The Role of ERG Gene in Prostate Cancer

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BACKGROUND

The second most prevalent cancer among men with a 5-year survival rate of 30%, prostate cancer is a pressing issue, especially in the developed world. There were 1.28 million reported cases of prostate cancer in 2018 and it is infamous for quickly metastasizing to the bone and lymph nodes. Prostate cancer begins when normal epithelial cells become a prostate intraepithelial neoplasia (PIN). The PIN becomes a low-grade carcinoma, which with time becomes a high-grade carcinoma, eventually leading to metastasis. It has been observed that 50% of prostate cancer cells overexpressed the ERG gene due to a translocation fusion of TMPRSS2 and ERG. ERG is a putative proto-oncogene within the ETS transcription factor family and is not regularly expressed in healthy prostate cells. TMPRSS2 is an androgen hormone binding site, so when TMPRSS2 fusion with ERG causes ERG transcription initiation because of the androgen hormones binding to the TMPRSS2 receptors. The expression of ERG in the cell plays a role in tumorigenesis, but the underlying mechanisms are not completely understood. To better understand the ERG gene and its relation to prostate cancer, I decided to do a literature review.

METHODS

I started my literature review on the University of Houston Libraries Database to access peer-reviewed publications. I started off my search very generally with keywords such as “ERG” and “ERG:TMPRSS2 translocation.” The same process was done using the Google Scholar Database, yielding publications from various journals. Understanding more about the distinction between epithelial cells in prostate cancer lead me to ERG’s loss of differentiation ability. Reading overviews about the ERG gene in relation to prostate cancer lead me to research more about the upstream and downstream genes and transcription factors regulating or regulated by ERG. In this way, I started looking into TDRD1, a direct downstream target gene of ERG overexpression. ERG’s relationship with the PTEN gene also sheds light on its control over cell differentiation.

RESULTS

Cell Differentiation and ERG

The two main epithelial cell types in the prostate are luminal and basal cells. Luminal cells are differentiated and secrete proteins of prostatic fluid. Basal cells interact with the stroma and express more stem cell properties. Primary untreated prostate cancer is unlike the general definition of cancer because it is caused by luminal cell expansion and absence of undifferentiated basal cells, prostate tumorigenesis paradoxically involves a loss of normal plasticity. Studies have shown that luminal cells express the ERG gene, such that ERG overexpression leads to luminal cell lineage. PTEN is a tumor suppressor gene that provides instructions for making an enzyme that is found in almost all tissues in the body. ERG and PTEN knockout resulted in increased basal cell differentiation.

TDRD1 and ERG

Tudor Domain Containing 1 (TDRD1) is a protein-coding gene thought to function in the suppression of transposable elements during spermatogenesis. Through comprehensive analyses using published datasets from the MSKCC Prostate Oncogene Project, it was found that the expression of TDRD1 was the most significantly increased in ERG-positive tumors. TDRD1 is a novel prostate-specific biomarker. Other studies have emphasized the use of TDRD1’s therapeutic properties in experiments assessing the mechanism between TDRD1 and ERG. ERG can disrupt a tissue-specific DNA methylation pattern at the TDRD1 promoter. As a result, TDRD1 becomes transcriptionally activated in TMPRSS2:ERG positive prostate cancer.

Androgen Deprivation Therapy and TMPRSS2:ERG

Androgen Deprivation Therapy (ADT) is a prostate cancer treatment where androgen hormone levels in the body are suppressed to prevent prostate cancer growth. In most prostate cancers, ERG overexpression is a result of activation by androgens binding to the translocated TMPRSS2 gene. Cohort studies with prostate cancer patients indicate that men with *TMPRSS2:ERG* positive tumors may have longer prostate cancer survival after ADT.

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