Unmoderated Posters: Basic Science, Physiology and Research

UP-03
Capsaicin May Reduce the Metastatic Burden in the Transgenic Adenocarcinoma of the Mouse Prostate (TRAMP) Model

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Introduction and Objectives: A large body of evidence supports the role of dietary factors in prostate cancer development and progression. We are interested in investigating the chemopreventive potential of capsaicin, the active component in chilli peppers that is traditionally used topically to treat various pain-related syndromes. Recently capsaicin has been reported to have anti-carcinogenic properties. In our study, we aim to study the chemopreventive properties of capsaicin using the transgenic adenocarcinoma of the mouse prostate (TRAMP) model, a mouse model that closely resembles the progression of human disease.

Methods: Thirty-five 6-week old TRAMP mice were randomized into two groups. Mice received either capsaicin (5 mg/kg body weight) or vehicle 3-times a week by oral gavage. Body weight (BW) was measured thrice weekly. All mice were sacrificed at 30 weeks. BW, genito-urinary (GU) weight, tumour burden were assessed. Serum, prostate, seminal vesicles, lung, liver, esophagus, lymph nodes and pancreas were obtained for analysis. All tumours were scored by an on-site pathologist according to the histopathologic grading scale and analyzed using proliferative and mechanistic markers.

Results: Interim results revealed that higher percentage of high-grade cancer in control group (n=18). The presence of PIN-like pre-cancerous lesions in only the treatment group and not the control group (n=18), and capsaicin treated mice also had a reduced proportion of metastatic cancers compared to the control group. There were no significant changes in the GU wet weight between groups. Immunohistochemical analysis of the prostate tumour is ongoing. There were no pathological liver or esophagus or gastrointestinal toxicities or changes in BW between grouped.

Conclusions: Interim results suggest that oral administration of capsaicin is well tolerated and may reduce the metastatic burden in the TRAMP model. Ongoing studies to delineate the mechanism of action are underway.

UP-04
Androgen Leads to Tumour Growth Control Through IKKε Expression in a Mouse Xenograft Model of Prostate Cancer

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Objectives: Following androgen depletion therapy (ADT), prostate cancer (PCa) can progress from a hormone sensitive (HS) to castrate resistant (CR) state. We have previously demonstrated the specific high expression of IKKε in advanced stages of PCa. We are performing experiment to determine whether androgen and hormon-dependent influence the role of IKKε in late stage disease.

Methods: We used HS 22Rv1 PCA cells that overexpress IKKe in a doxycycline inducible manner (22Rv1-6TR-IKKε). We injected 22Rv1-6TR-LacZ and 22Rv1-6TR-IKKε cells into SCID mice and compared 72 castrated and 72 unastrated animals fed with or without doxycycline. In order to study the implication of the AR itself, we are deriving constitutive AR knockdown clones (22Rv1-6TR-IKKε/shAR). Cell proliferation and invasion experiments will be conducted. Furthermore, we will describe how proliferation is affected. On the other hand, xenografts with 22Rv1-6TR-IKKε/shAR clones will reinforce this study.

Results: As expected, due to the hormone-sensitivity of 22Rv1 cells, growth of 22Rv1-6TR-LacZ xenografts is negatively affected by castration but not by doxycycline. Interestingly, growth of 22Rv1-6TR-IKKε xenografts is decreased when IKKε is expressed. This effect is weakened upon castration. In vitro and complementary in vivo experiments with our new clones modified for AR expression are being conducted to better understand these results.

Conclusions: Our results demonstrate that the presence of androgen co-constituent with IKKε expression had a positive effect on the survival of mice xenografted with HS cells. Unexpectedly, this benefit seems to be reduced upon castration, suggesting that the positive tumour growth activity of IKKε is contextual, and influenced by androgen.

UP-05
Demonstration of the Direct Impact of Ketamine on Urothelium Using a Tissue Engineered Bladder Model

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Introduction: Ketamine is an anaesthetic agent used for induction of general anaesthesia and for the relief of chronic pain. It is associated with side effects like hallucinations, confusion and out of body experience. These effects, pleasurable to some, have led to its consumption as a recreational drug. In the last decade reports described severe lower urinary tract symptoms linked with ketamine consumption. This led to the creation of a new clinical entity: Ketamine Induced Cystitis (KIC). To better understand the mechanisms involved in this condition, the effects of ketamine were evaluated on a human three-dimensional tissue engineered bladder model.

Methods: An entirely human tissue engineered bladder model produced using the self-assembly method unique to our laboratory, was used for these experiments. Human urothelial cells were plated on a stratum layer made of dermic fibroblasts and incubated at the air/liquid interface to allow their differentiation. Various concentrations of ketamine solutions were then put on the mature urothelium using paper and agarose vectors. The models were then incubated for 2 days. After incubation, histological sections and immunofluorescence studies were made to assess the impact of ketamine on the urothelium.

Results: Ketamine had an important deleterious effect on urothelium through the induction of apoptosis. Its presence markedly affected the structure and did so in a concentration dependent fashion.

Conclusions: It seems that one of the potential mechanisms involved in the urothelial damages of KIC could be a direct attack of ketamine, which is excreted in the urine. To our knowledge this is the first time that a direct effect of ketamine on human urothelium is shown. Our tissue engineered vesical equivalents are among the models that are the closest to human urothelium and their use will certainly help better define the mechanisms implicated in KIC and eventually help develop and test treatments.