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A protocadherin that crosstalks with the androgen receptor axis to control neuroendocrine transdifferentiation in human prostate cancer

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astration-resistant prostate cancers that relapse after androgen deprivation therapies are overwhelmingly responsible ✓ for the mortality from prostate cancer. These tumors progress despite castrate androgen levels and respond poorly to most therapeutics including chemotherapy. Although mechanisms enabling recurrent activity of Androgen Receptor (AR) are certainly involved in the growth of castrate resistant tumors, how these tumors convert from a hormone-sensitive to a castrate resistant phenotype remains unclear. Protocadherin-PC (PCDH-PC) is a putative androgen-repressed gene on the Y-chromosome, and a potential marker of apoptosis-resistance and neuroendocrine phenotype in the commonly used prostate cancer cell line, LNCaP. In recent investigations, we explored the dynamic expression pattern of PCDH-PC following androgen deprivation in human prostate cancer specimens as well as in cultures of LNCaP cells. Potential relationships between Androgen Receptor (AR), PCDH-PC and NE differentiation were also studied in various cell lines as well as their sensitivity to chemotherapeutic agents. PCDH-PC expression as being especially up-regulated in short-term hormonally treated tumors and in cell cultures in association with increased NE differentiation was found. Furthermore, acquisition of an NE phenotype by prostate cancer cells correlated with the emergence of a chemoresistant state. Finally, it was found that androgen regulates the expression of PCDH-PC and that PCDH-PC inversely modulated the ligand-dependent AR transcriptional activity, thereby regulating the neuroendocrine phenotype in prostate cancer cells. Together these results suggest that PCDH-PC can serve as an early marker for the transition of prostate cancer from epithelial to neuroendocrine phenotype and support a model of transdiffentiation/adaptive mechanism as an important step towards chemohormonal resistance.

Biography

Stéphane Terry is a Molecular and Cellular biologist whose research has been focused on prostate cancer (PCa). He earned his PhD from the University of Paris-Sud (France) in 2008 for his work on cell signaling perturbations in PCa cells following androgen ablation. After a post-doctoral training at the Weill Cornell Medical College on molecular characterization of PCa, he returned to France where he is currently a young investigator working closely with clinicians at the Institut Mondor de Recherche Biomedicale. His current interest is in identifying mechanisms by which PCa cells acquire neuroendocrine characteristics as a means to adapt and progress through treatments.

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