

SMARCD1 is a transcriptional target of specific non-hotspot mutant p53 forms

Researchers at DBT's Centre for DNA Fingerprinting and Diagnostics (CDFD), Uppal, carried out a study to identify the likely means by which mutant p53 can cause tongue cancer. For this, tongue cancer samples collected post-surgery from patients and were screened for modifications in the *TP53* gene (a sequence of nucleotides in the DNA that code for the production of the p53 protein). Interestingly, several p53 mutations unique to Indian patients (distinct from the common p53 mutations) were identified. Subsequently, using state of the art technologies, target genes of the mutant p53 were also identified, of which *SMARCD1* gene was the most prominent. *SMARCD1* encodes a protein that along with additional proteins constitutes a multi-protein complex involved in changing the structure of DNA enabling the production of proteins from genes.



Interestingly, *SMARCD1* was shown to be an exclusive target of unique India-specific p53 mutations. Our further studies showed the ability of *SMARCD1* to increase cancerous features in tongue cancer cells. *SMARCD1* is not previously shown to be a possible driver of any form of cancer. Therefore, the observations made in this study assume significance since they reveal a new and probable mechanism by which mutant p53 proteins encourage cancer development. The results of the study can be employed to develop therapies to treat tongue cancer, a common debilitating cancer in India.

Cancer is defined as a set of diseases involving abnormal and uncontrolled division of cells which attain the property to spread to and grow in other locations in the body. Various factors have been linked to cancer development including environmental factors, lifestyle choices (smoking, alcohol consumption, microbial infections, unhealthy diet, etc) and inheritance of cancer predisposing genes. In a normal cell, the p53 protein controls various fundamental processes including repair of damaged DNA, cell division and cell death. P53 achieves this by

binding directly to DNA leading to the production of essential proteins involved in these processes effectively blocking cancer development. However, if p53 gets modified (mutated), its ability to prevent cancer is significantly compromised. More importantly, recent studies have reported ability of specific and common mutated p53 forms to activate cancer growth.

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