Androgen Receptor (AR) has been suggested to play an important role in the metastatic progression in castration resistant prostate cancer (CRPC) and it is believed that AR is correlated with metastatic markers like matrix metalloproteinase 9 (MMP9) and vascular endothelial growth factor (VEGF). Phosphatidylinositol 4-phosphate 5-kinase alpha (PIP5K1α) and its phospholipid product PIP2 have been shown to have important roles in prostate cancer progression. A newly synthesized pharmaceutical called ISA-2011B has been shown to block PI3K/AKT phosphorylation by blocking PIP5K1α. In this study the role of AR in the metastatic progression and its associated to MMP9/VEGF pathway was analyzed in CRPC. The newly developed pharmaceutical ISA-2011B was used to analyzed its therapeutic effect against CRPC.

METHODS

Re-expression and overexpression of AR were performed on AR negative PC-3 cells and AR positive VCAP cells by transfection. Cells were treated with control treatment or dihydrotestosterone (DHT) supplemented in charcoal stripped serum. VCAP cells were treated with control treatment and ISA-2011B. This was followed with migration assay, Immunofluorescence analysis, organoid formation assay and Western Blot.

RESULTS

Re-expression and overexpression of AR lead to increased metastatic progression in CRPC. Results also revealed that AR is correlated with MMP9/VEGF pathway and PIP5K1α with PI3K/Akt pathw ay. Re-expression of AR in PC-3 cells lead to decrease in organoid formation amount indicating increased metastatic potential. ISA-2011B showed to have promising therapeutic effect against CRPC with inhibition of AR and MMP9/VEGF pathway by blocking PIP5K1α.

Conclusion

In this study we have shown that AR mediate the metastatic progression in castration resistant prostate cancer. AR is correlated with MMP9/VEGF pathway and PIP5K1α with PI3K/Akt pathway. Also, the newly synthesized ISA-2011B has a promising treatment effect against CRPC.

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Uméå University and Copenhagen Copenhagen University, Skåne University Hospital of Malmö and Oncorel AB
Per Mikael Johan Larsson
PhD
Division of Basal Tumor Biology and Division of Inflammation and Cancer
Department of Molecular Biology and Department of Microbiology and Immunology
Per.larsson@umu.se
073-2622025
https://www.umu.se/en/staff/per-larsson

In my research I am currently investigating the role of AR in the reconciliation of PCA and how it affect the metastatic progression of PCA.