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Androgen Receptor in Orientated Related Tumors

Zhihua Yang*

Department of Oncology, University of Freiburg, Germany

INTRODUCTION

The androgen receptor (AR) is expressed in many cell types, and its related signaling is widely investigated in hormone-dependent cancers such as prostate and breast. The significance of the AR, however, has been detected even in other cancers, including gastric, bladder, kidney, lung, hepatic, and pancreatic, in which growth and spreading are not strictly or notoriously dependent on sex steroid hormone action. The incidence and mortality of these cancers are, however, somewhat related to gender and, specifically, are higher in men than in women, with the ratio reaching 3-4:1 for bladder cancer.

DESCRIPTION

This direct correlation between cancer incidence, mortality, and gender makes sex one of the most important risk factors for these cancers and has incited investigation about the role of sex steroid receptors and their activating hormones in gender-related cancers. In these cancers, the AR is often expressed and seems to play a pivotal role in different processes contributing to cancer onset and progression such as growth, spreading, and epithelial to mesenchymal transition (EMT). This manuscript will offer an overview of the role of the AR in many cancers of the respiratory and gastrointestinal systems wherein its role has been at least partially analyzed. Understanding the role of the AR in these tumors could help us to identify a new biomarker for early diagnostic guidance and to develop better therapeutic approaches by directly targeting the AR or its downstream signaling in individual cells of hormone-related cancers at different stages.

Cancer ranks among the most common causes of death worldwide, and its incidence and mortality are expected to increase due to both the aging of the population and the major diffusion and worsening of some of the risk factors responsible for its onset, such as pollution or an unhealthy lifestyle. In addition to the classic environmental and genomic risk factors, the incidence and mortality of a lot of cancers are also determined by sex or gender. For this reason, an increasing number of scientists have been studying the role of sex steroid hormones in many cancers in addition to reproductive cancers, in which the hormone/hormone receptor action is absolutely the principal guide. To date, different cancers have shown gender disparities, not only in incidence but also in aggressiveness and disease prognosis. Except for breast, thyroid and other rare cancers located in specific sites of the digestive system, a lot of cancers, such as lung, kidney, bladder, gastric, colorectal, liver, and pancreatic, as well as hepatocarcinoma and many others, show a higher incidence in males. The mechanisms underlying this phenomenon are completely unknown, but there are some clear leading points that can help to understand these cancer-related gender disparities. Occupational risk factors, differences in levels of circulating hormones, and the expressions of their receptors could represent starting points to explain gender disparities in patients with cancers with a higher incidence in males. Even if, between the two sexes, there are no differences in the pivotal mutated genes participating in a cancer's development, as is the case with the BRAF gene in melanoma or K-RAS in pancreatic cancer, we must consider that there are whole groups of genes differentially expressed in response to sex steroid hormones able to influence several processes in cancer. For example, studies analyzing gene expression in clear cell renal carcinoma (ccRCC) have shown that, among the analyzed genes, about 90% were activated in a gender-specific way. Accumulating evidence displays that gender differences also influence the immune system, thereby contributing to the unequal disease outcomes and different efficiency in immune response to therapies in men and women.

CONCLUSION

Recently, the relationship between PCOS and other cancers, such as PaC or RCC, was analyzed and confirmed by many studies. These results suggest that diagnosis of PCOS may warrant increased education and clinical vigilance for PaC, but additional studies are required. All the results discussed in this review highlight the need to understand the role of androgens and their receptor in gender-related cancers in order to reduce their incidence and mortality by drawing up both preventive and therapeutic plans.

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Corresponding author Zhihua Yang, Department of Oncology, University of Freiburg, Germany, E-mail: ZhihuaYang124@yahoo.com

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