Etiology of Head and Neck Squamous Cell Carcinoma (HNSCC)

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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 microorganism infection

Risk factors

01 Tobacco
02 Alcohol
03 Betel Quid
04 Microbiota
05 HPV
Risk factor--Tobacco

Risk factor--Alcohol

Risk factor—Betel Quid

How Betel Quid affected development of HNSCC is unknown

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)

Risk factor--HPV

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

Case study in different HNSCC tumors

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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

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.

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.

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


Thank you!

Q&A