A NOVEL PROSTATE-RESTRICTED TUMOR-ASSOCIATED ANTIGEN: A POTENTIAL THERAPEUTIC TARGET

Zolila (Areli) Lopez Bujanda,1 Aleksandar Obradovic,2 Thomas Nirschl,3 Timothy O’Donnell,1 Uri Laserson,1 Rodney Macedo-Gonzales,1 Ran Reshef,1 Tiezheng Yuan,1 Mithil Soni,1 Emmanuel Antonarakis,2 Benjamin Lamaran,2 Pawel Muranski,1 Charles Drake,1 Zolila (Areli) Lopez Bujanda,1 Columbia University Irving Medical Center, New York, NY, USA; Johns Hopkins University, Baltimore, MD, USA; Icahn School of Medicine at Mount Sinai, New York, NY, USA; Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA

Background Prostate cancer is the second leading cause of cancer related death in men in the United States, mainly due to disease progression to metastatic castration-resistant prostate cancer (mCRPC). Although immunological treatment with the FDA-approved vaccine sipuleucel-T extends survival for 2–4 months by targeting the prostate-restricted antigen PAP, the identification of more immunogenic tumor-associated antigens (TAAs) continues to be an unmet need.

Methods We evaluated the differential expression profile of the subset of epithelial cells reported to give rise to CRPC from mice following an androgen deprivation/repletion cycle. The expression levels of a set of androgen-responsive genes was further evaluated in prostate, brain, colon, liver, lung, and skin normal tissues from murine and human databases. The expression of a novel prostate-restricted TAA was then analyzed in primary tumors across all human cancer types in The Cancer Genome Atlas (TCGA). Finally, the immunogenicity of this novel prostate-restricted TAA was evaluated in vitro by autologous co-culture assays with cells from healthy donors and in vivo by antibody profiling (PhIP-Seq) in the sera of a cohort of prostate cancer patients treated with AR blockade alone or in combination with the cell-based vaccine GVAX.

Results Here, we discovered a set of androgen-responsive genes exclusively expressed by the putative cell-of-origin for prostate cancer. We confirmed prostate-restricted enrichment of these androgen-responsive genes in normal tissues from murine and human databases. Among these prostate-restricted genes, we identified PAP, PSA, and a novel non-mutated TAA. This novel TAA was confirmed to be expressed in prostate cancer (mCRPC). Although immunological treatment with the FDA-approved vaccine sipuleucel-T extends survival for 2–4 months by targeting the prostate-restricted antigen PAP, the identification of more immunogenic tumor-associated antigens (TAAs) continues to be an unmet need.

Acknowledgements In conclusion, BVax tackles GBM immunosurveillance escape by using both cellular (CD8+ T-cell activation) and humoral (anti-tumor antibody production) immunity. Our study provides an efficient alternative to current immunotherapeutic approaches that can be readily translated to the clinic.

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