

Therapeutic targeting of NADPH Oxidase 4 (Nox4) in prostate cancer

Natalie Sampson

Department of Urology,
Division of Experimental Urology
Medical University of Innsbruck

Cédric Szyndralewicz

Genkyotex S.A.
Geneva
Switzerland

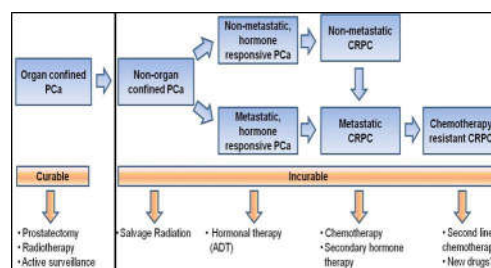
Need for NEW treatment strategies for prostate cancer

Despite improvements in screening programmes & development of new drugs, prostate cancer remains the 2nd leading cause of male cancer-related death in Western societies

⇒ urgent need for new treatment strategies

Current systemic treatment options target androgen-dependent growth of tumour cells

⇒ ultimately therapy resistance and development of recurrent tumours



Alternative therapeutic strategy:

targeting intimately connected neighbouring "stromal" cells that support tumour cell function

UROLOGY
Medical University Innsbruck

Nox4: central to tumour-driven corruption of the tissue microenvironment

pre-malignant/tumour cell

cancer-associated fibroblast (CAF)

TGFβ

TGFβ receptor

NOX4

ROS

CAF activation

tumour progression, therapy resistance, poor outcome

Aim: therapeutic potential of Nox4 inhibition as stromal-targeted strategy?

STATUS/OUTLOOK – see poster for details

- efficacy of Nox4 inhibitor in PCa in final phase of pre-clinical validation (tissue culture, animal models)
- currently in talks with Genkyotex to conduct clinical trials of Nox4 inhibitor for BPH and PCa

tilak

Nox4 TGFβ BE CA

Nox4 gene expression associated with aggressive PCa and poor prognosis

UROLOGY
Medical University Innsbruck

Innovation & translational success

“Model systems are like model students, they do exactly what you want them to do” Charles Weissmann, Biogen

- 1. Patient-orientated experimental approach:**
 - all experiments employ primary patient-derived tissue
 - ⇒ closely mimic patient situation (*relevance*)
 - ⇒ broad spectrum of patients (*data reproducibility*)
- 2. Stromal targeting as a novel therapeutic strategy:**
 - blocking essential bidirectional communication between stroma and the tumour cells
 - ⇒ complement current therapies, which do not specifically target stromal component of disease
 - in contrast to tumour cells, CAFs are genetically stable
 - ⇒ development of mutations that confer therapy resistance less likely

PCa tissue

cells

CAFs/NAFs

tissue culture

1 2

ctrl Nox4i

Acknowledgements

Department of Urology, MUI

Helmut Klocker
Elena Brunner
Martin Puhr
Gabriele Dobler

GenKyoTex S.A.

Cédric Szyndraleweiz
Philippe Wiesel

Division of Bioinformatics, MUI

Zlatko Trajanoski
Charoentong Pornpimol

Institute of Pathology, MUI

Georg Schäfer
Sarah Peer

DKFZ, Heidelberg

Holger Sültmann

Funding

FWF - Lise Meitner (M903) & Elise Richter (V216)
Austrian Cancer Research Society of Tyrol
Austrian Academy of Science