CANCER-ASSOCIATED FIBROBLAST-DERIVED CHARACTERISATION OF HTERT-IMMORTALISED INVOLVEMENT OF VERSICAN, A CHONDROITIN SULFATE PROTEOLGYCAN IN THE PATHOGENESIS OF MULTIPLE MYELOMA.

Introduction Multiple Myeloma (MM) is second most common haematological malignancy characterised by uncontrolled proliferation of abnormal plasma cells in bone marrow (BM). The growth of these myeloma cells is facilitated by BM niche consisting of numerous proteins, proteoglycans, cytokines and growth factors. One of the chondroitin sulfate proteoglycan, Versican (VCAN) has gained consideration in context of solid tumours where in it has been shown to promote tumour progression but there is dearth of literature in haematological malignancies including MM. Therefore, the involvement of VCAN in association with MM has been studied.

Material and methods 30 newly diagnosed MM patients and 20 controls were recruited. BM Mononuclear Cells (BMMNCs) were isolated from their BM aspirate. In representative samples (n=15), BM Stromal Cells (BMSCs) were harvested from BMMNCs by primary culture. The relative mRNA expression of VCAN and its four isoforms (V0, V1, V2 and V3) were investigated in BMMNCs, BMSCs and MM...
cell lines (RPM18226 and U266). Conditioned medium (CM) of primary cultured BMSCs was collected and examined for presence of VCAN by ELISA. Thereafter, the effect of BMSCs CM was studied on MM cells in presence or absence of VCAN antibody. To accomplish this, PCNA along with MTT assay for proliferation, VEGF for angiogenesis and Bcl-2, PUMA for apoptosis were investigated. Further, the signalling pathways involved in the action of VCAN were also identified.

**Results and discussions**

The relative mRNA expression of VCAN and its isoforms were found significantly higher in MM patients in both BMMNCs and BMSCs with higher expression in BMMCs than in BMMNCs. VCAN being produced in stroma found at lower levels in MM cell lines. Furthermore, BMMCs CM showed the presence of VCAN whose effect was evaluated in MM cell lines in vitro. Upon treatment with BMMCs CM, proliferation and angiogenesis increase while apoptosis decrease in cell lines, however, effect of CM neutralised in presence of VCAN antibody. The downstream signalling of VCAN was observed to entail phosphorylation of FAK and STAT3 which subsides by treatment with VCAN antibody.

**Conclusion**

Augmented levels of VCAN and its isoforms in BM of patients especially in BMSCs imply their involvement in BM microenvironment of MM. The neutralisation of the oncogenic effect of BMMCs CM upon treatment with VCAN antibody affirms the plausible role of VCAN in pathogenesis of MM. These findings open up new avenues for exploration of VCAN as a therapeutic target for treatment of MM in future.

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**PO-285 IMMUNOMODULATORY EFFECTS OF LACTOBACILLUS STRAINS: EMPHASIS ON IDENTIFICATION OF PROBIOTIC CANDIDATES WITH ANTI-TUMOUR RESPONSES**

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**Introduction**

Mucosal macrophages are essential for driving immune responses in mucosal membranes. In homeostatic environments, regulatory responses are predominated by the M2 subset, whereas inflammatory responses are mediated via their ability to switch to a pro-inflammatory M1 subset. Tumour-associated macrophages (TAMs) have been found to play a fundamental role in tumour development. Therefore, the aim of this study was to identify macrophage subset-specific responses to a panel of Lactobacilli with the objective of discovering candidates that elicit anti-tumour responses for future in vivo management of colorectal cancer.

**Material and methods**

A panel of candidate strains: L. planta-

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**PO-286 EVALUATING THE INFLUENCE OF MESENCHYMAL STROMAL CELLS DERIVATIVES ON EARLY STAGE OF BREAST CANCER**

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**Introduction**

Tumour microenvironment plays a decisive role in cancer development and metastasis, and affects the therapeutic effectiveness of anticancer drugs. Mesenchymal stromal cells (MSCs) are an important elements of tumour stroma. MSCs can both stimulate and inhibit tumour progression, depending on the components of microenvironment, genesis and stage of cell differentiation. Special attention focused on the paracrine effect of products secreted by MSCs. The aim of this study was to characterise the influence of derivatives from human bone marrow MSCs on proliferation, survival, receptor profile of MCF-7 in 2D and 3D cell cultures in vitro.

**Material and methods**

The monolayer MCF-7 cell culture was cultured in standard conditions in DMEM nutrient medium (Sigma, USA), with 2 mM l-glutamine (Sigma, USA), 40 mg/mL Gentamicin (Biopharma, Ukraine). The initial density of MCF-7 cells was $2 \times 10^4$ cells/cm$^2$. Human bone marrow multipotent mesenchymal stromal cells (MSCs) were used. MCF-7 cells were incubated in full nutrient conditioned media from MSCs in the ratio 1:1. For the initial generation of spheroids the DMEM nutrient medium with 2% carboxymethyl cellulose (Bio-Rad, USA) was used. Plates with spheroids were being incubated on an orbital shaker (PSU-10i, Biosan, Latvia) at 80 rpm for 3–5 hours. The spheroid culture was maintained for 7 days. Cell viability was evaluated by MTT assay. The Stemidi2000 software Axio Vision Red 4.7 (Zeiss, Germany) was used for processing the images. The