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Investigation of the BRCA2 gene SNP (rs144848) in prostate cancer patients with elevated PSA readings

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Abstract

Prostate cancer is the most commonly diagnosed male malignancy worldwide and a leading cause of cancer-related mortality. Germline variation in DNA-repair genes, particularly BRCA2, can modify prostate-cancer risk and aggressiveness; however, evidence from Iraqi populations is limited. We assessed BRCA2 rs144848 (c.1114C>A; p.Asn372His) frequency in Iraqi men with prostate cancer and elevated serum prostate-specific antigen (PSA), compared with apparently healthy controls. In this case-control study at a hospital in Erbil, Kurdistan Region, Iraq, 11 men with histologically confirmed prostate cancer and PSA >4 ng/mL and 10 age-matched male controls were enrolled. Genomic DNA was extracted from peripheral blood, and rs144848 was detected by allele-specific polymerase chain reaction (PCR) and 2% agarose gel electrophoresis. Demographic and clinical variables were summarized descriptively. The rs144848 variant was detected in all participants: 11/11 cases (100%) and 10/10 controls (100%); no variant-negative individuals were identified. Most participants were aged 66–82 years. Blood group B+ was the most frequent (36.4%), and overall reported serum PSA values ranged from 1.74 to 19.68 ng/mL. Because all participants carried the variant, this sample provides no evidence that rs144848 differentiates cases from controls; its association with prostate cancer cannot be estimated from these data. The small cohort also limits generalizability. These findings support larger studies using comprehensive BRCA2 sequencing rather than reliance on a single common polymorphism. Full-sequence testing reportedly identified clinically relevant pathogenic variants in this cohort, although their frequency and characteristics are not specified here. Thus, rs144848 genotyping alone should not substitute for comprehensive BRCA2 analysis in this population.

Keywords

Prostate cancer;
BRCA2;
Allele specific PCR;
Single nucleotide polymorphism (SNP);
Serum PSA;
Iraqi population

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1. Introduction

Cancer is characterized by uncontrolled cell proliferation and the acquisition of metastatic potential, driven largely by oncogene activation and/or tumour-suppressor gene inactivation [20]. Prostate cancer is now the most commonly diagnosed male malignancy worldwide, with more than 1.5 million new cases estimated in 2024 and rising incidence in many regions despite declining mortality [1][2][3]. Most prostate tumours are slow-growing and low-grade, but a clinically significant subset behaves aggressively, motivating continued search for biomarkers that distinguish indolent from lethal disease [4][5].

Prostate-specific antigen (PSA) remains the cornerstone of early detection, though its utility is debated in the general population; recent evidence supports targeted, rather than universal, screening in men at elevated genetic risk [6][7]. Germline mutations in DNA-repair genes — particularly BRCA2 — are now firmly established as modifiers of prostate-cancer risk and aggressiveness, and current European guidelines recommend germline testing for BRCA1/2, ATM and mismatch-repair genes in high-risk and metastatic disease [8][9][10].

BRCA2 encodes a protein central to homologous recombination repair of DNA double-strand breaks, and loss of this function predisposes carriers to earlier-onset, more aggressive prostate cancer [11][12]. The IMPACT study, the largest prospective trial of targeted PSA screening in BRCA1/2 carriers, recently confirmed a higher incidence of clinically significant prostate cancer in BRCA2 carriers versus non-carriers (3.1% vs 1.3%, p = 0.04), supporting systematic PSA screening in this group [13]. In addition to risk, BRCA2 status now has direct therapeutic implications: PARP inhibitors (e.g. olaparib) have clear value as therapy in mCRPC in men with germline or somatic mutations in the gene [14] [15]

To investigate if the common BRCA2 polymorphism rs144848 (c.1114C>A; p. Asn372His) is associated with prostate-cancer susceptibility among Iraqis, the authors analyzed this variant in prostate-cancer patients and healthy controls who had elevated PSA levels.

2. Materials and Methods

2.1 Study design and participants

This case-control study was conducted in a hospital in Erbil, Kurdistan region, in a Prospective fashion. Region, Iraq. A list of 11 men that have received a prostate cancer diagnosis from their pathologist. Ten apparently normal, age matched men were recruited along with the group with raised serum PSA >4 ng/mL. Normal male controls free of malignancy. Written informed consent was All participants were given an informed consent, and the study protocol was approved by the Ethics It is presented to the Committee of the University of Al-Hamdaniya (UH-2026-021).

Table 1 — Inclusion and exclusion criteria

Criterion	Details
Inclusion	tologically confirmed prostate cancer; elevated serum PSA (>4 ng/mL); age ≥40 years; written informed consent obtained
Exclusion	Prior malignancy other than prostate cancer; prior BRCA1/2 genetic testing; inadequate DNA yield or quality (<20 ng/μL or A260/A280 outside 1.8–2.0)

2.2 Sample collection and DNA extraction

Blood samples were obtained from peripheral veins and placed in EDTA tubes (3–5 mL). Leukocytes were used to isolate genomic DNA by silica membrane spin column kit, following the manufacturer's instructions. The concentration and purity of DNA were determined by spectrophotometric readings and the ratio of A260/A280 was between 1.8 and 2.0, indicating that the DNA was pure. The integrity of the DNA was checked by agarose gel electrophoresis.

2.3 Allele-specific PCR for BRCA2 rs144848

Allele-specific PCR was used to genotype the variant rs144848 (c.1114C>A; p.Asn372His) with primers specific to the two alleles at the polymorphic site. All reactions were 25 μL and included genomic DNA, the correct set of primers, dNTPs, Taq DNA polymerase, and $MgCl_2$. Amplification was initiated with a denaturation step at 95°C for 5 min followed by 35 cycles of DNA denaturation at 95°C for 30 s, annealing at 58 to 62°C for 30 s and extension at 72°C for 30 s. The last extension step was carried out at 72°C for 5 min.

Table 2 — PCR primer sequences and cycling conditions

Parameter	Detail
Target variant	BRCA2 rs144848 (c.1114C>A; p. Asn372His)
Amplicon size	67 bp
le-specific primer (variant, A allele / 372His)	5'-TGAAGAAGAACACCAACTA-3'
e-specific primer (wild-type, C allele / Asn372)	5'-TGAAGAAGAACACCAACTC-3'
Common reverse primer	5'-GTAAAACTTTCCAAGTGCT-3'
Annealing temperature	58–62°C
Cycle number	35
Expected band (variant-positive)	67 bp
Expected band (variant-negative)	band / 0 bp (ARMS-PCR: variant-specific forward primer yields no duct in homozygous wild-type samples, serving as negative control)

2.4 Gel electrophoresis and visualization

The PCR products were separated by a 2% agarose gel electrophoresis in 1× TBE buffer for 1 h at 120 V. After ethidium bromide staining the bands were detected by a UV transilluminator. Distances of fragments were estimated by loading 100 bp DNA ladder in the first and last lanes in the gel. A 67-bp amplicon was detected, which was considered a variant-positive genotype.

2.5 Statistical analysis

Data on demographic and clinical characteristics were presented as frequencies, percentages and ranges. The differences between patients and controls were analyzed by Fisher's exact test, as appropriate. Statistically significant results were accepted as $p < 0.05$. The data were analysed using SPSS version 26.0.

3. Results and Discussion

3.1 Demographic and clinical characteristics

The 11 prostate-cancer patients ranged in age from 50 to 82 years, with the majority (72.7%) aged 66 years or older. Blood group B+ was the most frequent (36.4%), followed by A+ and O+ (36.4% and 27.3%, respectively). Serum PSA ranged from 1.74 to 19.68 ng/mL, with the highest proportion (36.4%) in the 7.06-10.27 ng/mL range. Height ranged from 170 to 190 cm and weight from 60 to 90 kg. Four patients (36.4%) reported a history of smoking (Table 3, Figure 1).

Table 3 — Demographic and clinical characteristics of patients

Variable	Category	n (%)
Age (years)	50–61	3 (27.3)
	66–70	4 (36.4)
	72–82	4 (36.4)
ABO blood group	A+	4 (36.4)
	B+	4 (36.4)
	O+	3 (27.3)
Serum PSA (ng/mL)	1.74–3.06	2 (18.2)
	4.62–6.26	2 (18.2)
	7.06–10.27	3 (27.3)
	13.17–19.68	4 (36.4)
Height (cm)	170–180	9 (81.8)
	180–190	2 (18.2)
Weight (kg)	60–70	1 (9.1)
	70–80	8 (72.7)
	80–90	2 (18.2)
Smoking status	Yes	4 (36.4)
	No	7 (63.6)

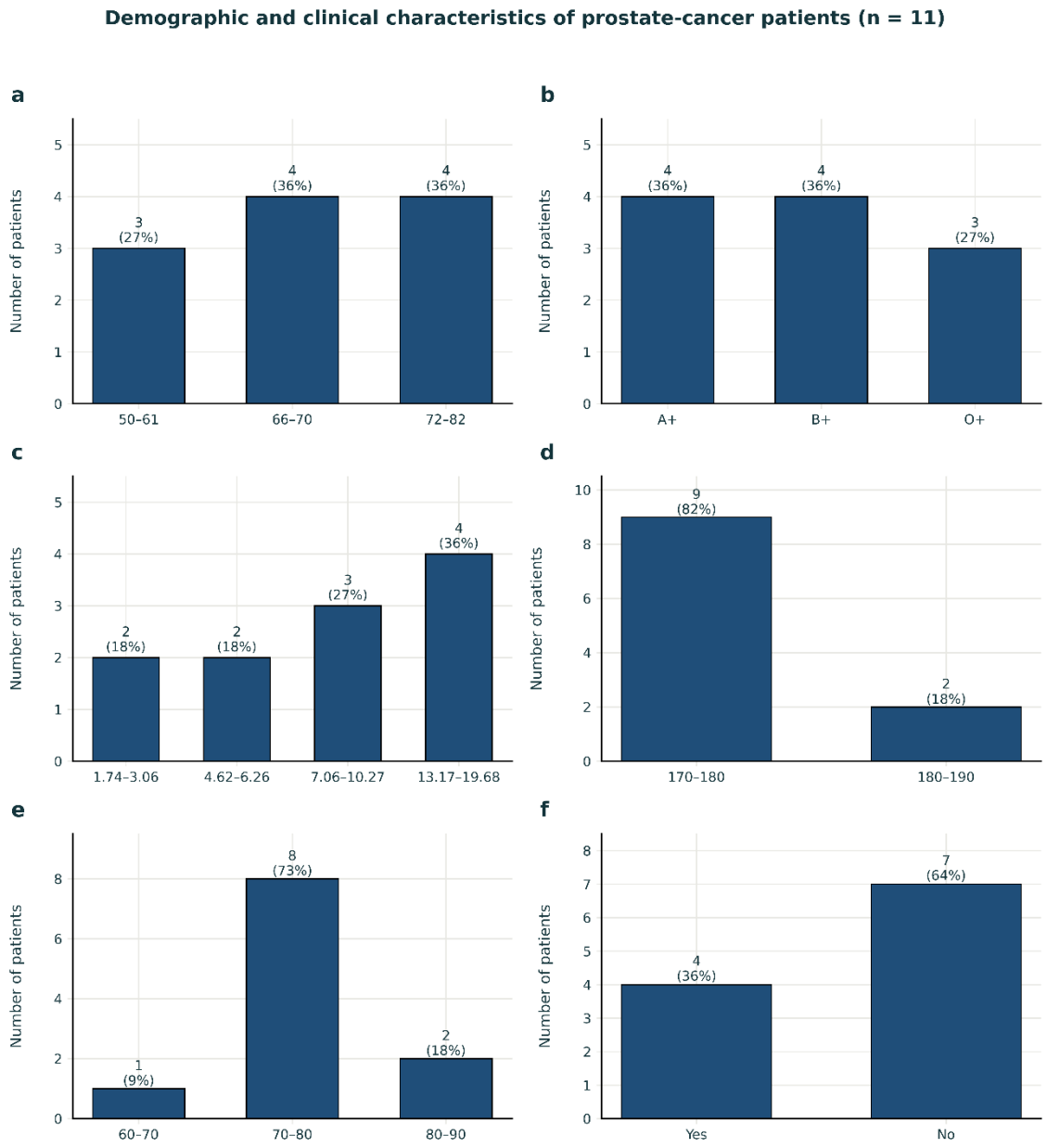


Figure 1. Demographic and clinical characteristics of the 11 prostate-cancer patients: (a) age distribution, (b) ABO blood group, (c) serum PSA distribution, (d) height distribution, (e) weight distribution, (f) smoking status. Values above bars indicate frequency and percentage.

3.2 BRCA2 rs144848 genotyping result

Allele-specific PCR followed by agarose gel electrophoresis detected the BRCA2 rs144848 variant in all 11 prostate-cancer patients and all 10 healthy controls, corresponding to a 100% variant-positive rate in both groups (Figure 2, Table 3). No variant-negative individuals were identified in either cohort.

Table 3 — BRCA2 rs144848 genotype distribution (new)

Group	Variant-positive	Variant-negative	Positive rate
ɔstate-cancer patients	11	0	100%
Healthy controls	10	0	100%
Total	**21**	**0**	**100%**

Statistical note: no comparison was possible (zero variance in both groups); Fisher's exact test is not applicable given identical 100% rates.

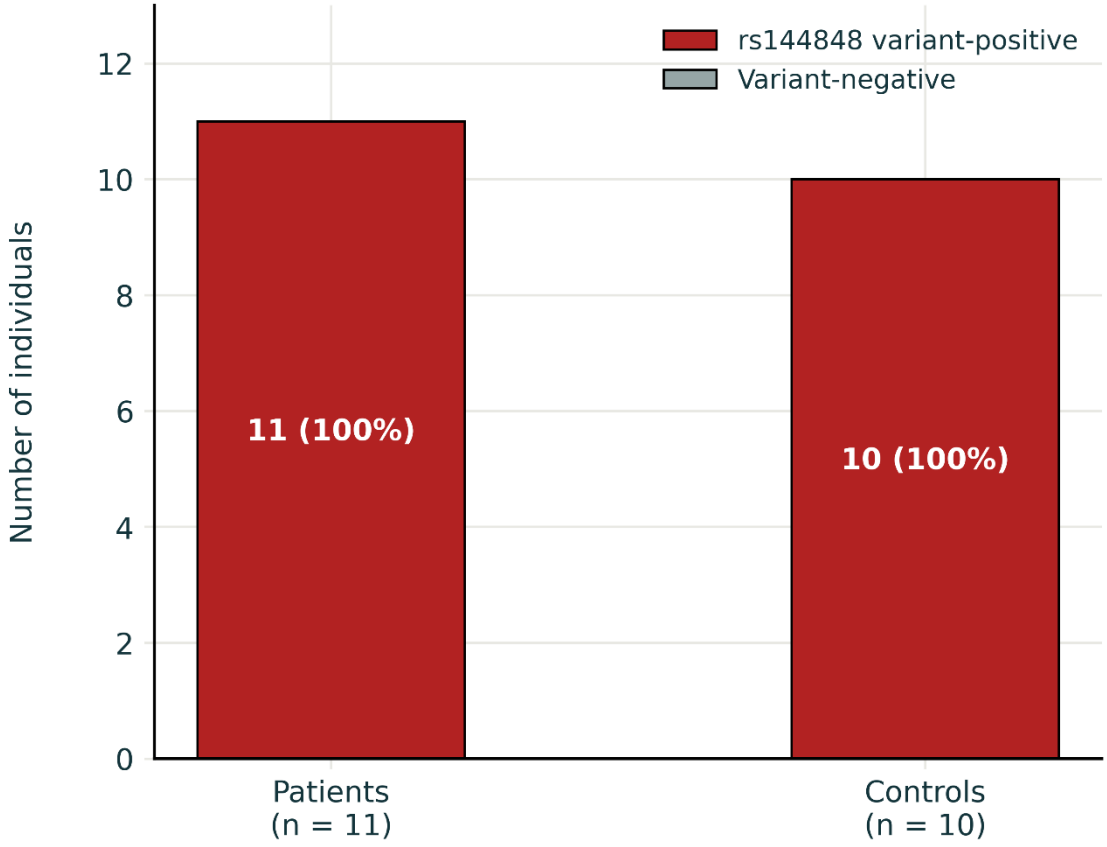


Figure 2. BRCA2 rs144848 genotyping results by allele-specific PCR in prostate cancer patients versus controls. The 67-bp amplicon is indicated; variant-positive banding patterns were observed in all samples from both groups.

3.3 Discussion

No association was observed between the presence of the BRCA2 rs144848 polymorphism and prostate cancer in the population studied since the polymorphism was present in all 11 patients and all 10 controls. This null effect occurs in line with the growing understanding that common SNPs, such as rs144848, account for only the minor part of the prostate-cancer

risk compared to rare pathogenic high-risk variants in genes such as BRCA2 and the other DNA-repair genes [8][9][10]. Recent data from the IMPACT study confirmed this difference, as clinically significant prostate cancer was significantly more common in pathogenic-variant carriers of BRCA2 than in non-carriers, which was not the case for common polymorphisms, including rs144848 [13].

The consistent observation of the presence of rs144848 in all samples also illustrates a methodological drawback of allele-specific PCR for this locus, which only identifies one specific variant, not the complete spectrum of BRCA2 variation. Whereas single-variant assays are recommended solely for lower risk prostate cancer, current guidelines explicitly call for next-generation sequencing (NGS) and appropriate depth of coverage (DOC) (at least 200×) when evaluating the BRCA1/2 status in high-risk prostate cancer, because the unusual mutant variants (not common SNPs) represent the clinically relevant risk and treatment implications [10]. This reflects the overall trend towards more extensive germline testing in prostate cancer, which has now been recommended by both American [13] and international guidelines for people with metastatic, high-risk and/or family history prostate cancer.

The null finding from a therapeutic perspective does not impact the need for BRCA2 assessment in this population. PfSpar inhibitors have shown PFS/OS benefit in metastatic CRPC specifically in patients with BRCA1/2 mutations or larger benefit in the subgroups of patients with BRCA2 mutations [14][15]. Sequencing-based strategies are thus the next step for Iraqi cohorts, which lacks this information, and the identification of patients who have pathogenic BRCA2 variants is the clinically actionable target.

The combination of these results leads to the conclusion that this single-SNP is not a useful marker for discriminating prostate-cancer susceptibility risk in the Iraqi population studied, and recommends the need for the use of comprehensive BRCA2 sequencing in future studies of this population.

4. Conclusion

The BRCA2 rs144848 (c.1114C>A; p.Asn372His) variant was detected by allele-specific PCR in all 11 Iraqi men with prostate cancer and elevated serum PSA, and in all 10 apparently healthy controls, indicating no detectable association between this common polymorphism and prostate cancer in the cohort studied. Unlike rare high-penetrance BRCA2 pathogenic variants, which confer a substantial elevation in prostate-cancer risk, the uniform presence of rs144848 in every sample suggests that this locus is not informative for case–control discrimination in the Iraqi population examined. These findings are consistent with prior reports questioning the role of this polymorphism in prostate-cancer susceptibility, and they underscore the need for sequencing-based approaches capable of capturing the full spectrum of BRCA2 variation — including rare pathogenic variants — in future studies of this population.

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Conflict of Interest

The author declares no conflict of interest.

Ethics Approval and Consent to Participate

The study protocol was approved by the Ethics Committee of the University of Al-Hamdaniya (UH-2026-021). Written informed consent was obtained from all participants prior to enrolment.

References

[1] Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263. https://doi.org/10.3322/caac.21834

[2] International Agency for Research on Cancer. Prostate cancer fact sheet. Lyon: IARC/WHO; 2024. Available from: https://www.iarc.who.int/cancer-type/prostate-cancer/

[3] Cao W, Chen HD, Yu YW, et al. Global epidemiological trends in prostate cancer burden: changing landscapes and future projections. 2025.

[4] Rebello RJ, Oing C, Knudsen KE, et al. Prostate cancer. Nat Rev Dis Primers. 2021;7:9. https://doi.org/10.1038/s41572-020-00243-0

[5] Rawla P. Epidemiology of prostate cancer. World J Oncol. 2019;10(2):63-89.

[6] Hugosson J, Roobol MJ, Månsson M, et al. A 16-yr follow-up of the European Randomized study of Screening for Prostate Cancer. Eur Urol. 2020;77(1):43-51. https://doi.org/10.1016/j.eururo.2019.09.016

[7] Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. Eur Urol. 2024;85(4):357-401. https://doi.org/10.1016/j.eururo.2024.03.024

[8] Mok K, Chung C, Zhen JC, et al. Frequency of hereditary cancer gene pathogenic variants in men with prostate cancer: a systematic review and meta-analysis. Br J Cancer. 2019;121(7):613-621. https://doi.org/10.1038/s41416-019-0502-7

[9] Agalliu I, Kwon EM, Salinas CA, et al. Genetic variation in DNA repair genes and prostate cancer risk: results from a population-based study. Cancer Causes Control. 2010;21(2):289-300.

[10] EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. Arnhem: European Association of Urology; 2025. ISBN: 978-94-92671-25-7.

[11] Venkitaraman AR. Cancer susceptibility and the functions of BRCA1 and BRCA2. Cell. 2002;108(2):171-182. https://doi.org/10.1016/S0092-8674(02)00615-3

[12] Yang H, Jeffrey PD, Miller J, et al. BRCA2 function in DNA binding and recombination from a BRCA2-DSS1-ssDNA structure. Science. 2002;297(5588):1837-1848. https://doi.org/10.1126/science.1076348

[13] Bancroft EK, Page EC, Castro E, et al. Targeted Prostate Cancer Screening in Carriers of BRCA1 or BRCA2 Mutations: Final Results from the IMPACT Study. Eur Urol. 2026.;89(2):142-154. doi:10.1016/j.eururo.2025.10.012

[14] Mateo J, de Bono JS, Fizazi K, et al. Olaparib for the treatment of patients with metastatic castration-resistant prostate cancer and alterations in BRCA1 and/or BRCA2 in the PROfound trial. J Clin Oncol. 2024;42(5):571-583. https://doi.org/10.1200/JCO.23.01436

[15] Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. Talazoparib enzalutamide in men with first-line metastatic castration-resistant prostate cancer (TALAPRO-2): a randomised, placebo-controlled, phase 3 trial. Lancet. 2023;401(10378):815-826. https://doi.org/10.1016/S0140-6736(23)00255-5

[16] Wang G, Zhao D, Spring DJ, DePinho RA. Genetics and biology of prostate cancer. Genes Dev. 2018;32(17-18):1105-1140. https://doi.org/10.1101/gad.315739.118

[17] Pomerantz MM, Spisak S, Jia L, et al. The association between germline variants and prostate cancer risk: a systematic review and meta-analysis. Eur Urol. 2021;79(6):739-752. https://doi.org/10.1016/j.eururo.2021.02.014

[18] Rani A, Dasgupta P, Murphy JJ. Prostate cancer: the role of inflammation and chemokines. Am J Pathol. 2019;189(11):2119-2137. https://doi.org/10.1016/j.ajpath.2019.08.002

[19] Waugh DJ, McGovern JA, McCusker S. The challenges and emerging opportunities of targeting cytokines and chemokine-driven inflammatory signals in metastatic castrate-resistant prostate cancer. Crit Rev Oncog. 2022;27(4):1-14. https://doi.org/10.1615/CritRevOncog.2022043357

[20] Dunn GP, Old LJ, Schreiber RD. The three Es of cancer immunoediting. Annu Rev Immunol. 2004;22:329-360. https://doi.org/10.1146/annurev.immunol.22.012703.104803