INVESTIGATING GENETIC VARIANTS IN ESOPHAGEAL CARCINOMA USING MASSIVELY PARALLEL (NEXT-GENERATION) SEQUENCING METHODS

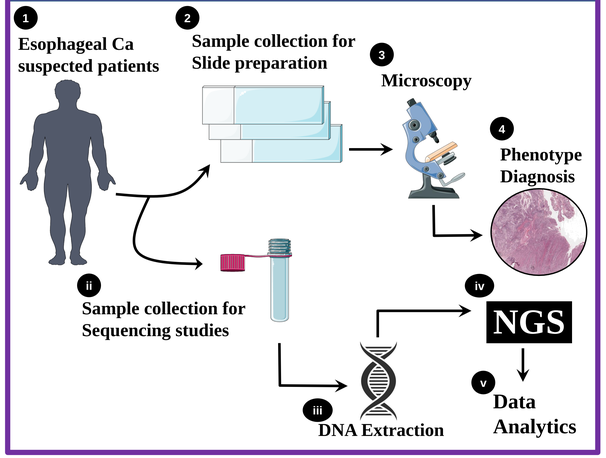
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INTRODUCTION

Esophageal cancers ranks amongst top-ten malignancies across the globe and its incidence is persistently rising in Pakistan. Data regarding genetic variants in esophageal malignancies in Pakistani population are scarce. In this study we aimed to perform Whole Exome Sequencing on esophageal cancer samples from Pakistani patients using massively parallel sequencing to identify genomic landscape of esophageal cancer patients in Pakistan.

METHODOLOGY



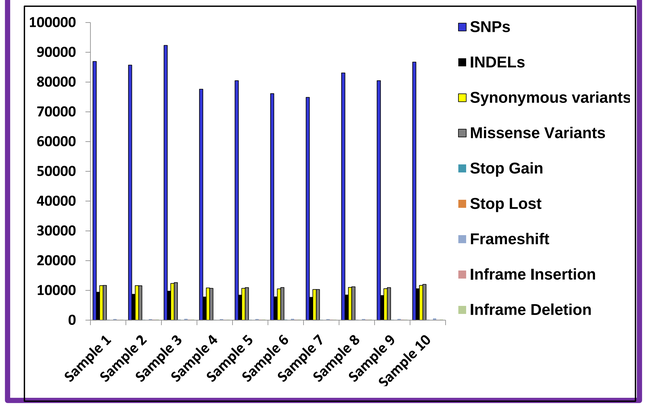
Samples conformed on Histopath were sequenced using NGS (Illumina platform). Filtered variants were annotated using SnpEFF and filtered with dbSNP alongwith with additional databases including ClinVar, dbNSFP, ACMG info.

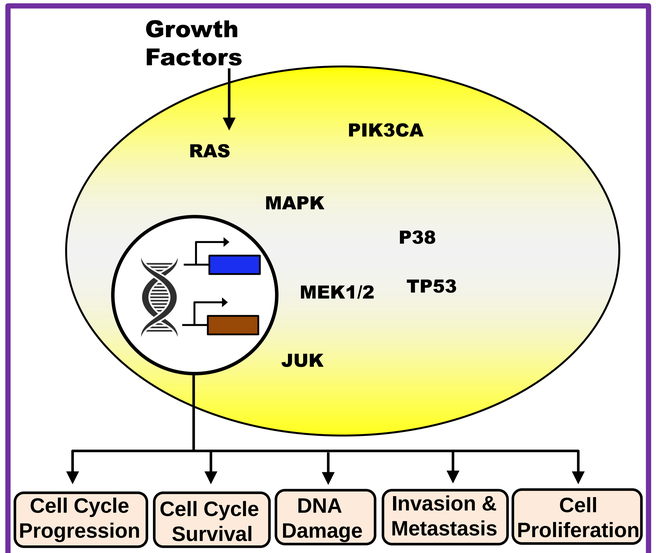
RESULTS

Quality Matrices of Sequences Samples

Samples	Total Yield (BP)	Total Reads	GC%	AT%	Q20%	Q30%
Sample 1	6567480750	43493250	58.25	41.75	96.98	92.3
Sample 2	6563307110	43465610	60.26	39.74	97.35	93.14
Sample 3	6663620336	44129936	58.94	41.06	97.18	92.81
Sample 4	6739591154	44633054	57.7	42.3	96.82	92.09
Sample 5	6490830432	42985632	58.42	41.58	97.29	92.98
Sample 6	6531621572	43255772	59.37	40.63	97.15	92.76
Sample 7	6820269548	45167348	59.84	40.16	96.92	92.28
Sample 8	6661332082	44114782	58.76	41.24	97.21	92.85
Sample 9	6653084764	44060164	58.93	41.07	97.21	92.88
Sample 10	6739711048	44633848	60.38	39.62	97.06	92.59

Overall distribution of Genetic Variants





Selected Mutations in Protein Coding Region

TP53	c.672+62A>G, c.-112G>A, c.215C>G, c.-123C>G
NOTCH1	c.2467+21G>A, c.2265T>C, c.1441+7C>T,c.312T>C,c.-607C>T
CDKN2A	c.*193G>C
PIK3CA	c.1060-17C>A, c.1809C>T
NFE2L1	c.511-1534dupG
CREBBP	c.3698+122T>C, c.3251-2583T>C, c.3251-2623G>A

DISCUSSION

Study Group	Genetic Variants	N
Gao et al (2014)	TP53, NOTCH1, NFE2L2, MLL2, CDKN2A, RB1, FBXW7, AJUBA, CREEBP, PTCH1	113
Song et al (2014)	TP53, NOTCH1, NFE2L2, CDKN2A, PIK3CA, RB1, FAM135, ADAM29	88
Lin et al (2014)	TP53, NOTCH1, NFE2L2, MLL2, CDKN2A, ZNF750, PIK3CA, RB1, PTEN, FAT1, EP300, FAT2, KDM6A	139
Zhang et al (2015)	TP53, CDKN2A, NOTCH1, ZNF750, AJUBA, PIK3CA, FBXW7, FAT1, PTCH1, CREBBP, PTCH1, BAP1	104
Sawada et al (2016)	TP53, NOTCH1, NFE2L2, MLL2, CDKN2A, ZNF750, PIK3CA, FAT1, EP300, FBXW7, AJUBA, CREBBP, NOTCH3, TGFBR2	144
Du et al (2016)	TP53, NOTCH1, NFE2L2, CDKN2A, MLL2, RB1, ZNF750, PIK3CA, AJUBA, CREBBP, FBXW7, PTEN, FAT1, CUL3, NOTCH3, KDM6A, TGFBR2, DCDC1	490
TCGA (2017)	TP53, NOTCH1, NFE2L2, MLL2, ZNF750, TGFBR2	97
Li et al (2018)	TP53, NOTCH1, NFE2L2, CDKN2A, MLL2, RB1, ZNF750, PIK3CA, AJUBA, CREBBP, EP300, FBXW7, PTEN, FAT1, CUL3, NAV3, NOTCH3, TENM3, PTCH1, KDM6A, TET2, TGFBR2, RIPK4, PBRM1, USP8, BAP1	549

CONCLUSION

To the best of our knowledge, it is the first report detailing WES, NGS based, on esophageal cancer samples from Pakistan. Extended to larger horizons, data generated from this study hold potential for identifying actionable variants of diagnostic, prognostic and therapeutic potential for esophageal cancer patients in Pakistan