Etiology of Head and Neck Squamous Cell Carcinoma (HNSCC)

香港中文大學
The Chinese University of Hong Kong

- 2nd year Mphil student: Emily Lei
- Supervisor: Professor Zigui Chen

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CU Medicine HONG KONG
香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

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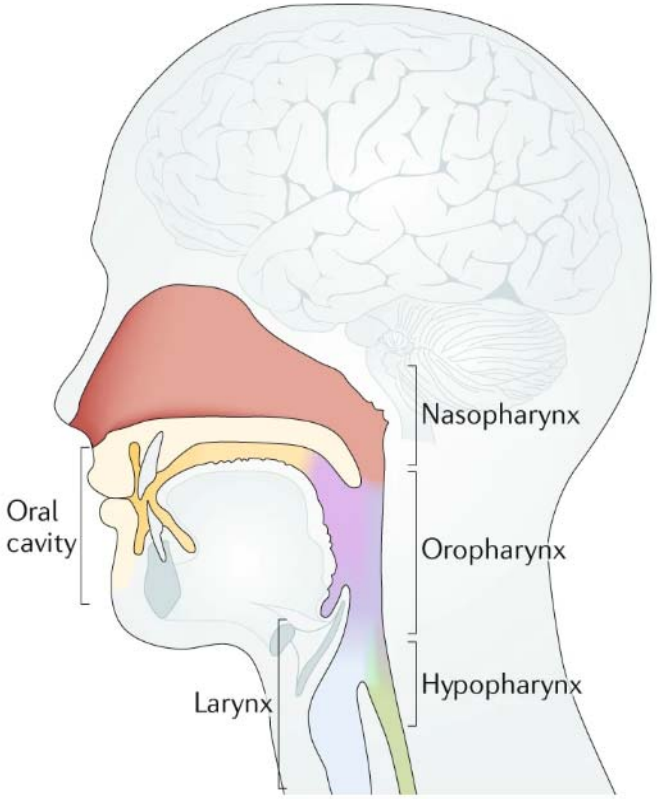
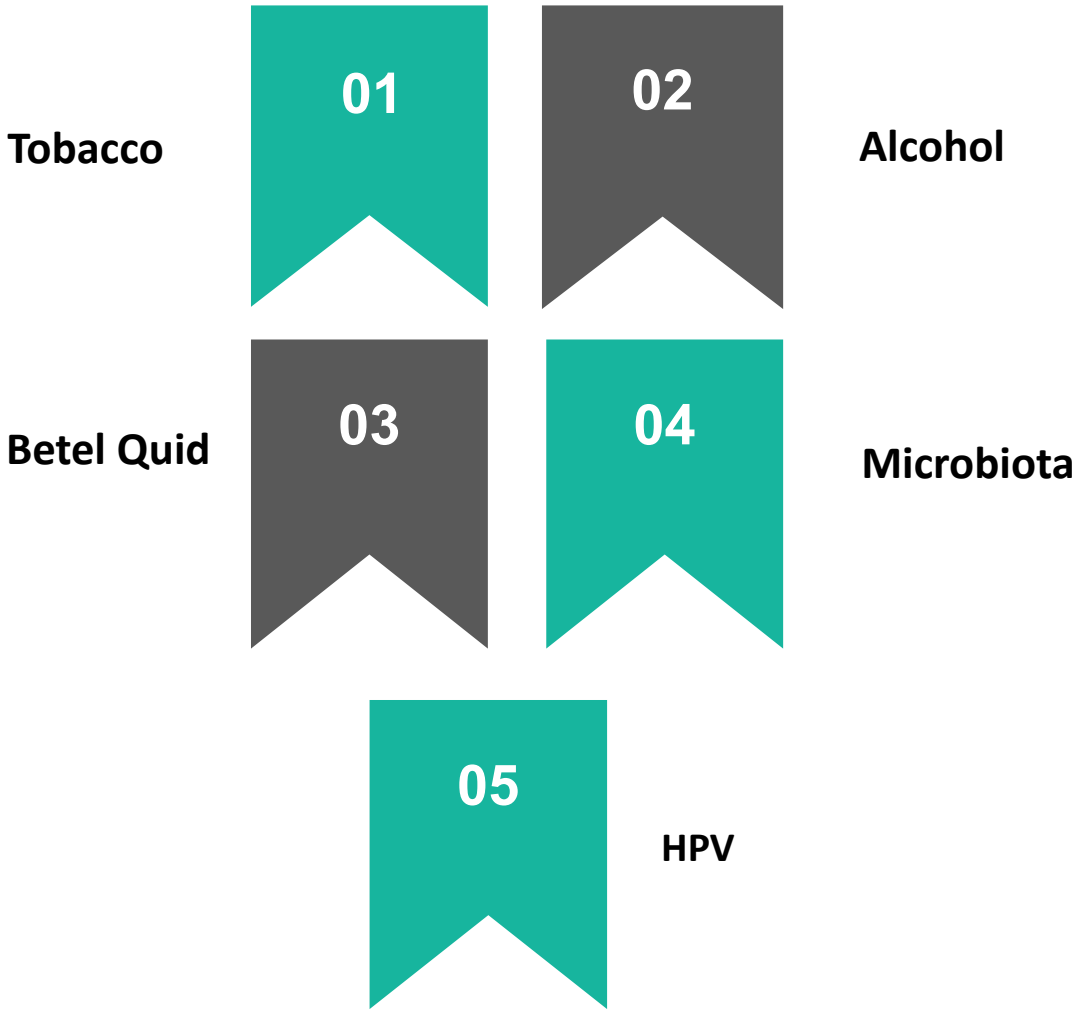
Background of Head and Neck Squamous Cell Carcinoma

- Head and neck squamous cell carcinoma (HNSCC) is the **6th** most common cancer, with > 500,000 cases diagnosed annually worldwide;
- At present, there is no accepted screening test for HNSCC at early stage, resulted in **low survival rate**;
- Many factors were associated with HNSCC including **host genetic and epigenetic changes**, **smoking**, **alcohol abuse**, **betel quid** and **mircoorganism infection**



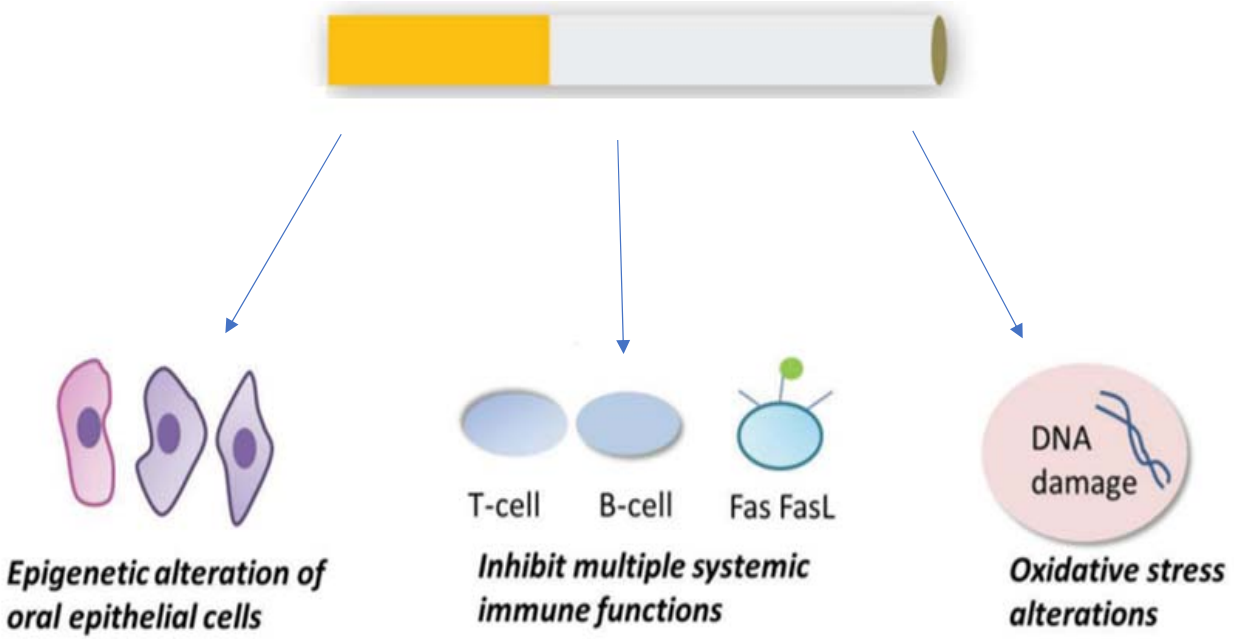
Cramer, John D., et al. "The changing therapeutic landscape of head and neck cancer." *Nature Reviews Clinical Oncology* 16.11 (2019): 669-683.

Risk factors



Risk factor--Tobacco

Carcinogenic factor



Jiang, Xiao ge, et al. "Tobacco and oral squamous cell carcinoma: A review of carcinogenic pathways." *Tobacco Induced Diseases* 17 (2019)

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Risk factor--Alcohol

Alcohol

Folate Cycle

Methylation (Epigenetic Events)

DNA synthesis (Cell Division)

Varela-Rey, Marta, et al. "Alcohol, DNA methylation, and cancer." *Alcohol research: current reviews* 35.1 (2013): 25.

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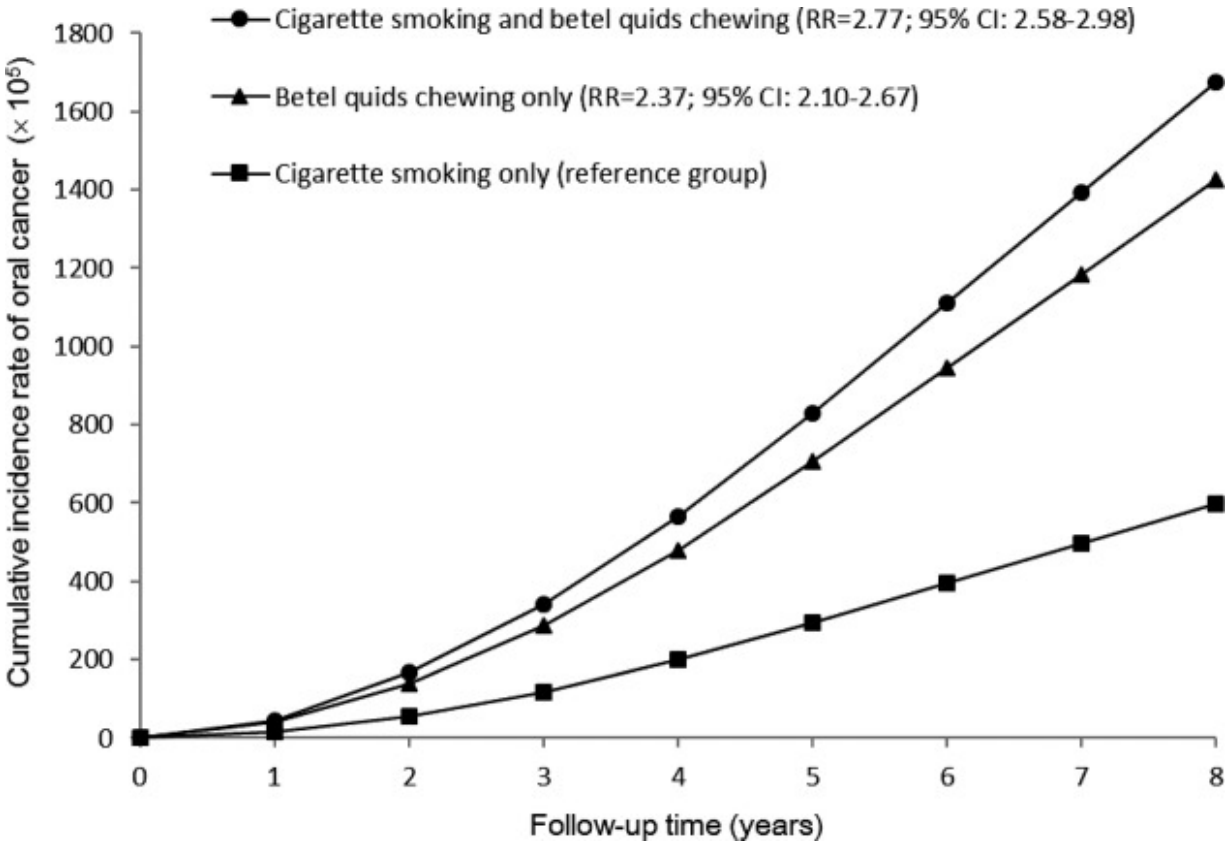
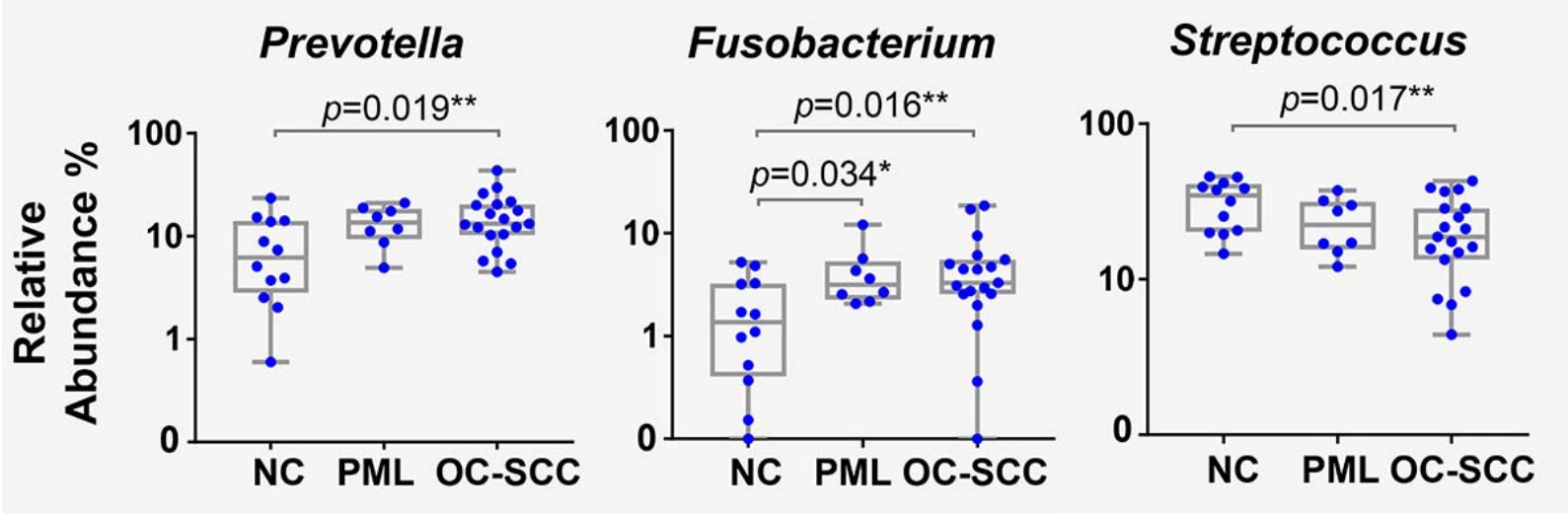
Risk factor-Betel Quid



How Betel Quid affected development of HNSCC is unknown

Chuang, Shu Lin , et al. "Population-based screening program for reducing oral cancer mortality in 2,334,299 Taiwanese cigarette smokers and/or betel quid chewers." Cancer 123.9(2017):1597-1609.

Risk factor--Microbiota

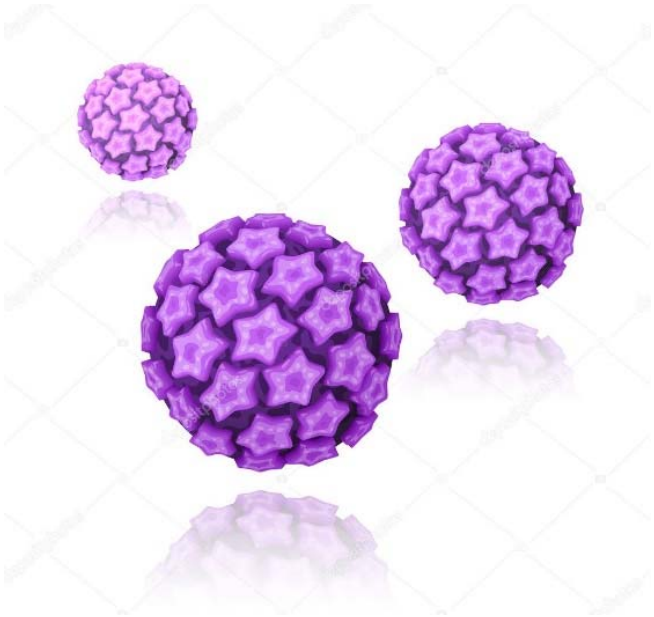


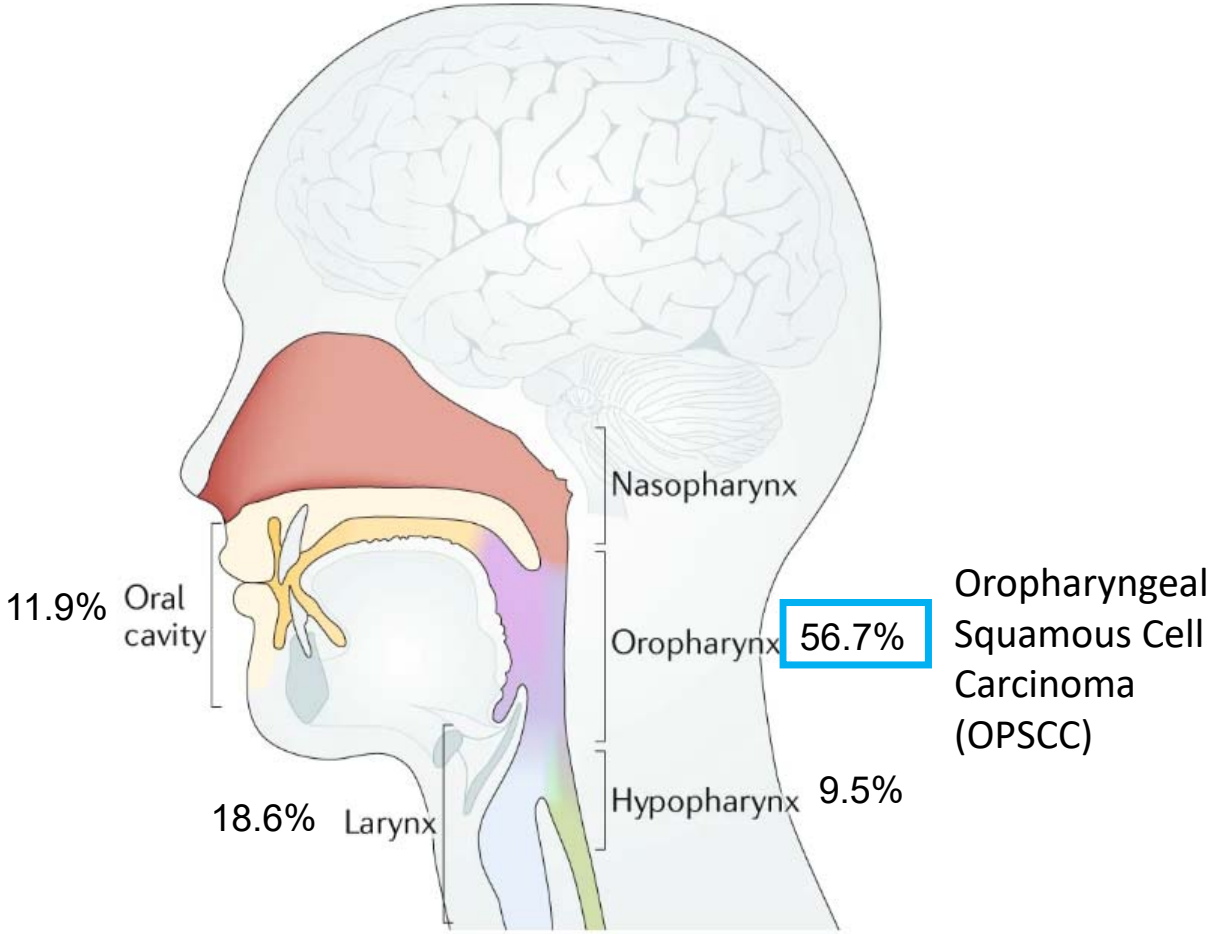
- *Fusobacterium* and *Prevotella* were significantly more abundant in OCSCC compared to NC, while *Streptococcus* was less abundant.
- *Fusobacterium* was significantly more predominant in PML than NC.

OCSCC: Oral cavity squamous cell carcinoma (18);PML: Premalignant lesion (8);NC: Negative controls (12)

Ganly, Ian, et al. "Periodontal pathogens are a risk factor of oral cavity squamous cell carcinoma, independent of tobacco and alcohol and human papillomavirus." International journal of cancer (2019).

Risk factor--HPV





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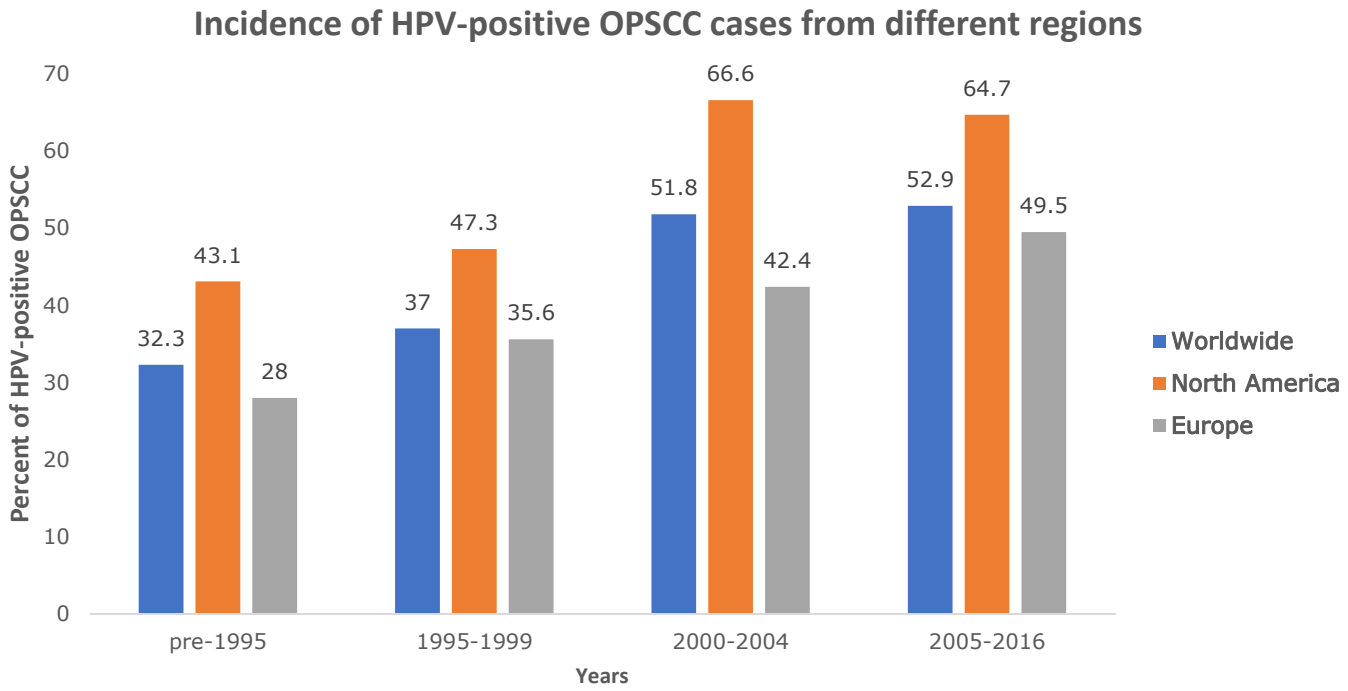
Incidence of HPV-positive OPSCC



- Frequency of HPV-positive OPSCC worldwide, in North America and across Europe
- Increasing trend of HPV-positive OPSCC incidence (>50%) worldwide

Stein, Andrew P., et al. "Prevalence of human papillomavirus in oropharyngeal cancer: a systematic review." Cancer journal 21.3 (2015): 138.

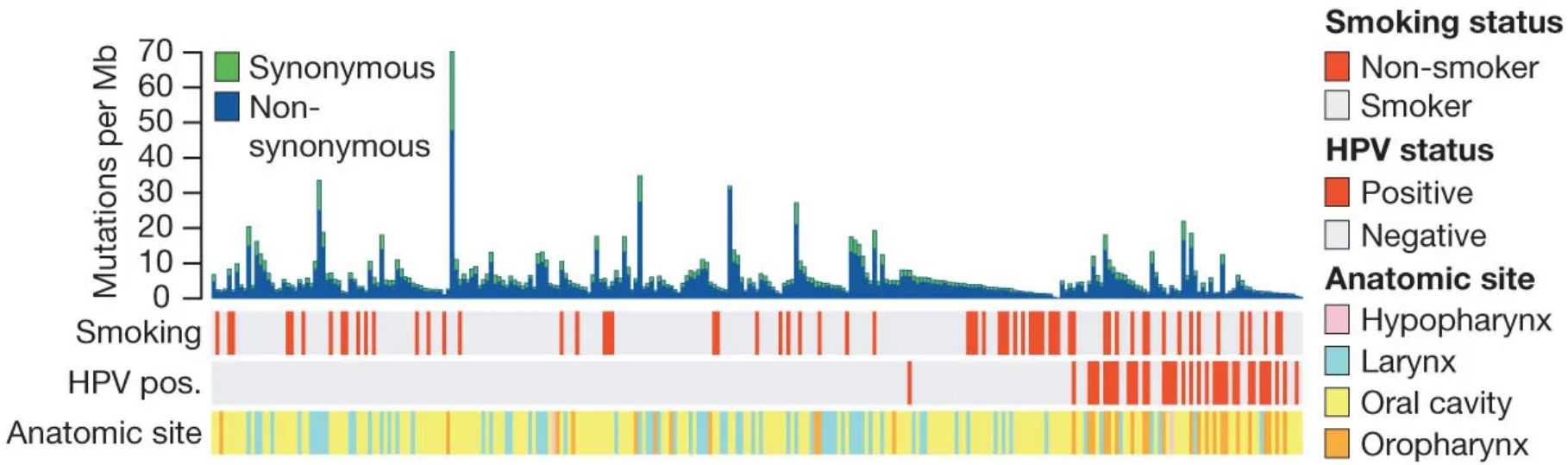
Case study in different HNSCC tumors

Published in final edited form as:
Nature. 2015 January 29; 517(7536): 576–582. doi:10.1038/nature14129.

Comprehensive genomic characterization of head and neck squamous cell carcinomas

The Cancer Genome Atlas Network *

36 HPV(+) and 243 HPV(-) tumors are found



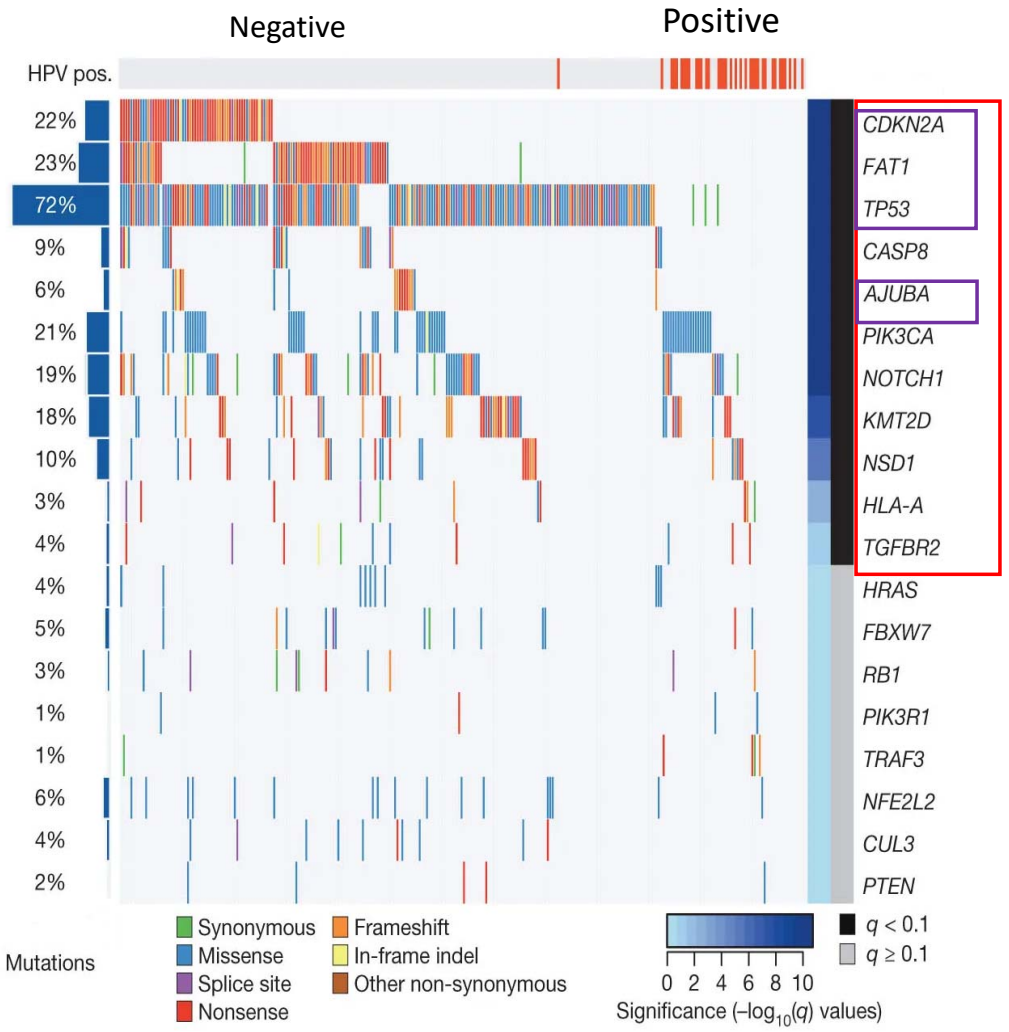
- This case investigated gene expression patterns of different patients' tumors from oral cavity(172/279), oropharynx(33/279), laryngeal sites(72/279)

- Most patients were heavy smokers

Cancer Genome Atlas Network. "Comprehensive genomic characterization of head and neck squamous cell carcinomas." *Nature* 517. (2015): 576.

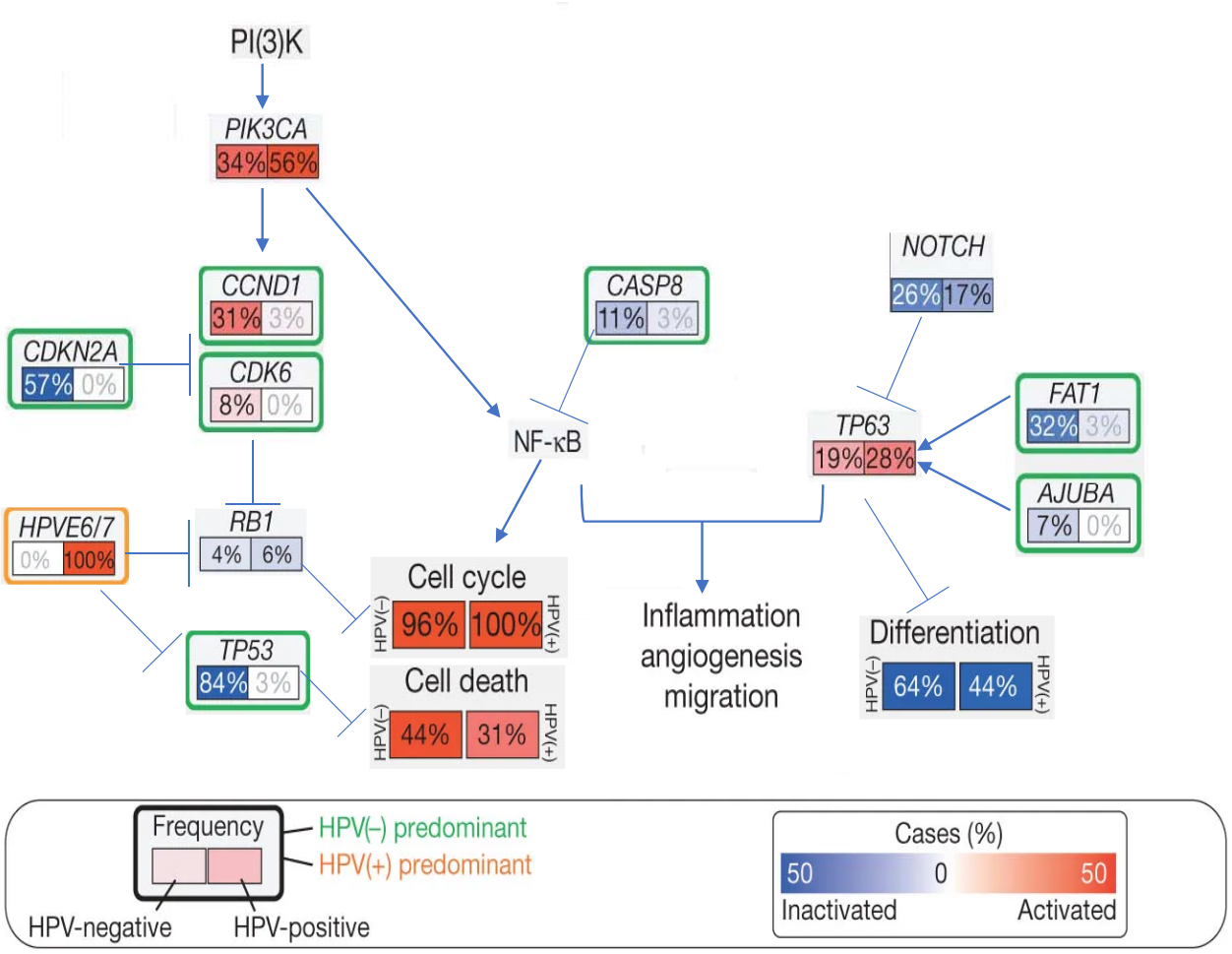
Gene mutations were found in both HPV(+) and (-)

- The study compared the HPV (+) and (-) patients' gene composition through RNA-sequencing
- 11 Genes were significantly identified with mutations
- Among inactivating mutations (missense, nonsense, splicing and frameshift), four genes (*CDKN2A*, *FAT1*, *TP53* & *AJUBA*) showed higher identifications in HPV(-) tumors compared to HPV(+) group.
- Mutations of gene *CASP8*, *PIK3CA* and *NOTCH1* that acquired missense mutations were found in both HPV(+) and (-) groups.



Cancer Genome Atlas Network. "Comprehensive genomic characterization of head and neck squamous cell carcinomas." *Nature* 517. (2015): 576.

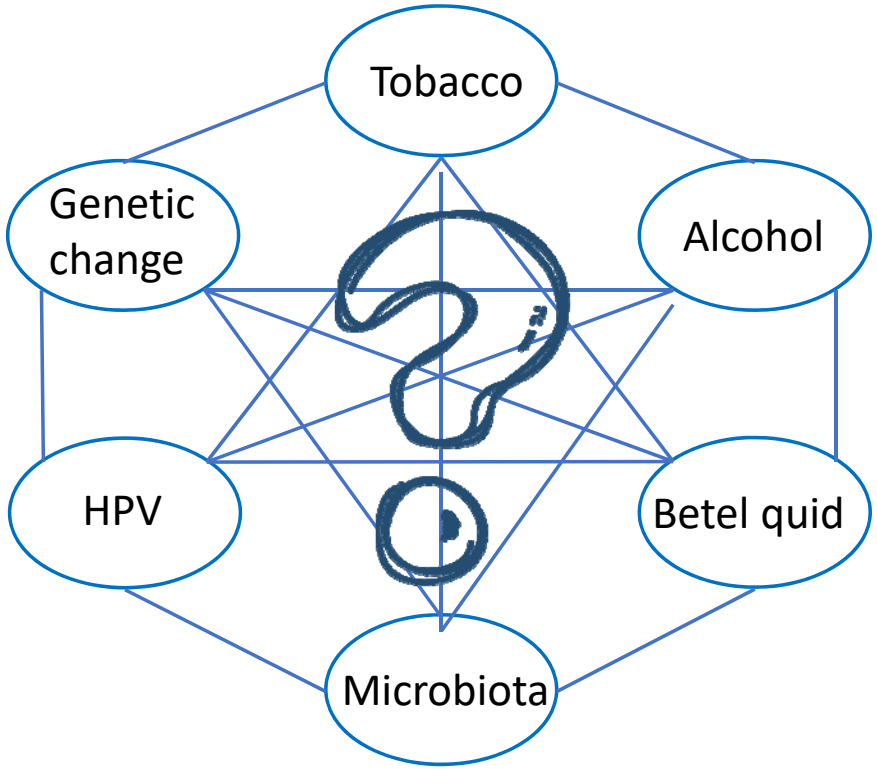
Overall pathway influenced by genes mentioned before



- Gene *Casp8*, *TP53*, *CDKN2A*, *NOTCH*, *FAT1*, and *AJUBA* were **inactivated** in both HPV(+) and HPV(-) tumors, but differences of cases percent between the two are shown
- *PIK3CA*, *CCND1*, and *TP63* were **activated**
- We can see the Cell cycle and Cell death are activated, but Cell differentiation is inactivated.
- Obvious difference in Cell death pathway and differentiation between HPV(+) and HPV(-) tumors

Cancer Genome Atlas Network. "Comprehensive genomic characterization of head and neck squamous cell carcinomas." *Nature* 517. (2015): 576.

Research gaps& Future study



- Although the previous study pointed out key targets (*TP53, PIK3CA* & *NOTCH1)* that associated with HNSCC, the exact functional roles need to be investigated, which could be the potential therapy targets.
- At present, there is no study clearly explain how these risk factors lead to the development of HNSCC
- The related pathways that trigger HNSCC still remained to be explored

References

1.Jiang, Xiaoge, et al. "Tobacco and oral squamous cell carcinoma: A review of carcinogenic pathways." *Tobacco Induced Diseases* 17 (2019)

2.Varela-Rey, Marta, et al. "Alcohol, DNA methylation, and cancer." *Alcohol research: current reviews* 35.1 (2013): 25.

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Thank you!

Q&A