effects against Kainic Acid (KA) induced excitotoxicity. Moreover, we have shown through gelatinase assay that these effects are mediated through MMP-9 inhibition. Currently, we are exploring in vivo neuroprotective effects of TIMP-1 NPs.

Keywords: Matrix Metallo-Proteinase, Nanoparticles, Neuroprotection.

SUN-349

An in vitro study on the risk of non-allergic type-I like hypersensitivity to *Momordica charantia*

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Background: *Momordica charantia* (MC) is a tropical plant that is extensively used in folk medicine. However, the knowledge about side effects of this plant is relatively little according to knowledge about its therapeutic effects. The aim of this study is to reveal the effects of non-allergic type-I like hypersensitivity to MC by an experiment which was designed in vitro.

Methods: In the present study, the expression of CD63 and CD203c on peripheral blood basophils against different dilutions of MC extracts was measured using flow cytometry and compared with one another. In addition to this, intra-assay CV's of testing extracts were calculated for precision on reproducibility of test results.

Results: It was observed that the fruit extract of MC at 1/100 and 1/1000 dilutions significantly increased active basophils compared to same extract at 1/10 000 dilution.

Conclusion: In conclusion, *Momordica charantia* may elicit a non-allergic type-I like hypersensitivity reaction in especially susceptible individuals.

Keywords: None.

SUN-350

Toxic molecular mechanisms induced by magnetite nanoparticles in human pulmonary fibroblasts

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The control of biomolecules-nanoparticles interaction from molecular to cellular levels is crucial for potential risks of adverse effects on human health.

The aim of our study was to investigate the molecular mechanisms involved in the inflammatory and cell death processes in human pulmonary fibroblasts (MRC-5 cell line) after magnetite nanoparticles (MNP) exposure.

In order to accomplish these, MRC-5 cells were exposed to 12.5 μg mL MNP for 24, 48 and 72 hours. As inflammatory markers, the level of prostaglandin-E2 (PGE_2), nitric oxide (NO) and the production of interleukin (IL)-6 and -8 were assessed using biochemical analyses. MNP potential to induce cell death in MRC-5 cells was evaluated by quantifying caspases activity and apoptotic cells through Annexin V-PI staining.

Results have shown a significant stimulation of NO and PGE_2 synthesis after 72 hours by 81% and 82% respectively, compared to control. A slight increase in IL-6 production occurred starting after 48 hours but no significant changes were observed in IL-8 levels. MNP caused no apoptotic events in pulmonary fibroblasts during the analyzed period but an increase of the caspase-1 activity by 35%, 21%, 25% after 24 h, 48 and 72 h compared to controls was noticed. It may be that activated caspase-1 regulated the release of pro-inflammatory cytokine as IL-1β generating the release of NO and PGE_2 into the extracellular milieu. The synthesis of PGE_2 could also be caused by IL-6.

Our findings suggest that human pulmonary fibroblasts exposed to MNP generates an inflammatory response through activation of caspase-1 and release of NO and PGE_2.

Keywords: nanoparticles, inflammation, cell death.

SUN-351

Toxicogenomic analysis of *Capparis ovata* water extract (MSCov)

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Capparis ovata water extract (*MSCov*) has been used for the treatment of multiple sclerosis and other immune diseases. However, its potential toxicity has not been completely investigated. The aim of the study was to determine the toxicology of *MSCov* in C57BL/6 mice and to investigate the underlying cellular mechanism further by microarray analysis. For this purpose, *MSCov* was prepared by using the plant's fruit, bud and flower parts (Turkish Patent Institute, PT 2012/04 093). Doses of *MSCov* at 500 mg/kg for 21 days were administered by oral gavage for subchronic toxicity in C57BL/6 mice. At the end of the experimental period, the animals were sacrificed, the liver tissues were isolated. Changes in the hepatic gene expression were identified with toxicology pathway PCR arrays to study the hepatotoxic mechanism of *MSCov*. A number of changes in the body weight and food consumption, absolute and relative liver weight, biochemical analysis were not observed after the subacute exposure to *MSCov*. A total 384 genes were screened which 14 genes were found to be significantly altered (2-fold, $P < 0.05$), including 14 up-regulated genes and no down-regulated genes. According to our biological pathway analysis, the *MSCov* resulted in aberrant gene expression in metabolic pathways such as phospholipids, cholesterol and asis and fatty acids. Real-time PCR analyses of several genes verified these results. Consequently, our gene expression microarray study will be useful for future *MSCov* toxicity studies. These results strongly suggest that *MSCov* has no or very very of low potencial of toxicity and considered to be safe as an alternative or complementary therapeutics in MS treatment at the studied dose regime.

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Keywords: Toxicogenomic, Capparis ovata, multiple sclerosis.

SUN-352

Transcription factor hypoxia-inducible factor (HIF)-1alpha is relevant for necrosis of *Mycobacterium avium*-induced granulomas

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Mycobacterial infections are characterized by the formation of granulomas. Granulomas are well-organized aggregates of immune cells, namely infected macrophages. The granuloma's main function is to constrain and prevent dissemination of the mycobacteria while concentrating the immune response to a limited area. In some cases these granulomas undergo central necro-

sis leading to their caseation although the underlying mechanisms are still poorly understood. It has been reported that reduced vascularization of granulomas may be one essential mechanism for caseation and some studies have demonstrated severely hypoxic regions at the center of the granuloma. The hypoxia-inducible factor 1alpha (HIF-1α) has been shown to be important in some diseases, such as cancer and infections. HIF-1α is able under hypoxic conditions to transcriptionally regulate gene expression, allowing macrophage adaptation to hypoxia [1]. The Appelberg laboratory has developed a granuloma necrosis model that mimics the human pathology of *Mycobacterium tuberculosis*, using C57BL/6 (WT) mice infected intravenously with a low dose of a highly virulent strain of *Mycobacterium avium* (ATCC 25291). Such mice develop granulomas that, at 4 months of infection, exhibit central necrosis [2]. To determine the relevance of HIF-1α during *M. avium* infection we used a mouse strain deleted of HIF-1α under Cre/lox system in the myeloid cell lineage (HIF1αKO). Infected mice were euthanized at different times during the infection and the lungs, liver and spleen were aseptically collected. Bacterial loads were determined in the organs of infected animals. Morphometric analysis of granulomas was performed in haematoxylin-eosin stained liver sections. The localization of macrophages in the livers from infected mice was studied by immunohistochemistry by evaluating the expression of F4/80. The analysis of liver and spleen cell populations were determined by flow cytometric analysis. IFN-gamma and HIF-1α production has been evaluated *ex-vivo* by ELISA. The results obtained indicate that HIF1α KO mice are more susceptible to the infection and the onset of necrotic granulomas is faster.

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Keywords: Granuloma, Hypoxia, Mycobacteria.

SUN-353
Urinary hydroxyproline levels in prediabetic patients

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Objective: The metabolic stage between normal glucose homeostasis and diabetes mellitus (DM) is called prediabetes. Prediabetes is categorized as impaired glucose tolerance (IGT) and increased fasting glucose (IFG), both established risk factors for DM. Although the relationship between type 2 DM (T2DM) and bone metabolism has been widely investigated, study results have been contradictory. But it is clear that fracture risk is higher in these patients. Recently, it was reported that urinary hydroxyproline increased markedly in diabetic patients. We investigated the urinary hydroxyproline concentrations in patients with prediabetes and T2DM and compared the results to those of normoglycemic individuals at baseline and 2 hours after glucose loading.

Material and Methods: The ADA 2013 criteria were used to identify subjects. These persons were defined as having IFG (100–125 mg/dL) or IGT (2-h values in the oral glucose tolerance test (OGTT) of 140–199 mg/dL) as prediabetes. Based on a 75 g OGTT, subjects were divided into a group with normal glucose tolerance (NGT; n = 28), prediabetes (n = 29) or T2DM (n = 24). Urine concentrations of hydroxyproline were measured by spectrophotometric assay. The hydroxyproline results were expressed as mg/g creatinine. Creatinine in urine samples was determined by Jaffe's method.

Results: Urinary hydroxyproline levels in patients with T2DM were found to be significantly higher compared with NGT ($p < 0.05$). Urinary hydroxyproline levels in prediabetic patients were higher than NGT group. But it was not found statistically differences ($p > 0.05$).

Conclusion: We suggest that urinary hydroxyproline could be an useful biochemical markers for monitoring possible bone mineral metabolism disorder in T2DM patients. Larger investigations are needed to understand the urinary hydroxyproline levels and bone metabolism in prediabetic patients.

Keywords: diabetes mellitus, hydroxyproline, prediabetes.

SUN-354
Variation within the CASP3 gene and the risk of Achilles teninopathy in a British case-control cohort

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Achilles tendon pathology (ATP) is a degenerative condition with known genetic risk factors[1]. Excessive tenocyte apoptosis has been observed in tendinopathy and components of the apoptosis pathway have previously been implicated in the aetiology of ATP[2]. Caspases play a key role in the execution and regulation of apoptosis, with caspase-3 being an important mediator of apoptosis[3]. Our aim was to determine whether a single nucleotide polymorphism (SNP) within the *CASP3* gene (rs1049253) was associated with ATP in a British cohort. We recruited 264 (133 ATP cases and 131 asymptomatic controls) British Caucasian participants for this genetic association study. ATP cases were clinically diagnosed with insertional tendinopathy, noninsertional tendinopathy, Achilles tendon rupture, or more than one pathology. TaqMan assay technology was used to genotype all participants using real-time PCR. A Pearson's chi-squared (χ^2) test was used to analyse for differences in genotype and allele frequency for the rs1049253 variant. We compared the collective ATP group against controls. We also conducted several sub-analyses taking into account the different types of tendinopathy. We found no significant difference in genotype ($p = 0.643$) or allele ($p = 0.635$) frequencies between the ATP group and controls. However, we did find a tentative genotypic association ($p = 0.025$) between male insertional tendinopathy cases and male controls. These data must be viewed with caution due to the relatively small sample size and replication in a larger cohort would be necessary to increase confidence. In conclusion, our preliminary data infer a possible role for the rs1049253 variant as a risk factor for insertional tendinopathy in British males. These results could further implicate the involvement of the apoptosis pathway in the development of ATP.

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Keywords: Apoptosis, Caspase-3, Tendinopathy.