Cancer Genomics: Chapter 14. Prostate Cancer Genomics as a Driver of Personalized Medicine

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Prostate cancer (CaP) is the most commonly diagnosed malignancy in men in the Western world. In North America, more than 275000 men are diagnosed annually whereby approximately 1 in 6 men will be diagnosed with CaP in their lifetime, and 1 in 34 men will die from castrate-resistant metastatic disease. Unfortunately, current clinical prognostic factors explain only a proportion of the observed variation in clinical outcome from patient to patient. Furthermore, over-treatment of indolent and low-risk cancers leads to inappropriate morbidity following radiotherapy or surgery. As such, better predictors of individualized prognosis and treatment response are urgently needed to triage patients to customized and intensified CaP treatment. Recent developments in next-generation sequencing have made it possible to identify prognostic and predictive signatures based on genomic profiles. Herein, we review the recent genetic data pertaining to prostate cancer carcinogenesis, progression, castrate-resistance and metastases. We discuss the genetic basis of CaP progression from localized to systemic disease (e.g. point mutations, copy number alterations and structural variants) and important considerations for CaP biology including intra- and inter-prostatic heterogeneity, multifocality and multiclonality, TMPRSS2–ERG and other ETS-family gene fusions and the role of the tumor microenvironment (e.g. hypoxia and the contribution of caner-associated stroma). Finally, we focus on the use of genomic markers as prognostic factors for local failure and for systemic disease, as novel risk stratification tools, in triaging patients to existing treatment options and, ultimately, the potential of genomics for the identification of molecular targets for CaP therapy. We conclude by summarizing selected outstanding questions in CaP biology that can be addressed effectively through international cooperation between genome sequencing projects such as The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC).

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