IDENTIFYING DIFFERENTIAL DNA METHYLATION PATTERNS IN PEOPLE WITH AND WITHOUT HEAD & NECK CANCER

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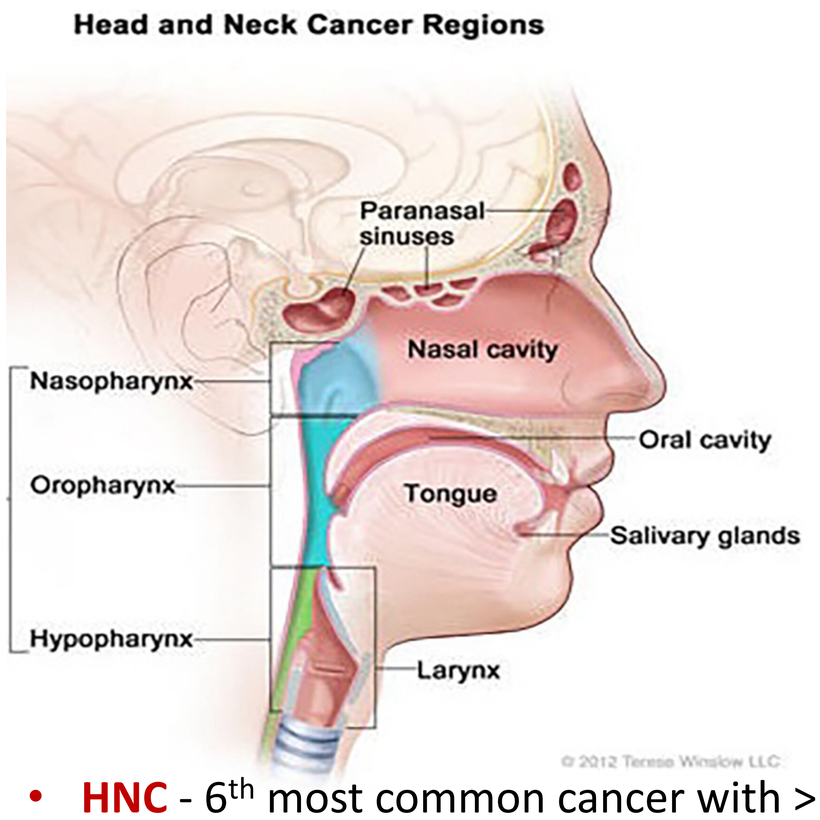
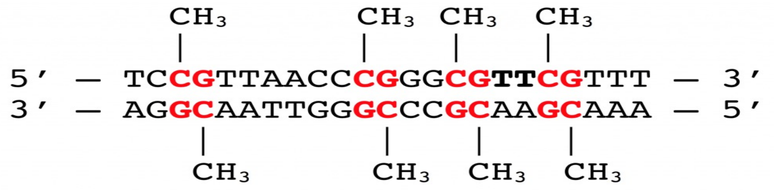
BACKGROUND



- **HNC** - 6th most common cancer with > half million annual diagnoses.[1]
- One of the highest morbidity & suicide rates among all cancers.[2]
- 7900 new HNC cases & 2100 deaths.[3]
- Major risk factors (tobacco, alcohol, HPV) increase HNC risk through epigenetic changes.
- **DNA methylation (DNAm)** – addition of –CH3 group to CpG dinucleotide in DNA sequence, alters transcription and gene expression.[4]
- Global hypomethylation -> oncogene activation[5,6] and Gene-specific promoter region hypermethylation -> inactivates tumor suppressor genes, cause genomic instability.[7]
- These epigenetic changes can be used to identify individuals with ↑ HNC risk.

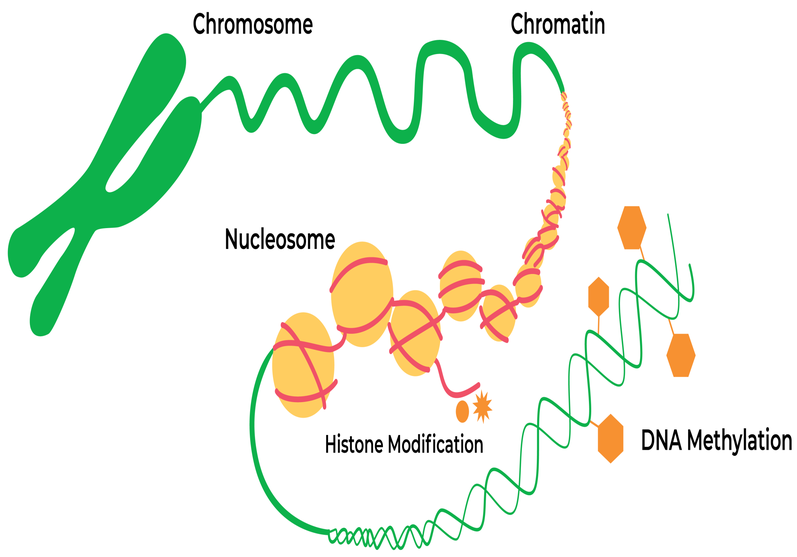
RATIONALE



- This project is part of a major research investigating the associations among epigenetic events (DNAm), life course exposures, and HNC risk.
- Here, we specifically aim to estimate the extent to which differentially methylated regions (DMRs) differ in patients with and without HNC.

OBJECTIVES

1. To identify DMRs between tumour tissue of HNC cases & oral mucosal tissue of non-cancer controls.
2. To identify DMRs shortlisted in Aim1 that are related to the carcinogenic process alone, by comparing contralateral non-cancerous oral mucosal tissue & tumour tissue from the same HNC cases.



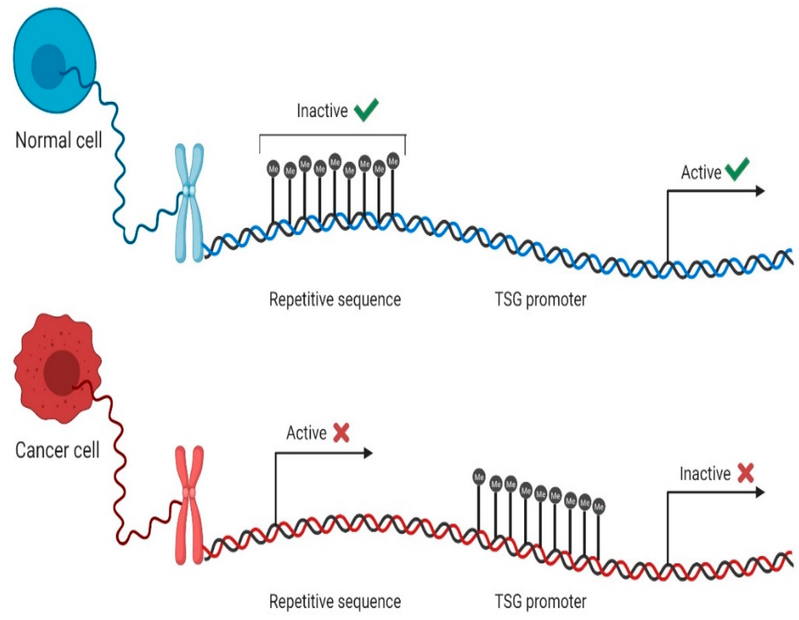
https://zymoresearch.eu/what-is-epigenetics

METHODS

- **Study Design:** Hospital Case Control; 460 incident HNC cases & 458 controls frequency matched (by age & sex) recruited from four main referral hospitals in Montreal.
- **In-person interviews** collected information on lifetime exposures to tobacco, alcohol & HPV infection using life grid tool & questionnaire.
- **Sample collection:** Brush biopsy from tumor & healthy mucosa in cases, oral mucosa in controls, oral rinse in both.
- **DNA Extraction** from biopsy samples & oral exfoliated cells.
- **DNAm Analysis** at Genome Center, Montreal: Bisulfite treatment

  Illumina® methylation EPIC Bead Chip (850k) to quantify DNAm.

  Illumina manifest file to define gene promoter & body regions.



Nunes SP et al. Cells. 2020

- **Data Analytical Strategy** – Bayesian curve credible band approach to identify DMRs between comparison groups in Aim 1 & 2.
- **BCurve** – flexible mixed effect model, considers spatial correlation between CpG sites.
- Construct confidence bands for average methylation levels in comparison groups.
- Identify regions where the confidence bands do not overlap i.e., DMRs.

ANTICIPATED RESULTS

- We anticipate identifying distinct DNAm patterns among HNC cases & controls.
- Results will be subsequently used to investigate whether DNAm patterns are associated with life course exposures & HNC risk.

SIGNIFICANCE

- Pioneering effort investigating epigenetics (DNAm patterns) and its link with increased HNC risk.
- Provide insights into HNC etiology.
- Potential identification of early carcinogenic biomarkers.

References:
*1.Cancer today 2020, 2.Zeller JL. 2006, 3.*Canadian Cancer Statistics 2023,
4.Bird A. 2007, 5.Smith et al. 2007, 6.Jones PA & Baylin SB 2002,
7.Deaton AM & Bird A 2011

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