PRESENTATION NUMBER: LBA-47
CHONDROPROTECTIVE AND ANTI-INFLAMMATORY EFFECTS MEDIATED BY EXTRACELLULAR VESICLES FROM PLASMA- AND SERUM-BASED BLOOD-DERIVED PRODUCTS FOR OSTEOARTHRITIS THERAPY

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Purpose: Plasma- or serum-based blood-derived products are intra-articularly injected into osteoarthritic joints to favour pain relief, reduce inflammation and promote cartilage regeneration. Preparations of platelet-rich plasma anti-coagulated with citrate (CPRP) are often applied, but also anticoagulant- and cell-free alternatives such as hyperacute serum (hypACT) are investigated. In addition to growth factors, blood products contain extracellular vesicles (EV) which are around 30-1000 nm sized membraneous particles and are carriers of signal molecules such as lipids, proteins or RNAs. These open up new levels of complexity at understanding mechanisms of action of blood products. Therefore, this study outlines roles of EVs isolated from blood products and characterises their contribution to the regenerative potential of these blood products.
Methods: To attribute potential chondroprotective and anti-inflammatory effects elicited by the EV fraction of blood products, ultracentrifugation was used to enrich EV from blood products. Concentration and mode size of enriched EVs was assessed via nanoparticle tracking analysis (NTA). Presence of EV marker proteins and depletion of frequently co-isolated components such as lipoproteins was monitored via Western Blot. Primary OA chondrocytes were then treated with the EVs in presence or absence of IL1β. Gene expression changes were analysed via reverse transcription quantitative PCR (RT-qPCR) and Western Blot. Cytokine release was monitored via enzyme-linked immunosorbent assay (ELISA) in sandwich format.
Results: Gene expression analysis revealed increased levels of type II collagen (COL2A1), SRY-box transcription factor 9 (SOX9) and aggrecan (ACAN) compared to full blood products, but also of the catabolic marker and tissue remodeling factor matrix metalloproteinase 3 (MMP3). hypACT EVs prevented increased type I collagen (COL1A1) expression compared to CPRP EVs. CPRP blood product increased SOX9 protein expression, whereas CPRP EVs prevented SOX9 expression and decreased COX2 levels. In contrast, hypACT EVs elevated COX2 expression, while promoting SOX9 expression. Enzyme-linked immunosorbent assay (ELISA) targeting IL6 released from chondrocytes showed a dramatic decrease in presence of EVs from hypACT or CPRP compared to the respective blood products.
Conclusions: The Results indicate that blood EVs are sufficient to promote chondrogenic gene expression changes in OA chondrocytes, while preventing pro-inflammatorsy cytokine release compared to full blood products. This highlights the potential of blood-derived EVs as regulators of cartilage extracellular matrix metabolism and inflammation as well as candidates for new cell-free therapeutic approaches for OA.

PRESENTATION NUMBER: LBA-48
ARTICULAR CARTILAGE REGENERATION BY ACTIVATED SKELETAL STEM CELLS

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Purpose: Here we investigate the ability of resident skeletal stem-cell (SSC) populations to regenerate cartilage in relation to age, a possible contributor to the development of osteoarthritis (OA).
Methods: We tested if microfracture (MF) surgery could stimulate expansion of SSCs on the chondral surface of adult limb joints in mice by inducing a localized regenerative response. We then tested if exogenously applied factors could skew the differentiation of the activated SSCs towards hyaline cartilage.
Results: We find that although activated SSCs tended to form fibrous tissues, localized co-delivery of BMP2 and soluble VEGFR1 (sVEGFR1), a VEGF receptor antagonist, in a hydrogel skewed differentiation of MF-activated SSCs towards articular cartilage.
Conclusions: These data indicate that following MF, a resident stem-cell population can be induced to generate cartilage for treatment of localized chondral disease in OA.

PRESENTATION NUMBER: LBA-49
THROMBOCYTE DERIVED PRODUCT EFFICACY IN KNEE PTOA TREATMENT

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Purpose: to study efficacy and safety of the platelet autologous plasma (PAP) comparing to standard treatment in young patients with symptomatic knee post traumatic OA (PTOA)
Methods: Study included 62 patients (mean age 38.29±3.51 years) with established symptomatic knee PTOA (mean time from trauma - 46.87±2.09 months), I-II stages (X-ray). Patients with prominent known primary OA risk factors (obesity, metabolic diseases), after knee surgery, with other arthritis or any other uncontrolled diseases and disorders were not included in the study. All patients were concented to participate in the study and were divided into 2 groups -Gr.1 received standard treatment (NSAIDs, exercises, multimodal physiotherapy), Gr.2 - received the course of 3 intra-articular injections of PAP in addition to the standard treatment. Efficacy and safety was evaluated by KOOS, VAS, laboratory investigations.
Results: During early observation period (first 2 weeks) all patients with PTOA demonstrated significant improvement in pain and functional activity, comparing to baseline values but patients from Gr.2 demonstrated better daily living activities and better points in KOOS sport and recreation subscales. In 4 weeks the difference between groups were more prominent, with better results of treatment in group treated with PAP. Later, during the late observation period, second group still demonstrated better outcomes (both comparing to the baseline and to the first group), while Gr. 1 patients partly returned to the baseline levels; after 3-6 months one third of Gr. 1 patients experienced 1-2 OA exacerbations, accompanied by repeated NSADs use; in Gr.2 only 6.45% of patients has had 1 OA exacerbation (p&l0.05). At 12 months period the majority of Gr.2 patients still had better knee functional capacity and less pain comparing to the baseline, while Gr.1 patients showed no significant difference with baseline in all KOOS parameters. No significant complications were observed during PAP use, except of temporary local pain at the injection site.
Conclusions: Use of the PAP intraarticular injections in addition to the standard PTOA treatment improves both early and late Results of treatment, decreases the number of OA exacerbations and need in NSAIDs use during 12 months after treatment.

PRESENTATION NUMBER: LBA-50
THERAPEUTIC MOLECULES FOR OSTEOARTHRITIS TREATMENT. ROLE OF PHLORETIN, IPRIFLAVONE AND RALOXIFENE IN LIPOPOLYSACCHARIDE INDUCED OSTEOARTHRITIC CHONDROCYTES

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Purpose: The search of novel molecules for the treatment of osteoarthritis (OA) is complex as any new therapeutic approach should encompass these requirements: inhibition of cartilage degradation, protection of bone and inhibition of inflammation. In the last years, different drugs have been proposed though most of them did not succeed in fulfil these requirements. Moreover, few of them have been encapsulated in drug delivery systems to improve their therapeutic potential to achieve a sustained or controlled release compared to the administration of equivalent doses of the free compounds. Nanoscience has arisen in the last decades as a potential field of study in drug delivery because nanomaterials may overcome the main current limitations to achieve an efficient and localized drug delivery by improving the targeted delivery and providing a sustained or controlled delivery to prolong the therapeutic effect. On the other hand, different polyphenols and aromatic organic compounds are known to possess anti-