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Deciphering the Diversity of Somatic Alterations and Salmonella Infection in Gallbladder Cancer by Whole Exome Sequencing

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Abstract

Introduction: Gallbladder cancer is relatively a rare lethal malignancy with dismal prognosis. While in India there is high incidence (3.9-8.6/1, 00,000) with majority of patients having advanced disease. Recent developments in next generation sequencing technologies have enabled the discovery of new molecular therapeutic targets in many human cancers.

Objectives: Interrogate the landscape of somatic alterations in Indian gall bladder cancer using whole exome sequencing technology.

Material and Methods: We interrogated the coding region of 27(10 paired and 7 unpaired) Indian gall bladder cancer samples using whole exome sequencing at an average coverage of 100X and above. We further validated the findings using an additional set of 27 FFPE samples.

Results: Using a bioinformatics filtering approach, we identify a total of 5060 somatic variants found across 17 tumors consisted of 3239 missense, 1449 silent, 131 nonsense, 135 indels and 106 splice site mutations The average mutation rate considering the paired tumors is about 7.7 mutations/mb. We found *TP53* (35.2%), *ERBB2* (17.6%), *SF3B1* (17.6%), *ATM* (17.6%) and *AKAP11* (17.6%) mutations in more than two samples by exome sequencing analysis. Furthermore, we examined our exome sequencing data for identifying *Salmonella* sequences as well as presence of 143 HPV types using computation subtraction based on HPVDetector. Based on our evaluation we found association of typhoidal *Salmonella* strains in 11 of 26 gall bladder cancer samples and non-typhoidal *Salmonella* species in 12 of 26 samples, 6 samples were co-infected with both.

Conclusions: The profiling of somatic alterations and identification of non typhoidal *Salmonella traces* may aid in changing the current treatment paradigm of gall bladder cancer.

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