29P KEY CANCER GENE EXPRESSION FEATURES OF HEREDITARY BREAST CANCER IN KAZAKH POPULATION

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It is known that breast cancer(BC)is a pathogenically polymorphic disease, and it can hardly be assumed that all subgroups of patients will receive the same result from a particular therapy. With the development of genetic engineering and the creation of high-tech molecular analysis techniques, there is a real possibility of simultaneously assessing the expression of genes involved in controlling tumor growth, that is, the possibility of creating a molecular genetic portrait of the tumor.

The purpose of the study was to study the molecular genetic features of the development of breast cancer in young women of the Republic of Kazakhstan.

MATERIALS AND METHODS

The study included 235 patients of the Kazakh ethnic group with a diagnosis of breast cancer under the age of 40 years. A set and analysis of clinical material with a family history was carried out, biopsy material of a breast tumor was studied with the study of immunohistochemical (IHC) parameters (ER, RP, Her2, Ki67).Next-generation sequencing was performed using TruSightCancer Kit on the MiSeq platform. Studio Variant was used to annotate and interpret genetic variants.

TruSight Cancer 94-Gene pre-disposition Panel for detecting Germline mutations

AIP	BUB1B	DDB2	EXT2	FANCL	MEN1	PALB2	RB1	SLX4	WRN
ALK	CDC73	DICER1	EZH2	FANCM	MET	PHOX2B	RECQL4	SMAD4	WT1
APC	CDH1	DIS3L2	FANCA	FH	MLH1	PMS1	RET	SMARCB1	XPA
ATM	CDK4	EGFR	FANCB	FLCN	MSH2	PMS2	RHBDF2	STK11	XPC
BAP1	CDKN1C	EPCAM	FANCC	GATA2	MSH6	PRF1	RUNX1	SUFU	
BLM	CDKN2A	ERCC2	FANCD2	GPC3	MUTYH	PRKAR1A	SBDS	TMEM127	
BMPR1A	CEBPA	ERCC3	FANCE	HNF1A	NBN	PTCH1	SDHAF2	TP53	
BRCA1	CEP57	ERCC4	FANCF	HRAS	NF1	PTEN	SDHB	TSC1	
BRCA2	CHEK2	ERCC5	FANCG	KIT	NF2	RAD51C	SDHC	TSC2	
BRIP1	CYLD	EXT1	FANCI	MAX	NSD1	RAD51D	SDHD	VHL	

RESULTS

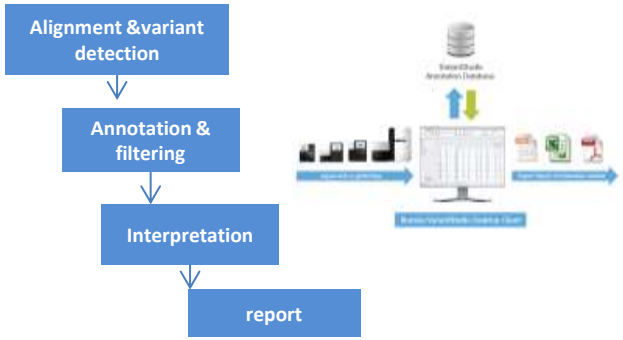
According to the results of the IHC study, luminal A type was found in 30 (12.8%) patients, luminal B-type in 65 (27.6%), luminal B + type in 38 (16.2%) triple negative type in 75 (31.9 %) cases, Her2 enriched in 27 (11.4%). In 31 (13.1%) burden of family history of breast cancer was found, of which 1 degree of kinship in 22 (70.9%) patients, 2 degrees of kinship in 9 (29.1%) maternal patients.

Bioinformation analysis showed that the most common pathogenic mutations in the genes BRCA1 (24 variants (37.5%)) and BRCA2 (18 (28.1%)). A hereditary history was recorded in 24.8% and 25.6% of representatives of the group with pathogenic mutations in the BRCA1 gene and with BRCA2 mutations, respectively. This indicator is much higher compared to the group of patients without pathogenic mutations and to the group of patients with mutations in BRCA-negative genes. The triple negative molecular subtype of the tumor was found most in the group of BRCA1-associated patients, twice as high as in the group of patients without pathogenic mutations.

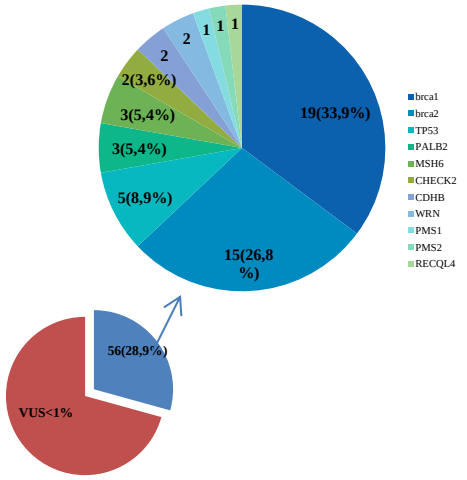
RESULTS

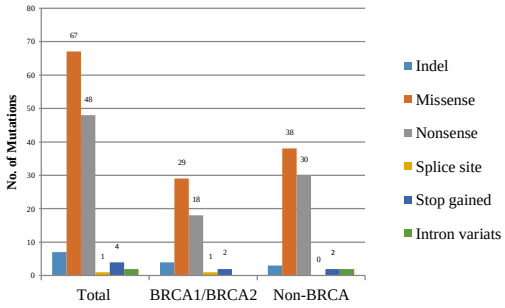
Pathogenic mutations in the BRCA1 and BRCA2 genes are often associated with the presence of family burden and the aggressive phenotype of so triple negative breast cancer in the Kazakh population.

BIOINFORMATICS



NGS data analysis of mutations





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