The hallmarks of castration-resistant prostate cancers.
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Abstract
Prostate cancer has become a real public health issue in industrialized countries, mainly due to patients' relapse by castration-refractory disease after androgen ablation. Castration-resistant prostate cancer is an incurable and highly aggressive terminal stage of prostate cancer, seriously jeopardizing the patient's quality of life and lifespan. The management of castration-resistant prostate cancer is complex and has opened new fields of research during the last decade leading to an improved understanding of the biology of the disease and the development of new therapies. Most advanced tumors resistant to therapy still maintain the androgen receptor-pathway, which plays a central role for survival and growth of most castration-resistant prostate cancers. Many mechanisms induce the emergence of the castration resistant phenotype through this pathway. However some non-related AR pathways like neuroendocrine cells or overexpression of anti-apoptotic proteins like Hsp27 are described to be involved in CRPC progression. More recently, loss of expression of tumor suppressor gene, post-transcriptional modification using miRNA, epigenetic alterations, alternatif splicing and gene fusion became also hallmarks of castration-resistant prostate cancer. This review presents an up-to-date overview of the androgen receptor-related mechanisms as well as the latest evidence of the non-AR-related mechanisms underlying castration-resistant prostate cancer progression.

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