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Opinion

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P53 mutational signature in cancer

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Abbreviations: DNA, deoxyribonucleic acid; TD, tetramerization domain; DBD, DNA binding domain; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; HCC, hepatocellular carcinoma

Opinion

P53 is tumor suppressive gene located on chromosome no 17p13.1 and 20kb in size. This contains 11 exons and the first one is non-coding exon. The p53 protein contains five main domains: N-terminal Transactivation domain (1-61aa), Pro-rich domain (61-101aa), DNA binding domain (101-300aa), tetramerization domain (326-356aa) and C-terminal basic domain (364-393). The N-terminal transactivation domain TAD is required for activation of different transcription factor i.e. TFIID and TFIIH and also mediates the interaction with histone acetyltransferases CBP with E3 ubiquitin ligase MDM2. PRD play important role in p53 stability, transcription activation, and induction of transcription independent apoptosis, DBD is responsible for binding with the p53 co repressor. The TD involved in regulation of the oligomeric state of p53 and BD regulates the sequence specific binding of DBD. P53 act as polestar protein of complex signaling network that control cell proliferation, cell death in response to different stimuli, including DNA damage, nutrient deprivation, nucleotide depletion, hypoxia, oxidative stress, and hyper proliferative signals. Activated p53 perform their function in different ways. It acts as transcription factor to bind with the promoter region of different genes and regulate their expression level to induce cell cycle arrest, apoptosis, and DNA repair. The p53 is most commonly mutated protein that is almost found in all types of cancer. The mutation mainly occurs in DNA binding domain (DBD) followed by tetramerization domain (TD). The mutational signature of p53 in cancer is diverse. It is reported that all exon of p53 (1-11) can mutate but the most frequently mutated exons are 5, 7 and 8. The type of mutation in cancer is mainly missense, nonsense and deletion but the pattern of mutation is different in different ethnic group depends on the geographical location. Studies show that the 34 % of p53 mutation affect 10 residues 175, 176, 213, 220, 245, 248, 273 and 282 but the three are mainly 175, 248 and 273. More than 90% of all the p53 mutation in cancer occurs in central core region (codon 101-300). The following table show all reported p53 mutation in different cancer cell lines (Table 1).

Table 1 p53 mutation in different cancer cell lines

Cell Line	Cancer Type	Mutation
MDA-MB-468	Breast cancer	CGGàTGG (273RàH)
T-47D	Breast cancer	CTTàTTT (194LàF)
MCF7	Breast cancer	
Hs 578T	Breast cancer	GTCàTTC (157VàF)
HCT 1	Colon cancer	CàT (241SàF)
DLD1	Colon cancer	CGTàCAT (273RàH)
SW620	Colon cancer	CGTàCAT (273RàH)
HT-29	Colon cancer	CCCàTCC (309PàS)
SW480	Colon cancer	CGGàTGG (248RàW)
COLO 320DM	Colon cancer	CGGàTGG (248RàW)
866MT	NSCLC	TGTàTGA (229Càstop)
A2182	NSCLC	WT
NCI-H292	NSCLC	WT
Calu6	NSCLC	CGAàCGT (196Ràstop)
A427	NSCLC	WT
Calu-1	NSCLC	Deletion
NCI-H358	NSCLC	Deletion
NCI-H1155	NSCLC	CGTàCAT (273RàH)
NCI-H157	NSCLC	GàT (298Eàstop)
NCI-H596	NSCLC	GGCàTGC (245àC)
A549	NSCLC	WT
NCI-N417	SCLS	GAGàTAG (298Eàstop)
MDS92	SCLS	ATGàATA (237Màl)
NCI-H446	SCLS	WT
NCI-H146	SCLS	Splice junction of intron3
NCI-H82	SCLS	GàC
HA22T/VGH	HCC	Deletion
HUH4	HCC	121 Sàstop
HEP 3B	HCC	Deletion
HUH7	HCC	TATàTGT (220Càstop)
SK-HEP-1	HCC	WT
MIA PaCa-2	Pancreas cancer	CGCàTGG (248RàH)
Capan-2	Pancreas cancer	CGTàCAT (273RàH)
AsPC-1	Pancreas cancer	CGTàCAT (273RàH)
FaDu	Oral cancer	CGGàCTG (248RàL)
SSC-4	Oral cancer	CCC?CTC (151P?L)
118 MG	Glioblastoma	GàA (213RàQ)
HCE7	Esophagus cancer	CàT (278PàS)

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Conflicts of interest

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