Dear Sir,

Cancer represents a multifactorial disease mediated by the interactions of several known and unknown risk factors. Molecular studies have decoded multiple pathways of carcinogenesis, aiding in the identification of key diagnostic markers and therapeutic targets. Despite the progress in cancer diagnostic and therapeutic, the overall mortality rate remains high. One of the most common reasons for the poor survival rate in cancer is due to the development of treatment resistance. Recent studies have linked specific genetic mutations to the development of resistance in cancer therapy. The present manuscript provides an overview of mutation-specific treatment resistance in cancer and emphasizes the need for formulating a mutation-specific therapeutic approach to overcome the resistance.

The advent of molecular biology had aided in decoding the molecular pathogenesis of many disease entities including cancer. Molecular tools allow a comparison between the clinicopathological progressions of the disease with its corresponding molecular profile. Given the increasing incidence of treatment resistance in cancer, much focus has been emphasized in identifying the underlying molecular mechanisms. Although cancer is indeed a result of mutations, there are specific gene mutations which have proven to be more than just mere participants in carcinogenesis. These specific mutations have rendered the cancer cells with the ability to resist standard treatment modalities. To overcome the resistance of cancer cells, it is important to first identify the specific mutations initiating resistance in various cancers. Mazza and Cappuzzo observation of T790M, PIK3CA mutation, and EGFR, MET gene amplification in cases of non-small-cell lung cancer was closely associated with its profound resistance to EGFR inhibitors. A similar observation was made by Bissada et al., K-RAS codon 12 mutations were linked to treatment resistance in head and neck squamous cell carcinoma.

Condorelli et al. noted that the mutations in retinoblastoma 1 gene were linked to the development of resistance to cyclin-dependent kinases 4/6 inhibitor in breast cancer.

Apart from the development of treatment resistance, these mutations were shown to alter the sensitivity of cancer cells to treatment modalities. In glioblastoma with wild-type calcitonin receptor, calcitonin could be an effective treatment modality. In contrary, calcitonin would be largely ineffective against glioblastoma with mutated calcitonin receptor. Thus, in such cases, targeting the downstream signaling pathways such as AKT, MEK, and JNK would be a better alternative.

The above data suggest that specific genetic mutations could determine the sensitivity of cancer cells to treatment modalities. Thus, classifying cancer based on their mutation profile could aid in determining the risk of treatment resistance and formulation of appropriate treatment strategies. To conclude, given the close association between mutations and treatment resistance, formulating mutation-specific treatment strategies could aid in overcoming therapeutic resistance and increasing the survival rate in cancer.

Archana A. Gupta1, Pooja Jaisinghani2, Narayanasamy Priyadharshini2, Chandini Rajkumar4, Shivaranjhany Sivakumar3

1Department of Oral Pathology and Microbiology, Dr. D. Y. Patil Dental College and Hospital, Dr. D. Y. Patil Vidyyapeeth, Pimpri, Pune, India, 2Medical Practitioner, Private Medical Practice, Pune, Maharashtra, India, 3Dental Practitioner, Private Dental Practice, Coimbatore, India, 4Department of Oral Pathology and Microbiology, Sathyabama University Dental College and Hospital, Chennai, Tamil Nadu, India, 5Clinical Resident, Sapphire Primary Care, Faculty of Dentistry, UiTM, Ministry of Higher Education, Selangor, Malaysia

Correspondence: Shivaranjhany Sivakumar. Clinical Resident, Sapphire Primary Care, Faculty of Dentistry, UiTM, Ministry of Higher Education, Selangor, Malaysia. E-mail: drshivaranjhany@gmail.com

Received: 11 September 2018; Accepted: 20 November 2018

doi: 10.15713/jns.jodm.16


References