

## **CELLULAR PLASTICITY AND REPROGRAMMING IN LETHAL NEUROENDOCRINE PROSTATE CANCER**

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**T**he major clinical challenge for prostate cancer treatment is targeting the highly aggressive and incurable disease that emerges under the pressure of contemporary androgen receptor (AR), pathway inhibitors (ARPIs) such as enzalutamide (ENZ): neuroendocrine prostate cancer (NEPC). The aim of our study is to understand what regulates the cellular plasticity that allows prostate cancer cells to shed their dependence on the AR and re-emerge as AR-indifferent NEPC. Our data suggest that NEPC trans-differentiation is aligned with dynamic cellular reprogramming which occurs as a response to AR pathway inhibitors. Our data reveals novel AR binding proteins that orchestrate the self-renewal and neuroendocrine trans-differentiation programs leading to aggressive disease form of prostate cancer. These reprogramming factors, including BCOR, FOXM1, BRN2 and EZH2, are also very attractive therapeutic targets. In addition, we have developed novel live-cell cellular plasticity imaging methods that allow us to capture the cellular reprogramming and neuroendocrine trans-differentiation live in in vitro prostate cancer models. By utilizing our models and imaging methods, we have identified novel players of cellular plasticity whose overexpression by ARPIs lead to a cellular morphology change and development of NEPC. The expression of the novel cellular modulators identified were validated in patients with incurable NEPC, and the morphology changes in vitro were validated using super-resolution confocal and scanning electron microscope imaging in both prostate cancer and neurodegenerative disease models. Taking together, by identifying and inhibiting the cellular plasticity and reprogramming processes in neuroendocrine prostate cancer, we hope to develop a better care for men with this fatal disease.

### **Biography**

Kirsi Ketola has completed her PhD from University of Turku and Postdoctoral studies from University of British Columbia School of Medicine. She is the Director of the Cellular Plasticity and Neuroendocrine Trans-differentiation program at the University Of Eastern Finland School of Medicine. He has published more than 20 papers in reputed journals and has been serving as an Editorial Board Member of reputed.

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