Study of some candidate genes for treatment in prostate cancer

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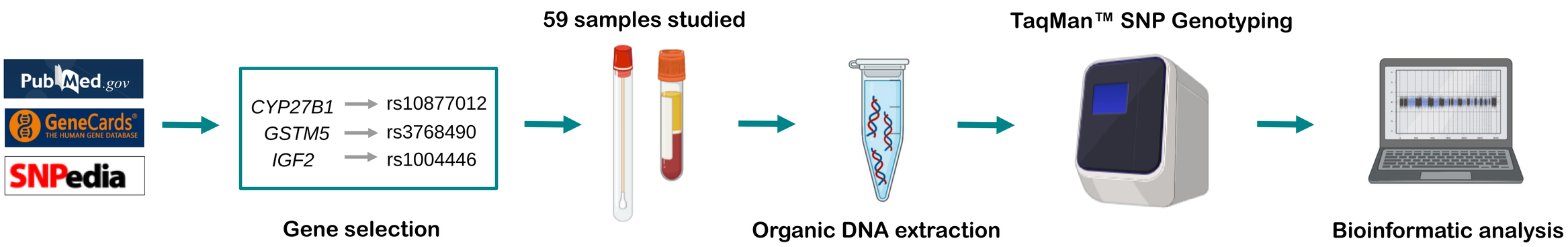
Introduction

The activation of the androgenic signalling pathway in prostate cancer (PC) is essential for carcinogenesis and tumour development. The importance of that pathway makes it the main target of treatments against PC, among which androgen deprivation therapy (ADT) stands out. This therapy is efficient in the early stages of tumour development, however, in most instances, the tumour evolves into castration-resistant prostate cancer. In such cases, the tumour becomes more aggressive and a metastatic process usually occurs [1, 2]. The heterogeneity of the response against the same treatment prompted us to seek for molecular biomarkers which enable the prediction of the response to therapy [2]. This work focuses on the characterization of the response to treatment in several patients of PC through the analysis of different genetic variants. Thereby, candidate genetic positions implicated in the development of resistance against ADT were selected. The search of single nucleotide polymorphisms (SNPs) was carried out to establish a possible connection between the genotype of each patient and the response to treatment.

Materials and Methods



Results and Discussion

Association between genotype and response to treatment show a trend to resistance in A/G genotype in **rs1004446 (*IGF2*)**. However, owing to the lack of statistical significance we cannot confirm a direct association. We consider that these inconclusive results are due to the low number of samples analysed.

Regarding the relationship with the Gleason score, an association between the genotype of the SNP **rs10877012 (*CYP27B1*)** and the aggressiveness of phenotypes was proved with statistical significance **(p=0.013)** as shown in **Table 1**.

Table 1. Association between genotype and Gleason *score.*

SNP	Gleason score ≤ 7	Gleason score > 7	p
rs10877012 (*CYP27B1*)			0.013
G/G	6 (25.00%)	22 (59.46%)	
T/T	1 (4.17%)	3 (8.10%)	
G/T	17 (70.83%)	12 (32.44%)	
rs3768490 (*GSTM5*)			0.908
G/G	11 (44.00%)	15 (42.86%)	
T/T	2 (8.00%)	4 (11.43%)	
G/T	12 (48.00%)	16 (45.71%)	
rs1004446 (*IGF2*)			0.784
G/G	13 (52.00%)	16 (43.24%)	
A/A	2 (8.00%)	4 (10.81%)	
A/G	10 (40.00%)	17 (45.95%)	

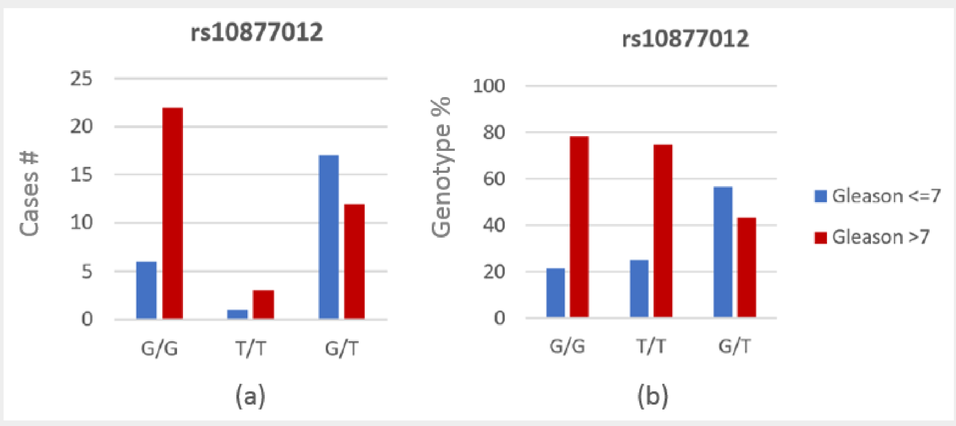


Figure 1. Representation of genotype association and Gleason score: (a) Expressed in number of cases; (b) Expressed as a percentage.

As represented in **Figure 1**, we observe that 78.57% of the patients with G/G genotype for rs10877012 had a Gleason score above 7, which is associated with greater aggressiveness of PC. In the case of the heterozygous genotype, it was found that 56.67% of those presented a Gleason score lower or equal to 7. In the case of the T/T genotype, no relevant conclusion can be reached since only 4 of all the samples that participated in the study presented that genotype.

This important fact would help to predict the future severity of the PC when the tumour is still in the early stages.

Conclusions

This study reveals that PC patients with A/G genotype in **rs1004446 (*IGF2*)** show a certain tendency to resistance to hormonal treatment, although a relationship with statistical significance was not confirmed. Besides, a significant statistical relation between aggressive phenotypes was confirmed in **rs10877012 (*CYP27B1*)**. Further confirmation of these results in a larger cohort will open up a wide range of possibilities for the clinical implementation of these SNPs.

References

1) Dai, C. *et al*. Androgen signaling in prostate cancer. *Cold Spring Harb. Perspect. Med.* 2017.
2) Alvarez-Cubero, M.J. *et al*. Prognostic role of genetic biomarkers in clinical progression of prostate cancer. *Exp. Mol. Med.* 2015.

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