

7018 **NFκB Activity Modulates the Oncogenic Potential of Stat3 in Prostate Cancer Development**

POSTER

J. Pencik¹, M. Schleder¹, M. Mair¹, M. Musteanu¹, V. Poli², R. Eferl¹, R. Moriggi¹, Z. Culig³, L. Kenner¹. ¹Ludwig Boltzmann Institute for Cancer Research, Vienna, Austria; ²University of Turin, Department of Genetics Biology and Biochemistry, Turin, Italy; ³Medical University Innsbruck, Urology Department, Innsbruck, Austria

Background: Prostate cancer is one of the most frequent tumours in the Western world. Approximately 27000 men die each year from prostate cancer in USA. The Jak/Stat pathway (Jak – Janus kinase, Stat – signal transducer and activators of transcription) is an important signaling cascade in prostate cancer. Stat3 seems to play an essential role in regulation of proliferation, apoptosis, angiogenesis and drug resistance in prostate cancer. The NF-κB pathway is a key player in inflammation. Deregulation of components of the NFκB cascade was observed in metastatic prostate cancer with activated Jak/Stat. Stat3 signaling was shown to cause growth inhibition and apoptosis of cancer cells. Although there has been evidence for an oncogenic function of Stat3, observations from several laboratories suggest the opposite. Under certain conditions activation of Stat3 leads to decreased growth of prostate cancer cells in vitro and can exert an inhibitory effect on prostate cancer xenografts.

Material and Methods: We conditionally deleted PTEN in prostate epithelial cells (PTEN^{ΔPEC}) taking advantage of Cre-recombinase under a prostate-specific probasin (PB) promoter (ARR2PB). To investigate the role of Stat3 in prostate cancer, we crossed PTEN^{ΔPEC} mice with Stat3 floxed mice (obtained from Valeria Poli) or with mice harbouring a constitutively activated Stat3 (Stat3^C). We analysed PTEN^{ΔPEC} Stat3^C mice by immunohistochemistry and immunofluorescence. Quantification of protein expression in tissue sections were measured using HistoQuest™ and TissueQuest™ software. In addition, we quantified RNA and protein expression using qRT-PCR and Western Blot techniques.

Results: Loss of Stat3 in PTEN^{ΔPEC} resulted in accelerated tumour growth, massive inflammation and increased angiogenesis. In contrast, constitutive active Stat3 in PTEN^{ΔPEC} mice led to decreased tumour formation. The PTEN^{ΔPEC} Stat3^{C/+} mice showed decreased inflammatory infiltrates (mast cells and T-cells) when compared to PTEN^{ΔPEC} mice. Western blot analysis of PTEN^{ΔPEC} Stat3^{C/+} mice revealed significant downregulation of IKKα, IKKβ and p65 when compared to PTEN^{ΔPEC} mice.

Conclusions: Stat3 in prostate cancer cells interferes with tumour growth. Activation of NFκB in PTEN^{ΔPEC} mice promotes inflammation and interactions between stromal and tumour cells. In further experiments we will focus on the molecular link between Stat3 and NFκB in prostate cancer development.

7019 **Potential Value of HOXB13 as a Progression Marker for Recurrent Prostate Cancer**

POSTER

T. Kang¹, K. Oh¹, N. Nguyen², Y. Kim², C. Choi³, M. Kim⁴, C. Jung⁵. ¹Chonnam National University Medical School, Urology, Gwangju, Korea; ²Chonnam National University Medical School, Anatomy, Gwangju, Korea; ³Chonnam National University Medical School, Pathology, Gwangju, Korea; ⁴Chonnam National University, Statistics, Gwangju, Korea; ⁵Chonnam National University, Anatomy, Gwangju, Korea

Background: Many patients with prostate cancer have disease recurrence after surgical removal of tumours and fail to respond to androgen-ablation therapy. Even with the help of a number of clinical/pathological factors, it is not possible to predict which patients will fall into this category. The results of our previous studies demonstrated that the HOXB13 homeodomain protein plays an important role in the development of prostate cancer and the progression of this malignancy. In addition, HOXB13 has been reported to predict estrogen-resistant breast cancer tumours. The purpose of this study was to study whether HOXB13 could be a molecular marker used to predict prostate cancer recurrence.

Materials and Methods: To examine the role of HOXB13 as a molecular marker with clinical/pathological data, the expression of HOXB13 was compared using immunohistochemistry in 57 organ-confined prostate cancer tumours obtained by radical prostatectomy.

Results: There was no significant correlation between the expression of HOXB13 and most clinical/pathological parameters including the tumour margin, invasion, pathological stage, and risk level. The HOXB13 expression level correlated with the Gleason score and there was a positive tendency for it to correlate with the preoperative PSA level. Accordingly, the tumour specimen from four patients that ultimately had biochemical failure (PSA >0.2 ng/mL) all showed a high expression of HOXB13, while their risk levels were either intermediate or high.

Conclusions: This is the first report that HOXB13 may increase the predictability in recurrent prostate cancer when it combined with other clinical/pathological factors. However, more extensive study with larger patient pool is required to confirm the clinical value of HOXB13 as a prognostic marker for prostate cancer.

7020 **Survival After Biochemical Failure – the “Far Away” in Prostate Cancer**

POSTER

C. González¹, J.A. Santos-Miranda¹, M. Muñoz-Fernández¹, B.D. Delgado-León¹, F. Herranz-Amo², A. Álvarez-González¹, P. Cuesta-Álvarez³. ¹Hospital Universitario Gregorio Marañón, Oncology, Madrid, Spain; ²Hospital Universitario Gregorio Marañón, Urology, Madrid, Spain; ³Universidad Complutense, Statistics, Madrid, Spain

Background: The biochemical relapse-free survival is the goal of the studies that analyze the effectiveness of local treatments for prostate cancer (CaP). However, patient's evolution after biochemical recurrence (BR) is a poor studied parameter. We analyze and compare the survival of patients initially treated with surgery or radiotherapy (RT) following diagnosis of RB.

Material and Methods: We report the experience of HGU Gregorio Marañón in follow up and treatment of patients with RB criteria, focusing in survival from recurrence, patterns of progression and efficacy of salvage therapies.

Results: 366 patients with RB treated with surgery (267) or RT (99) were considered eligible for analysis. Time to RB from initial diagnosis was higher in irradiated patients (51.5 vs 35.5 months). However, the median survival from RB to death or latest news was 62 months in the surgery group and 22 months in the RT cohort (p = 0.00). After a median follow up of 91 months, the 8 yr cause-specific survival was 93.5% in operated patients and 88% in those treated with RT (p = 0.01). 35 patients (9.5%) died of CaP.

In the surgical group, 162 patients (60.5%) received RT as salvage therapy. 13% of the operated and 27% of irradiated patients did not received treatment after RB. In patients treated with radical RT, only 17% had a local salvage treatment (cryotherapy or brachytherapy) and 56% received androgen deprivation ± chemotherapy. After RB, 41 operated patients (15%) and 21 after RT developed metastases, mainly in bone.

The poorest outcome was observed in patients who developed RB during adjuvant hormoneotherapy after RT and in patients with persistent elevated PSA after prostatectomy. Patients undergoing salvage RT after RB obtained the best survival rates.

Conclusions:

- In prostate cancer patients, median survival after RB is fairly long (51 months) and higher in operated patients.
- After RB, 15–20% of patients develop metastases.
- Defining criteria for treatment of irradiated patients with RB will help us to optimize their management and improve survival rates.

7021 **Multidisciplinary Management of Castration Resistant Prostate Cancer (CRPC) in France – a Survey Comparing Practices and Assessing Collaboration Between Urologists and Oncologists**

POSTER

T. de La Motte Rouge¹, D. Pouessel², A. Benchikh³, F. Dubosq⁴, X. Durand⁵, N. Gillion⁶, A. Plantade⁷, I. Alexandre⁸, F. Thibault⁹. ¹Groupe Hospitalier Pitié Salpêtrière, Service d'Oncologie Médicale (SOMPS), Paris, France; ²Hopital Saint Louis, Service d'Oncologie Médicale, Paris, France; ³Groupe Hospitalier Bichat-Claude Bernard, Service d'Urologie, Paris, France; ⁴Hopital Saint Louis, Service d'Urologie, Paris, France; ⁵Hopital d'instruction des armées du Val de Grace, Service d'Urologie, Paris, France; ⁶Hopital Mondor, Service d'urologie, Creteil, France; ⁷Hopital des Diaconesses, Service d'Oncologie Médicale, Paris, France; ⁸Centre Hospitalier de Lagny, Service d'Oncologie Médicale, Lagny, France; ⁹Groupe Hospitalier Pitié Salpêtrière, Service d'Urologie, Paris, France

Background: In France, multidisciplinary meeting to discuss individuals' cases is mandatory and helps collaboration between urologist and oncologist. The primary goal of this study was to analyze the putative differences in management of castration resistant prostate cancer (CRPC) among urologists and oncologists and to assess the quality of the collaboration.

Material and Methods: This nationwide study was performed from May to November 2010. A 24-items questionnaire was sent to the members of the French association of urologists (AFU) and to the oncologists involved in the management of CRPC patients. Answers from 450 urologists and 150 oncologists were expected. Information on the mode of clinical practice, local multidisciplinary meeting setting and management of CRPC was requested. The completed questionnaires were anonymously collected