GENE VARIANT MAPPING IN 7,587 INDIVIDUALS REFFERED FOR HEREDITARY CANCER.

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Introduction

Hereditary cancer accounts for about 10% of diagnosed cancers. The genetic investigation of hereditary cancer is important as it may help in clinical decision-making such as clinical follow-up, treatment approach and reduce the risk of developing new malignancies. The application of **Next Generation Sequencing (NGS)** technology allows the simultaneous analysis of many samples and genes.

Aim

The **purpose of the study** is to investigate the genetic predisposition in patients with referral for hereditary cancer.

Methods

In total, **7,787 individuals** were referred for multi gene genetic testing, in the period 2020-2023, to the Genekor laboratory and genetic testing using **NGS was performed** (Figure 1). Of those examined, 4,167 had been diagnosed with breast cancer, 492 with ovarian cancer, 151 with colorectal cancer, 148 with prostate cancer, 522 were healthy with a family history of cancer and 2,107 had another type of cancer or no information was available.

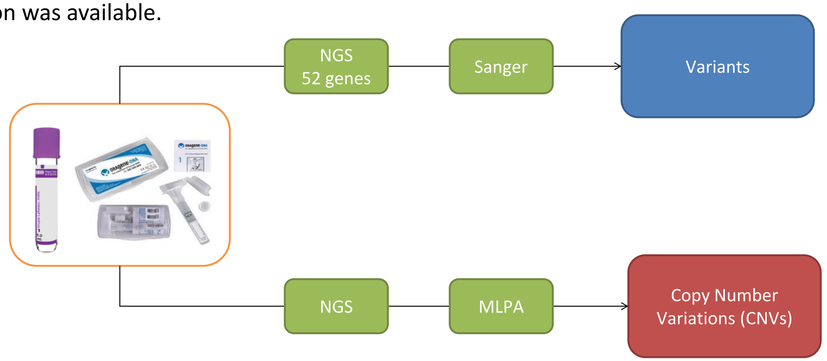

Figure 1. Methodology performed in this study.

Results

19.9% (1,511/7,587) of individuals tested carried a pathogenic variant (Figure 2A). Specifically, 43.6% (659/1,511) of patients carried a pathogenic variant in **a clinically important gene** (*BRCA1*: 11.2%, *BRCA2*: 10%, *APC*: 3.6%, *PALB2*: 3.4%, *MSH2*: 1.8%, *MLH1*: 1.5%, *MSH6*: 1.5%, *PMS2*: 1.5%, *RAD51C*: 1.5%, *RET*: 1.3%, *CDKN2A*: 1%, *RAD51D*: 1%, *MEN1*: 0.8%, *TP53*: 0.7%, *CDH1*: 0.7%, *CDK4*: 0.2%, *PTEN*: 0.2%, *VHL*: 0.2%) (**Figure 2B**). Among the different types of pathogenic variants detected, **a significant proportion** (6.7%, 59/982) represent **Copy Number Variations** (CNVs) (Figure 2C).

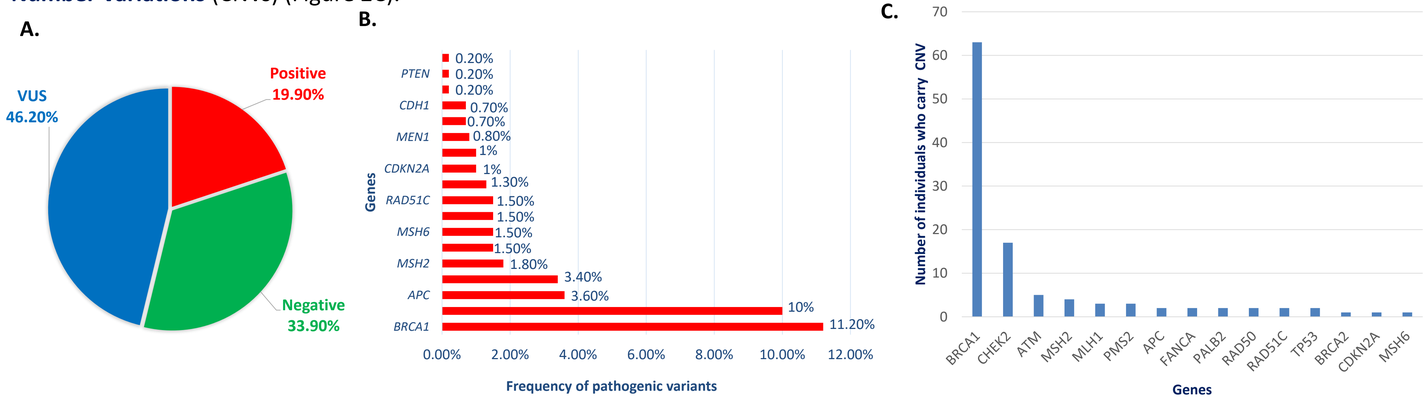

Figure 2. A. Results from the genetic testing of 7,587 individuals. **B.** Frequency of pathogenic variants in clinically relevant genes. **C.** Distribution of pathogenic CNVs by gene.

Conclusions

- **Comprehensive** multi gene genetic testing is essential for the most appropriate **clinical management** of carriers of pathogenic variants.
- In addition, the information obtained is important for determining the **risk of developing** malignancy in the other **family members** of the tested individuals.

References

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