Journal of Molecular Histology & Medical Physiology

Agarwal, J Mol Histol Med Physiol 2016, 1:2

Short Communication Open Access

# Cancer Genomics: Head and Neck Cancer

**Dr. Suraj Agarwal***

*Guru Gobind Singh Dental College, Burhanpur, India*

## Introduction

Head and neck cancer accounts for 4% of all malignancies worldwide, though it constitutes 40% of the cancer burden in India [1,2]. The distinct geographic predilection of head and neck squamous cell carcinoma (HNSCC), a major portion of the burden being laryngopharyngeal cancers, may be due to prevalence of risk factors and genetic susceptibility. Advances in treatment strategies have not been accompanied by a parallel improvement in the survival rates. The major reasons being late presentation, high occurrence rate and the development of multiple primary tumors (10-30%) [1-3]. Detection and identification of patients who are likely to respond to treatment so as to avoid unnecessary toxicity through identifying response/resistant markers are the critical questions that need to be addressed through a comprehensive and systemic approach.

With the advent of improved sequencing technologies such as Next Generation Sequencing (NGS), profiling a tumor to detect therapeutically relevant mutations is becoming an increasingly viable option. NGS based tests can typically profile a few hundred genes causally implicated and clinically relevant in cancer. This deep sequencing technology can detect mutations with far greater sensitivity than other conventional sequencing methods, thus making it ideal to study tumors. According to the COSMIC (database for somatic mutations in cancer, Dated 5 June 2016) database, the most frequently mutated genes in head and neck cancer include TP53, CDKN2A, PIK3CA, MET, HRAS, EGFR, PTEN, BRAF, KRAS, PIK3R1, IL6ST, JAK3, NFE2L2 and FBXW7. In depth assessment of the impact of these mutations such as with the Strand Somatic-48 gene test can yield therapeutically relevant insights and aid in prediction of clinical behaviour of the tumor depending on the mutation pattern. Hence, NGS based multigene testing helps build a larger actionable landscape of mutations thus facilitating minimal loss of time before arriving at the effective therapy option.

Mutation profile of the tumor could indicate poor response to a particular regimen that would be typically considered for the patient. Some mutations may be indicators of overall prognosis or response to certain types of chemotherapy. Chemotherapy and radiotherapy are very important treatment modalities in head and neck cancer patients; mutations in genes such as ATM, FBXW7 and TP53 can provide valuable information regarding responsiveness. It is increasingly being accepted that tumors of different origins can have the same driver mutations and hence can be targeted using the same drug. For example, cetuximab has been approved by FDA for colorectal cancer and more recently for head and neck cancer as well. More than 90% of the head and neck cancer patients overexpress EGFR, either due to amplification of the EGFR gene or polymorphic mutations [4,5], and thus, anti-EGFR drugs provide a therapeutic window. Although the results are promising, there are a few caveats to be considered. Firstly, in tumors treated with cetuximab, presence of an activating mutation in the downstream RAS/RAF/MEK pathway such as codon 12 or 13 mutation in KRAS would make the tumor refractory to anti-EGFR drugs. Such head and neck cancer patients will probably respond better to inhibitors of downstream proteins such as MEK inhibitors, trametinib or selumetinib [6,7]. Secondly, various clinical studies have reported that after the early response to cetuximab, head and neck tumors gradually acquire resistance to treatment [8,9]. In such cases, NGS based mutation profile can help in charting out a second line of treatment or a more aggressive first line of treatment. Head and neck cancer patients often harbour activating mutations in PIK3C, PTEN or AKT1 resulting in constitutive activation of the PI3K/m TOR/AKT pathway and thus, possibly sensitizing the tumors to mTOR inhibitors such as everolimus or temsirolimus [3].

Strand Somatic 48-gene test based molecular profiling and interpretation gives insight into patient responsiveness to approved treatment, potential treatment regimen inferred from other tumor types and patient prognosis. Treatment regimens aided by such an approach are likely to translate into tailored, less toxic and more cost-effective care.

### References

1. Partridge M, Li SR, Pateromichelakis S, Francis R, Phillips E, et al. (2000) Detection of minimal residual cancer to investigate why oral tumors recur despite seemingly adequate treatment, Clinical Cancer Research 6: 2718-2725.
2. Shah JP (1990) Cervical lymph node metases- diagnostic, therapeutic and prognostic implications. Oncology (Williston Park, NY) 4: 61-69.
3. Day GL, Blot WJ, Gina L (1992) Second primary tumors in patients with oral cancer. Cancer 70: 14-19.
4. Li H, Wawrose JS, Gooding WE, Grandis JR, et al. (2014) Molecular profiling of HNSCC cells and tumors reveals a rational approach to preclinical model selection. Mol Cancer Res 12: 571-582.
5. Wheeler S, Siwak DR, Chai R, LaValle C, Seethala RR, et al. (2012) Tumor epidermal growth factor receptor and EGFRPY 1068 are independent prognostic indicators for head and neck squamous cell carcinoma. Clin Cancer Res 18: 2278-2289.
6. Peeters M, Price TJ, Cervantes A, Sobrero AF, Ducreux M, et al. (2010) Randomized phase III study of panitumumab with fluorouracil, leucovorin and irinotectan (FOLFIRI) compared with FOLFIRI alone as second line treatment in patients with metastatic colorectal cancer. J Clin Oncol 28: 4706-4713.
7. Walters DM, Lindberg JM, Adair SJ, Newhook TE, Cowan CR, et al. (2013) Inhibition of the growth of patients augmented by combined treatment with the epidermal growth factor receptor/ HER2 inhibitor lapatinib. Neoplasia 15: 143-155.
8. Boeckx C, Baay M, Wouters A, Specenier P, Vermorken JB, et al. (2013) Anti-epidermal growth factor receptor therapy in head and neck squamous cell carcinoma: focus on potential molecular mechanisms of drug resistance Oncology 18: 850-864.
9. Rebucci M, Peixoto P, Dewitte A, Wattez N, De Nuncques MA, et al. (2011) Mechanisms underlying resistance to cetuximab in the HNSCC cell line: role of AKT inhibition in bypassing this resistance. Int J Oncol 38: 189-200.

***Corresponding author:** Suraj Agarwal (Oral and Maxillofacial Medicine and Radiology) Guru Gobind Singh Dental College, Burhanpur Consultant Oromaxillofacial Radiologist, Axis Imaging Centre, Agra Consultant, Oral Oncologist, SRL Pathology Lab, Agra, India, Tel: 9927488170; E-mail: dr.surajagarwal@yahoo.in

**Received** June 24, 2016; **Accepted** July 15, 2016; **Published** August 05, 2016

**Citation:** Agarwal S (2016) Cancer Genomics: Head and Neck Cancer. J Mol Histol Med Physiol 1: 107