

## PROSTATE CANCER JUNIOR CLINICAL RESEARCH UNIT

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### OVERVIEW

Prostate cancer (PrCa) is the most common cancer diagnosis in men and, despite its potential to be cured in almost 90% of early stages, its metastatic spread causes about 6,000 deaths every year in Spain alone, whilst in the US over 30,000 men succumb to the disease each year.

During the last few years, our Group has focused precisely on the development of new methods to identify and treat the most aggressive and lethal forms of prostate cancer, in order to accelerate precision medicine for the disease. In particular, over the last 8 years, our group has made significant contributions in:

→ Establishing and developing several biomarkers based on the concept of liquid biopsy.

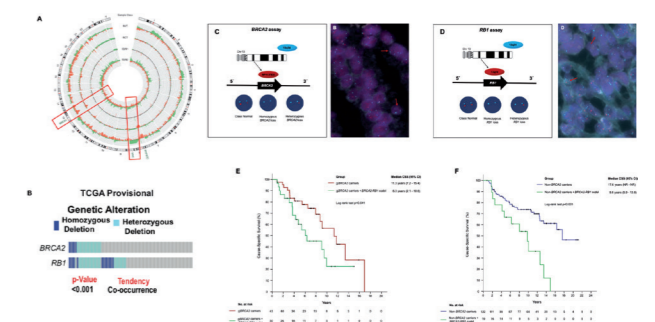
→ Understanding the implication of gene alterations leading to DNA repair deficiency in this disease.  
→ Developing new treatments for prostate cancer.

Our work has been widely recognised with several highly cited publications in top journals in our field, including *The New England Journal of Medicine*, *The Lancet Oncology*, *The Journal of Clinical Oncology*, *European Urology*, *Annals of Oncology*, and many others.

### RESEARCH HIGHLIGHTS

During 2020, our Group was recognised with the 1st *CRIS* Excellence in Research Award. This award will help, among other aspects, to continue our work on understanding gene alterations that could be synergistic with DNA repair defects promoting oncogenesis and prostate cancer progression, and therefore to be exploited as potential new targets. For example, at the 2020 American Society of Clinical Oncology meeting, we presented the results of the PROREPAIR-A study, in which we reported that *BRCA2* defects are frequently associated to *RB1* loss and/or *MYC* amplification, and that their combination is associated to poor outcomes. We also advanced in our understanding of *ATM* defects in prostate cancer. As part of the thesis project of our student Ylenia Cendón, we established that *ATM* may contribute or not to cancer oncogenesis and progression depending on the genetic background (i.e., it may be synergistic in an *RB1* suppression or *MYC* overexpression context, and the opposite in a *PTEN* loss context). Our aim is to publish these results during 2021.

In addition, the group actively participated in several clinical trials, and this included our participation in the steering committees of large phase II trials. We particularly contributed to the approval of olaparib as the first targeted treatment for precision medicine in metastatic prostate cancer. Like everyone around the world, we were also affected by the Covid-19 pandemic. Our research efforts, especially in the clinic, had to be slowed down as doctors in our teams and



**FIGURE** PROREPAIR-A study: (A) aCGH plot comparing PrCa tumours from patients with and without germline *BRCA2* mutations; (B) *BRCA2* and *RB1* loss co-occur also in sporadic PrCa shown by TCGA data; (C) and (D) FISH assays illustrating *BRCA2* and *RB1* co-deletion; (E) gBRCA2 PrCa patients; and (F) sporadic PrCa patients. In both Kaplan-Meier curves showed that patients with somatic co-deletion of *BRCA2* and *RB1* had worse survival outcomes.

other associated researchers had to focus on delivering patient care. Still, we also tried to contribute through international collaborations to understanding the role of *TMPRSS2*, a key AR-regulated gene, which could be involved in SARS-CoV-2's entry into the cell. ■

### PUBLICATIONS

- Hussain M *et al.* (incl. Olmos D); PROfound Trial Investigators (2020). Survival with olaparib in metastatic castration-resistant prostate cancer. *New Engl J Med* 383, 2345-2357.
- de Bono J *et al.* (incl. Olmos D) (2020). Olaparib for metastatic castration-resistant prostate cancer. *New Engl J Med* 383, 2091-2102.
- Khalaf DJ *et al.* (incl. Aragón IM, Lozano R, Cendón Y, Pacheco MI, Olmos D, Castro E) (2020). HSD3B1 (1245A>C) germline variant and clinical outcomes in metastatic castration-resistant prostate cancer patients treated with abiraterone and enzalutamide: results from two prospective studies. *Ann Oncol* 31, 1186-1197.
- Lorente D *et al.* (incl. Castro E, Lozano R, Cattrini C, Olmos D) (2020). Association between second progression-free survival (PFS2) and overall survival in metastatic castration-resistant prostate cancer. *Eur Urol* 77,763-766.
- Perez-Ruixo C *et al.* (incl. Olmos D) (2020). Efficacy and safety exposure-response relationships of apalutamide in patients with nonmetastatic castration-resistant prostate cancer. *Clin Cancer Res* 26,4460-4467.
- Cattrini C, Soldato D, Rubagotti A, Zinoli L, Zanardi E, Barboro P, Messina C, Castro E, Olmos D, Boccardo F (2020). Epidemiological characteristics and survival in patients with de novo metastatic prostate cancer. *Cancers* 12, 2855.
- Lozano R, Castro E, Aragón IM, Cendón Y, Cattrini C, López-Casas PP, Olmos D

(2020). Genetic aberrations in DNA repair pathways: a cornerstone of precision oncology in prostate cancer. *Br J Cancer* 124, 552-563.

- Correa R *et al.* (incl. Olmos D) (2020). Influence of the technique and comorbidities in hypofractionated radiotherapy for prostate cancer. *Clin Transl Oncol* 22, 311-318.
- Messina C, Cattrini C, Soldato D, Vallome G, Caffo O, Castro E, Olmos D, Boccardo F, Zanardi E (2020). BRCA mutations in prostate cancer: prognostic and predictive implications. *J Oncol*, 4986365.
- Rescigno P *et al.* (incl. Olmos D, Castro E) (2020). Early post-treatment prostate-specific antigen at 4 weeks and abiraterone and enzalutamide treatment for advanced prostate cancer: an international collaborative analysis. *Eur Urol Oncol* 3, 176-182.

### AWARDS AND RECOGNITION

- David Olmos:
  - Member of the Board of Directors, European Organization for Research and Treatment of Cancer (EORTC).
  - Impact Award (Partnering PI). US Department of Defense, Congressionally Directed Medical Research Programs.
  - CRIS Excellence in Research Award, Spain.
- Elena Castro: Faculty Board Member, ESMO Preceptorships in PrCa.
- Rebeca Lozano: awarded the "Merit Award", ASCO Annual Meeting 2020.
- Carlo Cattrini: awarded the "Merit Award", ASCO Genitourinary Cancers Symposium 2020.
- Nuria Romero: awarded the "Merit Award", ASCO Annual Meeting 2020.