OMICs role in Hereditarian prostate cancer

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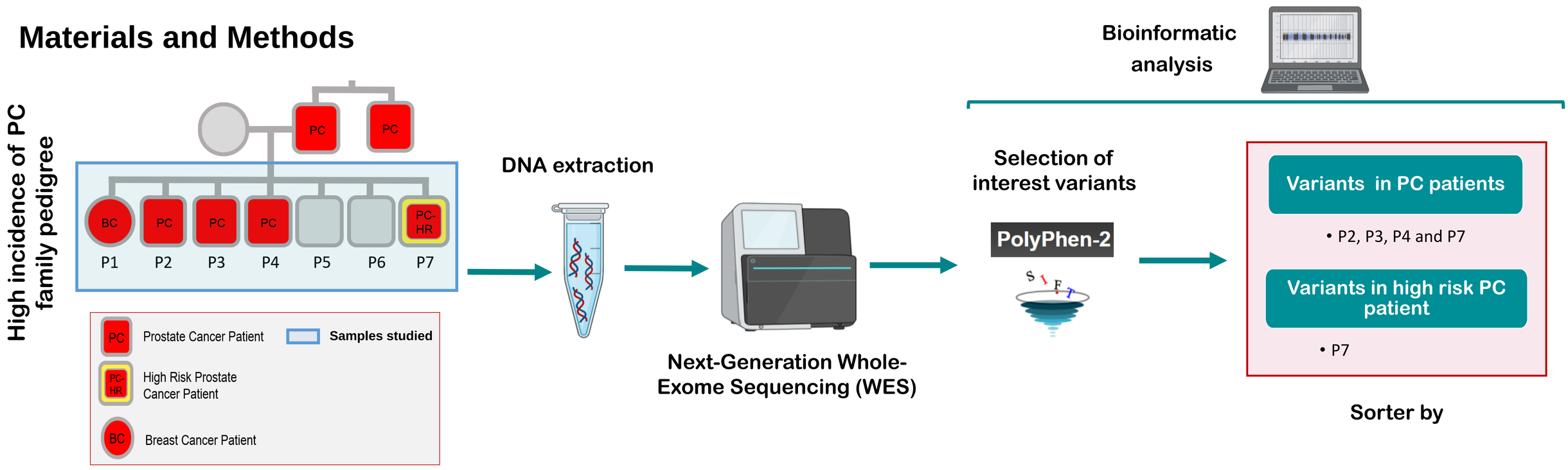
Introduction

Although all men are at increased risk for prostate cancer (PC) developing with increasing age, a family history of PC in a first-degree relative multiplies that risk approximately twofold. Most cases of PC occur sporadically in people with no family history of the condition. However, approximately 5% to 10% of PC cases are believed to be primarily caused by a genetic predisposition to the condition. Approximately 43% of men with a diagnosis of PC before age 55 have hereditary prostate cancer (HPC). Nevertheless, the biologic behaviour or molecular biomarkers for HPC remains unclear.

Next-Generation Sequencing (NGS) has turn in to a significant tool for finding new altered genes, allowing the diagnosis of many diseases and with a special important role in those less known diseases. However, by the moment, there is scarce data about large families cohorts to find out more details of HPC malignancy. With this study we make a deep analysis of exome analyzed by NGS in a high incidence PC family.

Materials and Methods



Results and Discussion

Sequencing analyses reveal i) the presence of variations in five genes for only the patients with PC. All of them, except ***STK31***, are also found in the patient with breast cancer. ii) The patient with aggressive PC shows a total of ten genes with unique variations, not present in the other patients.

Table 1. List of main variations obtained after bioinformatics analysis in PC patients.

Variations in all PC patients		Variations in high risk PC patient	
Gene	**SNP**	**Gene**	**SNP**
DPP4	rs116302758	*ACE*	.
HIBCH	rs291466	*ALDH3B2*	rs7947754
MOK	rs56377169	*CD63*	.
PPP4R3A	.	*EFCAB13*	rs2271803
STK31	.	*FAM86HP*	rs16834628

Although scarce data, there are previous publications relating ***HIBCH*** with PC clinical response or accelerating PC progression following androgen deprivation therapy in ***DPP4*** [1]. These data support our results as hopeful marks of aggressiveness mainly due to a poor response of the therapy, which is also confirmed in other tumours such as colorectal cancer in ***HIBCH*** [2].

Moreover, high-risk patient has unique additional variants such as ***ACE, CD63 and EFCAB13***, that have already been associated with PC. These results provide a new set of promising biomarkers that can help in the stratification and diagnosis in HCP.

Conclusions

Our data revealed the association between variations in some genes, such as ***HIBCH*** and ***DPP4,*** and hereditary prostate cancer. These results provide a new set of promising biomarkers which can help in the stratification and diagnosis in hereditary prostate cancer.

References

1) Graff, J.N. *et al.* Sustained complete response to *CTLA-4* blockade in a patient with metastatic, castration-resistant prostate cancer. *Cancer Immunol. Res*. 2014.

2) Shan, Y. *et al.* Targeting *HIBCH* to reprogram valine metabolism for the treatment of colorectal cancer. *Cell Death Dis*. 2019.

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