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Integrating endocrine regulatory mechanisms in prostate cancer progression

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Abstract

Prostate cancer (PCa) ranks first in incidence among cancers in American males and second as a cause of death by cancer. Beside age, etiologic and progression factors are still not fully identified. Accumulating evidence point to changes in signalling molecules and pathways as means to confer survival and/or growth advantages to tumor cells as they evolve with time and become resistant to androgen deprivation- and chemo-therapies. Our studies on the non-receptor Fak and Fer tyrosine kinases (TKs) indicate that beside their up-regulation in PCa, these kinases are key elements controlling PCa cell motility and survival/growth, respectively. Notably, Fak signaling complexes with Src, paxillin and integrins are involved in PCa cell response to neuroendocrine (NE) products, eliciting selective patterns based on androgen receptor (AR) expression in PCa cells. The Fer TK integrates signals emanating from interleukin (IL)-6 and to a lesser extent growth factors (EGF, IGF-1) and also androgens. This occurs through STAT3 and AR, both identified as Fer substrates and binding partners and accumulating into the nucleus where they regulate transcription. Altogether, these mechanisms favor the adaptation of androgen-sensitive luminal-like tumor cells and the concomitant selection of androgen-independent tumor cell subsets (stem, NE). They concur to cell heterogeneity of tumors and metastases as observed during PCa progression.

Biography

Simone Chevalier completed her Ph.D at the age of 25 years from “l’Université de Montréal”, Montréal, Canada and postdoctoral studies from the Department of Biochemistry, University of British Columbia, Vancouver, and the Department of Medicine (Endocrinology), Maisonneuve-Rosemont Research Centre, Montréal. She is associate professor in Surgery, Urology Division, McGill University and the McGill Urology Director of Research. She is also affiliated to the Medicine and Oncology Departments. Devoted to the cause of prostate cancer, she directs the PROCURE Québec Prostate Cancer Biobank since 2007. She published more than 90 papers in reputed journals and 350 presentations at national and international meetings.