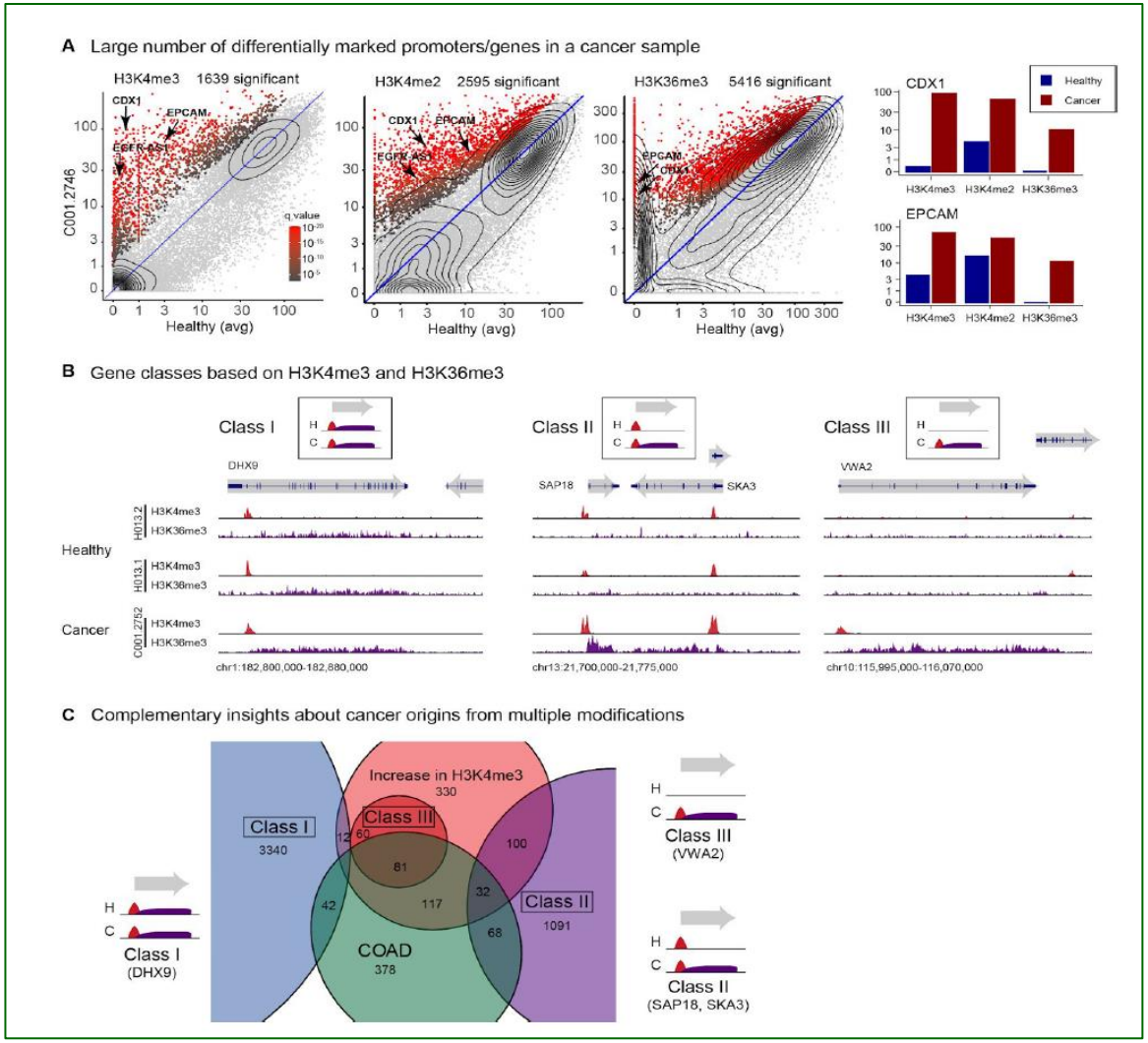
# cfChIP recaptures the transcriptional program of cells



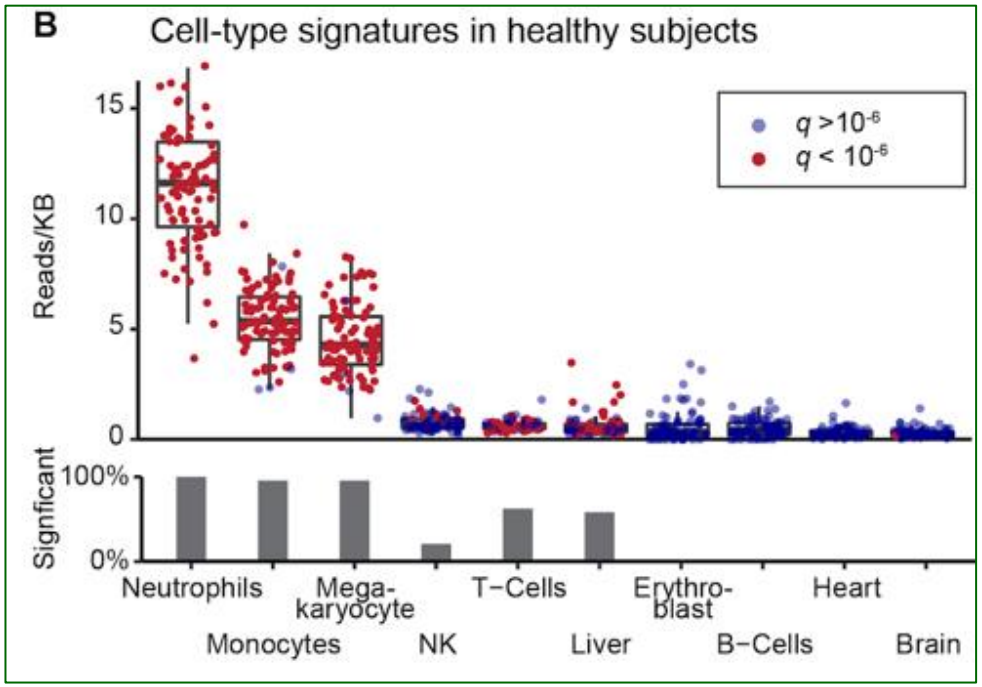

Sadeh *et al*, Nature biotechnology, 2020

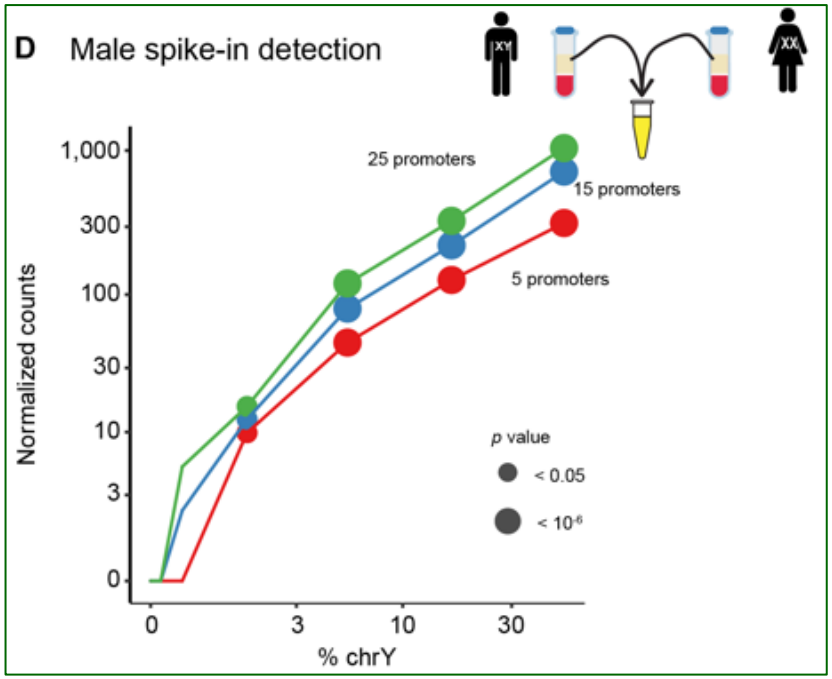
# cfChIP-seq of multiple marks is informative on gene expression




Sadeh *et al*, Nature biotechnology, 2020

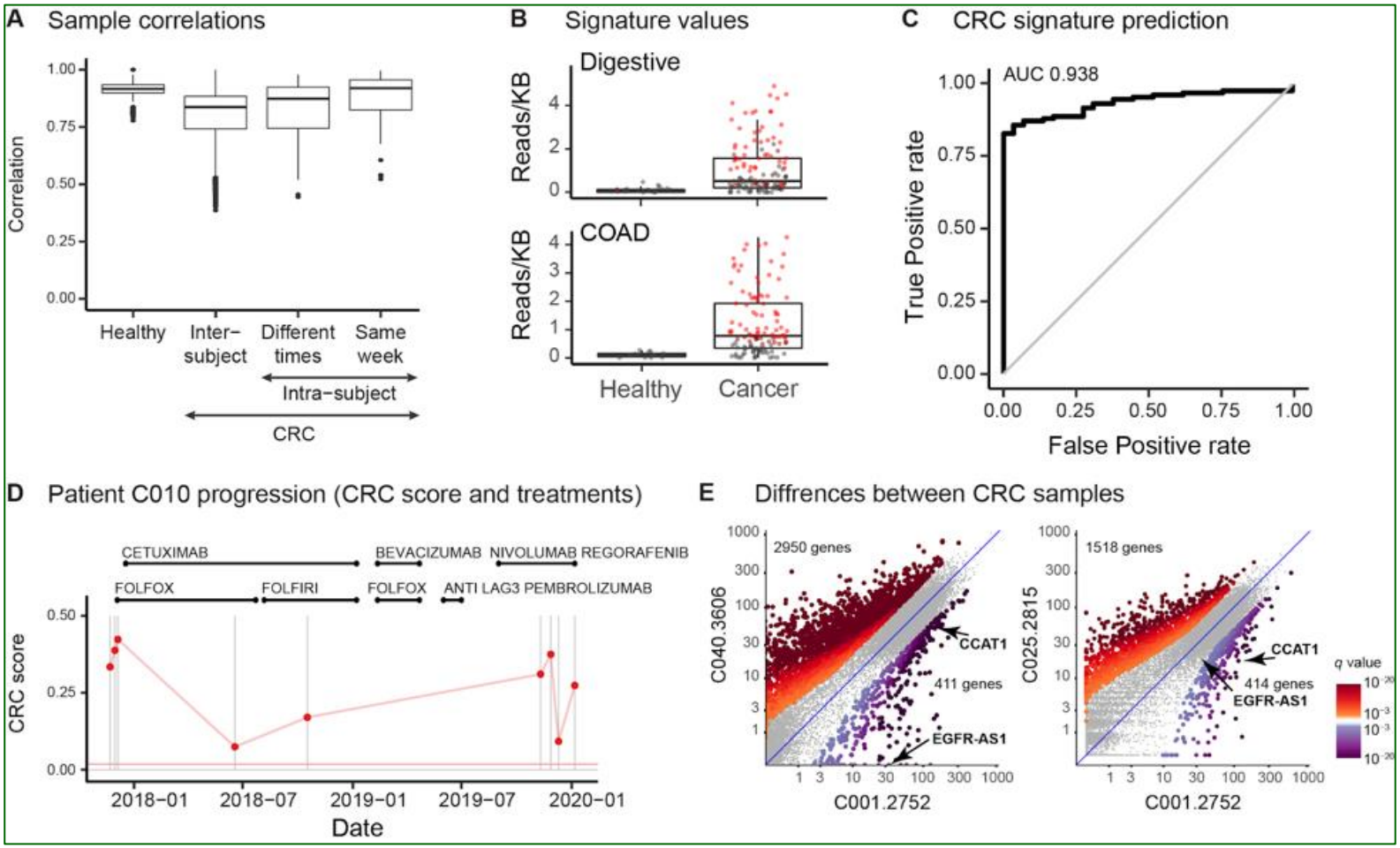
# cfChIP is sensitive



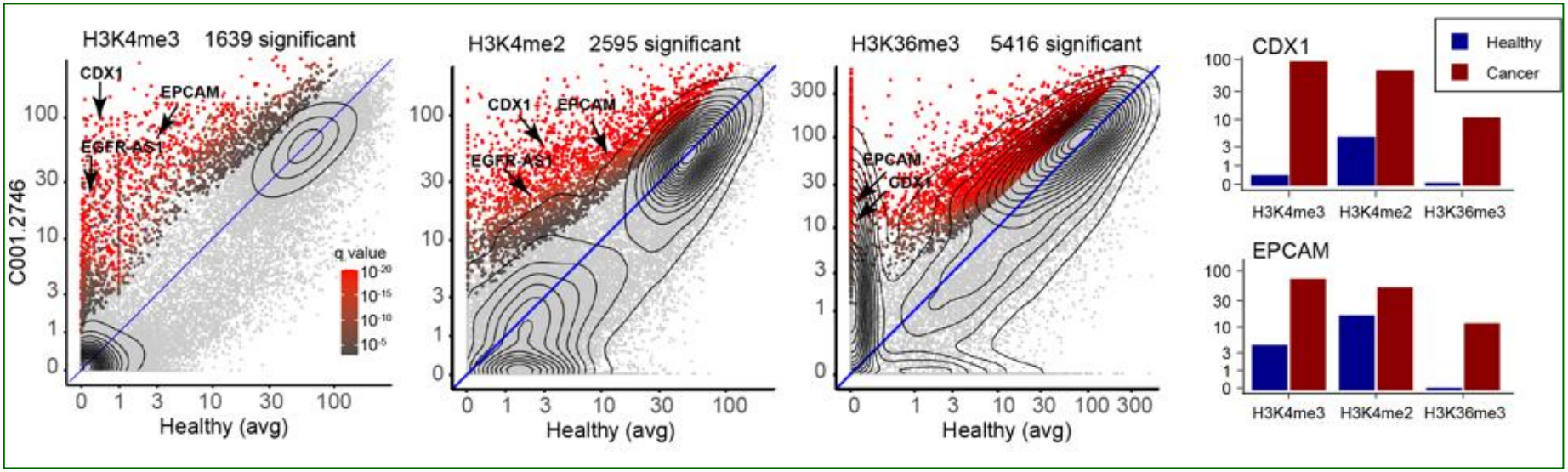

Sadeh *et al*, Nature biotechnology, 2020

# cfChIP identifies unique expression patterns in different cancer patients



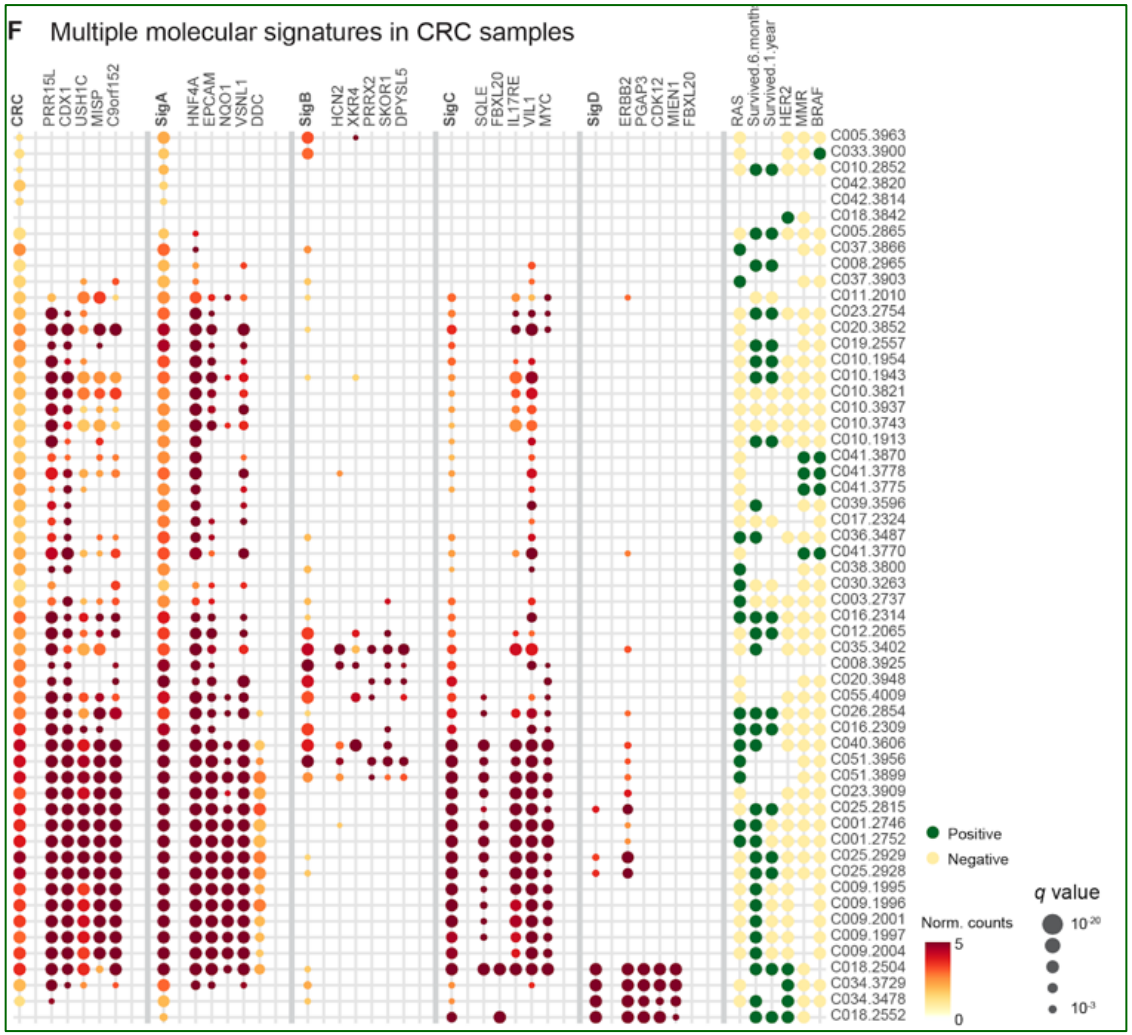

Sadeh *et al*, Nature biotechnology, 2020

# cfChIP finds a large difference between healthy and colon cancer patients



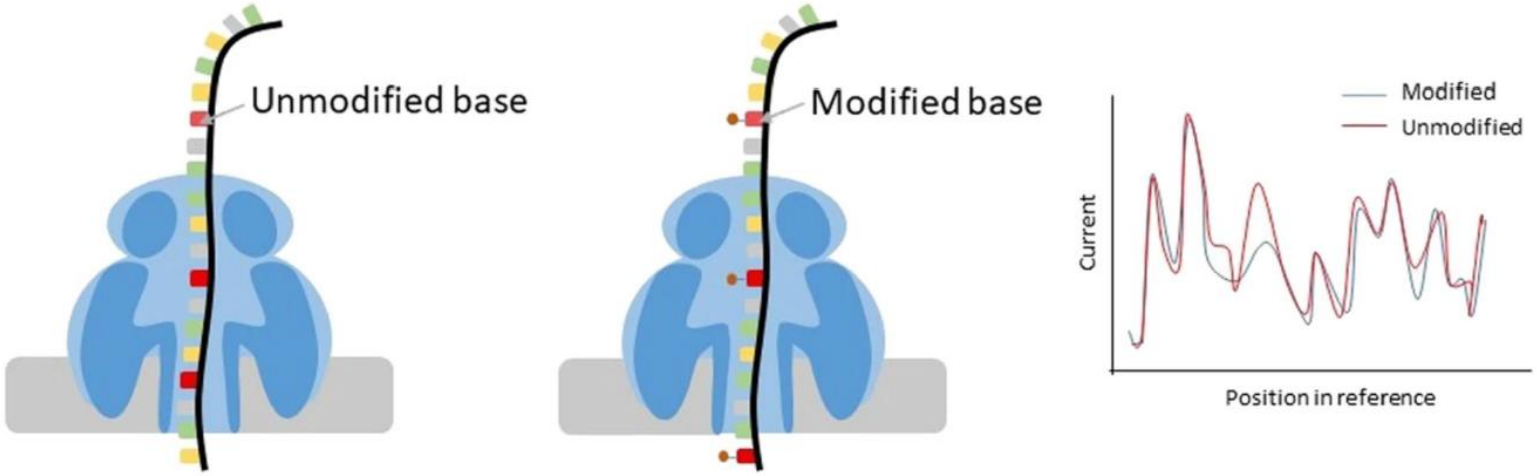

Sadeh *et al*, Nature biotechnology, 2020

# cfChIP identifies HER2 activation




Sadeh *et al,* 2021, *Nat Biotechnol.* May;39(5):642.

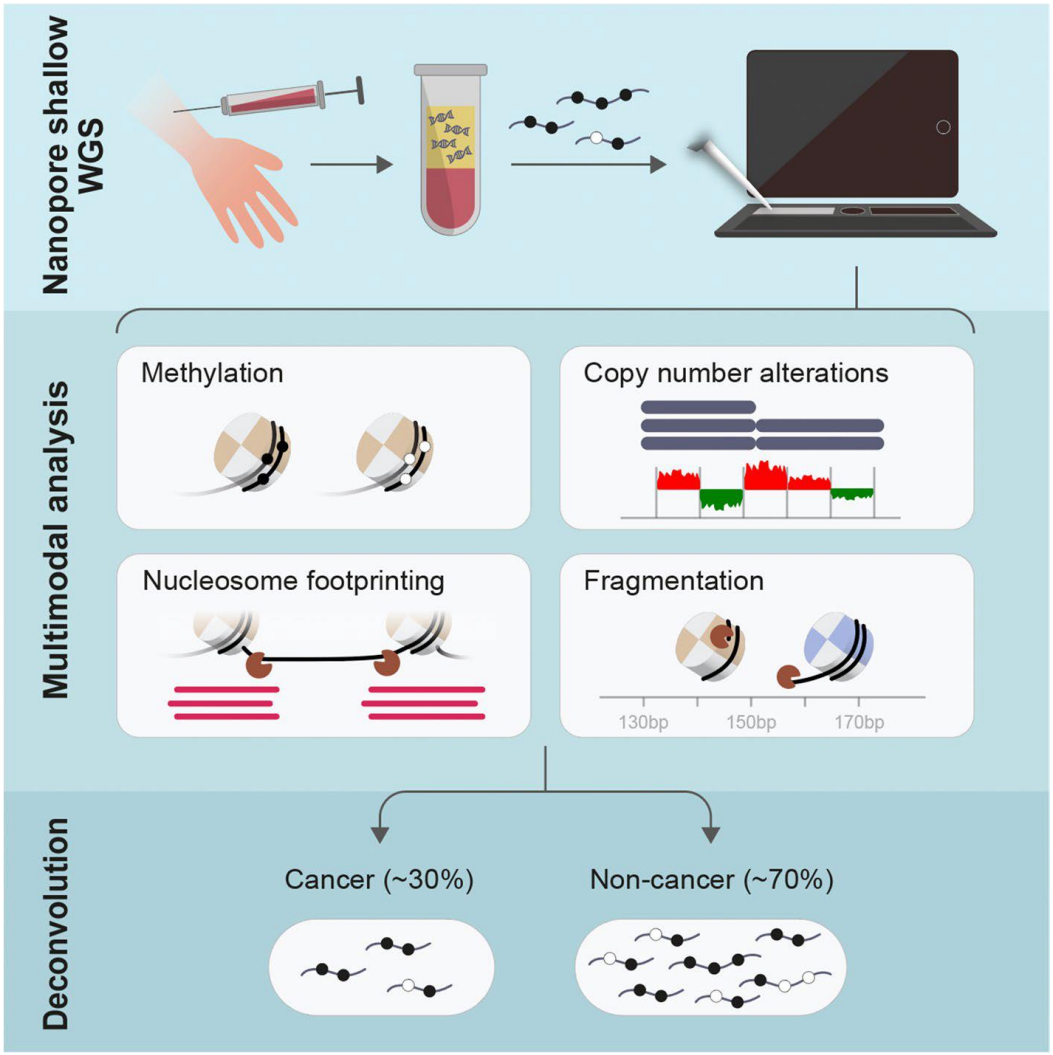
# Oxford Nanopore: Direct detection of DNA methylation




Adapted from Prof. Ben Berman

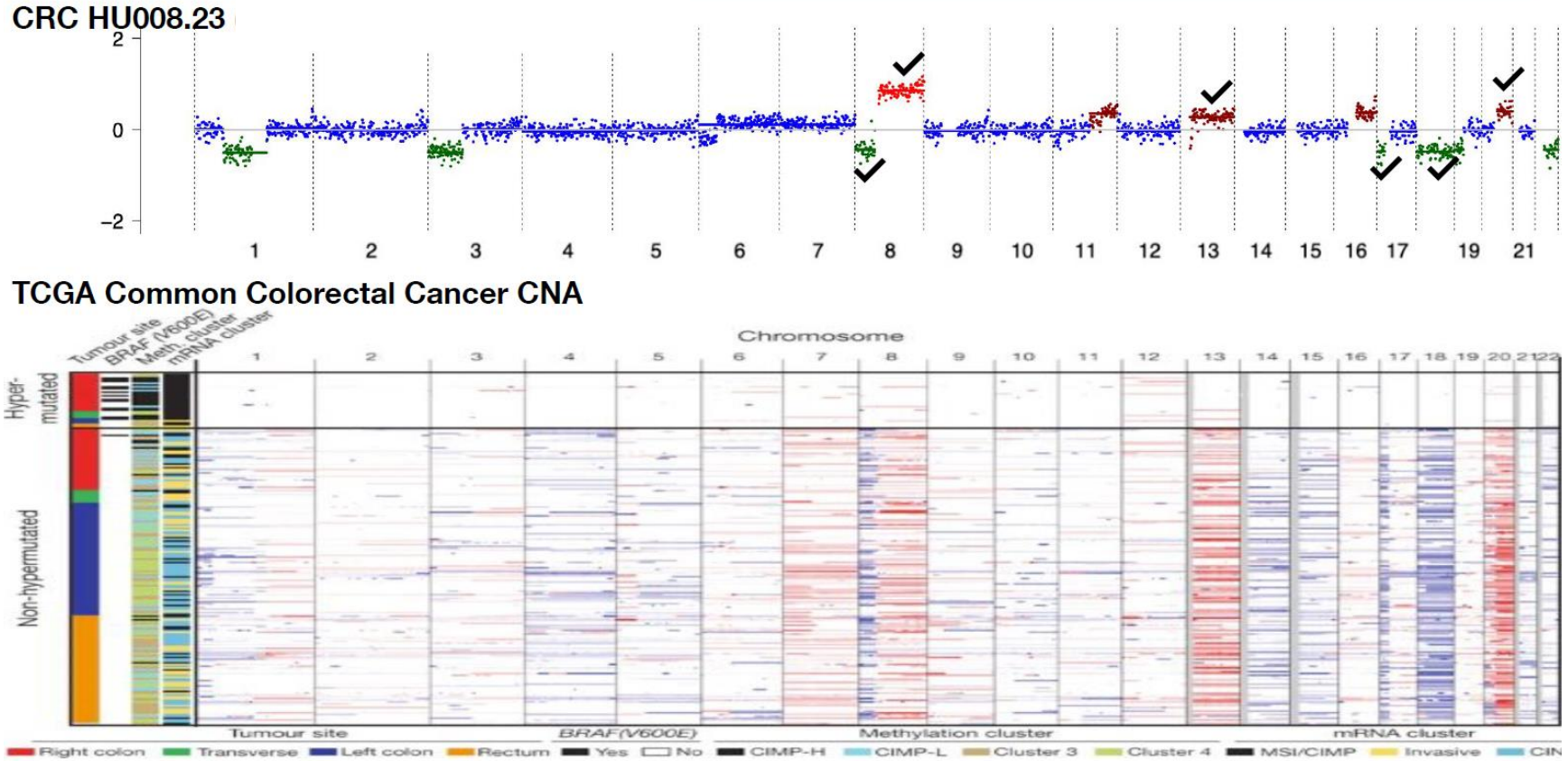
Xu and Seki, Journal of Human Genetics, 2020

# cfNano: Nanopore shallow WGS detects ctDNA



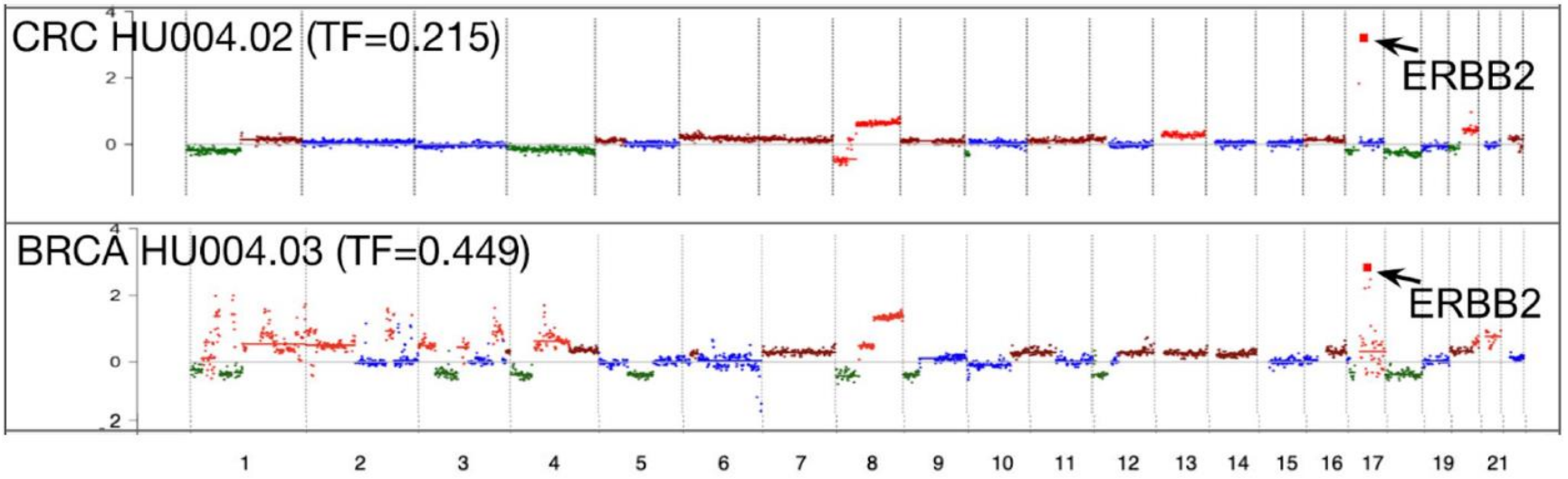

Katsman et al. *Genome Biology* 2022

# cfNANO detects copy number alterations in ctDNA



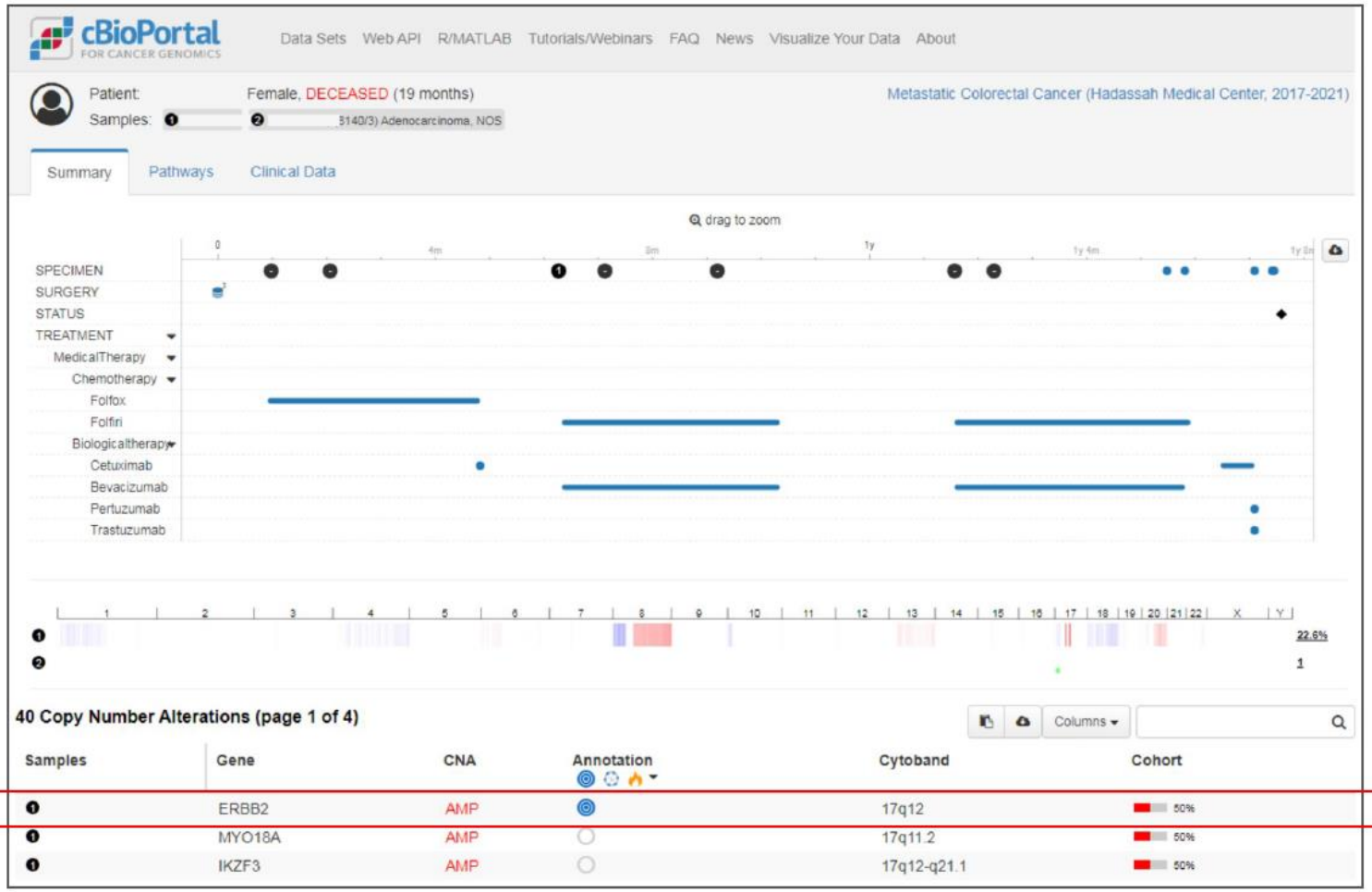

Berman *et* al, unpublished 2022

# cfNANO detects *ERBB2* amplifications




Berman *et* al, unpublished 2022

# cBioPortal allows an integrated view of clinical and pathological information




Berman *et* al, unpublished 2022

# Conclusion

Epigenetic cfDNA can be used in the clinical setting

Can identify response to chemotherapy

Can identify critical expression patterns such as HER2

# Future plans

Integrate Epigenetic cfDNA to routine practice as

- A tumor marker
- A tool for early detection of cancer
- Early detection tissue damage before clinically apparent.

Integrate Epigenetic cfDNA to clinical trials to identify predictive and prognostic markers as well as gain further understanding of the biological mechanisms underlying drug activity.

Thank you very much