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Targeted oncogenes analysis of colorectal cancer in Saudi Arabia; opening new doors for precision-based cancer treatment

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Background

Advances in Next-Generation-Sequencing (NGS) technologies have revolutionized cancer therapy by identifying driver mutations that contribute to cancer development. Further exploration and identification of these mutations and genes they dysregulate can aid in cancer diagnosis and guide precision-based therapy for cancer patients. Colorectal cancer (CRC) is a malignant tumor of the colon and rectum, for which no national policy of screening exists, despite its increasing incidence in the Saudi population.

Methods

FFPE tissues collection | DNA & RNA extraction | Oncomine Ion torrent NGS

- A total of 14 colorectal cancer samples collecting from KFMC.
- DNA & RNA extraction from each FFBE clinical research samples using Invitrogen kit.
- Run Oncomine sequencing using Ion AmpliSeq™ Kit for Chef DL8.
- Sequence analysis using Ion reporter software.

Objectives

- To Identify and establish somatic mutations database in CRC within the Saudi population using NGS technology.
- To develop protocols to drive knowledge-based targeted therapy according to CRC genes identified.

Results

- The basic analysis criteria classified the genetic variants based on three different types, Loss of function, missense and frameshift mutation.
- Variants were further subdivided based on genes related or not related to the phenotype.

Genes	No. of mutation	Amino acid change
PIK3CA	5	p.Glu726Lys
CDK4	1	p.Asp221Asn
MIR6759	1	p.Gly251Asp
KRAS	1	p.Gly12Asp
FGFR2	1	p.Asn549Lys
BRAF	1	p.Gly466Arg
MSH2	1	p.Asp303Asn
TP53	2	p.Pro190Ser
FANCI	1	p.Ser512Leu
MAP2K4	1	p.Arg134Trp

Table 1: A summary of the Gene Variants identified in colorectal cancer patients.

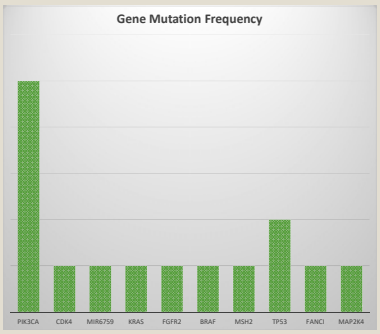
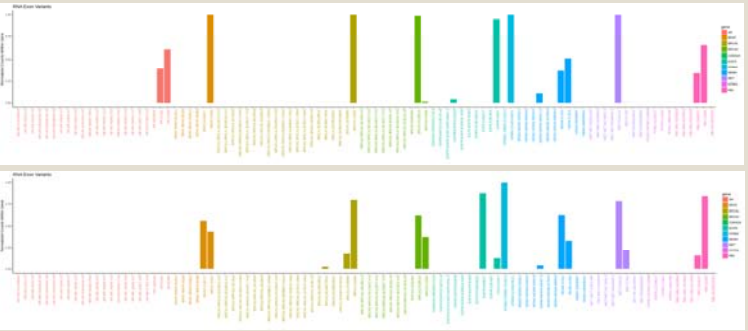


Fig1: Frequencies of somatic verses genes identified by the Oncomine Focus DNA assay in 14 patients with advanced colorectal cancer.



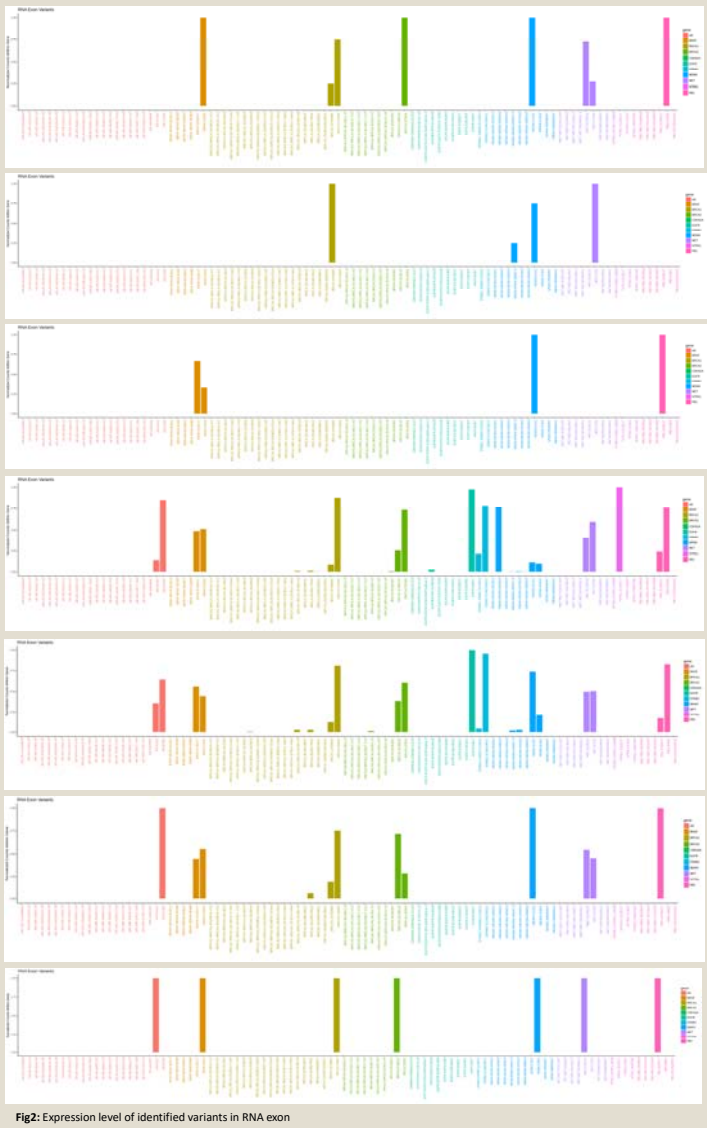


Fig2: Expression level of identified variants in RNA exon

Conclusions

Our findings suggest that *PIK3CA* mutation has the neutral prognostic found on CRC patients, oncogenic *PIK3CA* mutations are found in a significant fraction of human cancers. The use of oncomine sequencing in clinical practice will benefit the detection, management, and treatment of CRC in SA. We believe our analysis will help in identifying some new, clinically actionable mutations. This information will be used to guide optimal treatment regimens and CRC diagnosis. This will aid in further understanding the genomic landscape of CRC in SA and highlight the applicability of oncomine sequencing to aid cancer diagnosis and treatment. This will allow for more rapid and accurate CRC diagnosis and facilitate precision-targeted CRC therapy. This will ultimately improve patient outcomes and improve cancer therapy in SA.