Divergent Evolution in Bilateral Prostate Cancer: a Case Study

Roni Haas^{1,2,3,4,†}, Yash Patel^{1,2,3,4}, Lydia Y. Liu^{1,2,3,4}, Rong Rong Huang⁵, Adam Weiner^{2,3,4}, Takafumi N. Yamaguchi^{1,2,3,4}, Raaq Agrawal^{1,2,3}, Paul C. Boutros^{1,2,3,4,†}, Robert E. Reiter^{2,3,4,†}

- ¹ Department of Human Genetics, University of California, Los Angeles, USA
- ² Department of Urology, University of California, Los Angeles, USA
- ³ Jonsson Comprehensive Cancer Center, University of California, Los Angeles, USA
- ⁴ Institute for Precision Health, University of California, Los Angeles, USA
- ⁵ Department of Pathology, University of California, Los Angeles, USA

Abstract

Background

Multifocal prostate cancer is a prevalent phenomenon, with most cases remaining uncharacterized from a genomic perspective.

Methods

A patient presented with bilateral prostate cancer. On systematic biopsy, two indistinguishable clinicopathologic lesions were detected. We sampled the separate tumours from freshly frozen radical prostatectomy tissue. A benign prostate tissue was used as a reference control. DNA whole genome sequencing (WGS) was carried out to interrogate the genomic landscape and evolutionary relationship of the tumors

Results

We displayed somatically unrelated tumours with distinct driver CNA regions, suggesting independent origins of the two tumors. This involved CNA-driver regions, including MYC and NCOA2 gains on chromosome 8q and NKX3-1 deletion on chromosome 8p, typically seen in prostate cancer. By contrast Tumour B was characterized by PTEN deletion on chromosome 10, and RB1 deletion on chromosome 13.

Conclusions

We demonstrated that similar clinicopathologic multifocal tumours, which might be interpreted as clonal disease, can in fact represent independent cancers. Genetic prognostics can prevent mischaracterization of multifocal disease to enable optimal patient management.

Funding Acknowledgements

R.H is supported by EMBO Postdoctoral Fellowship ALTF 1131-2021 and the Prostate Cancer Foundation Young Investigator Award 22YOUN32. R.A is supported by the NIH grant T32GM008042. ABW was supported by the UCLA Dr. Allen and Charlotte Ginsburg Fellowship in Precision Genomic Medicine and the Prostate Cancer Foundation Young Investigator Award (23YOUN21). This work was supported by the NIH through awards P30CA016042, U2CCA271894, R01CA270108 and P50CA092131. It was supported by the DOD through awards W81XWH2210247 and W81XWH2210751. This work was supported by a Prostate Cancer Foundation Special Challenge Award to PCB (Award ID #: 20CHAS01) made possible by the generosity of Mr. Larry Ruvo.

Conflicts of Interest Disclosure Statement

P.C.B. sits on the Scientific Advisory Boards of BioSymetrics Inc and Intersect Diagnostics Inc., and formerly sat on that of Sage Bionetworks. All other authors declare they have no conflicts of interest.

[†] Corresponding authors