(IDO). The biologic activity of necrotic material towards MSCs is abolished once these DAMPs are oxidized.

Conclusions: MSCs are often found within tumor tissue and can influence the biologic behaviour of tumor and the host immune response to tumor. Tumor microenvironment is characterized by reducing conditions. Based on our results, oxidizing conditions should be considered for therapeutic approaches targeting tumor microenvironment.

WS/PP-005-05 Immunomodulatory properties of reactive carbonyls: linking oxidative stress to Th2 immunity

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Oxidative stress is widespread and entwined with underlying inflammatory processes seen in many related pathologies, and yet its linkage to adaptive immunity is poorly defined. Aldehydes, important elements of oxidative processes, can adduct reactive carbonyls (RCs) to proteins, targeting them to adaptive immunity. We have investigated the immunomodulatory roles of RCs, adducted to model proteins using the pathophysiologically-relevant aldehydes, glycolaldehyde, 4-hydroxy-2-nonenal, and malondialdehyde, in murine models. All aldehydes generated RCs on ovalbumin and hen egg lysozyme, resulting in induced immunogenicity of the model proteins in vivo as demonstrated by antigen-specific antibody and T cell responses. Antibody titres showed a highly significant correlation ($r = 0.761$, $p = 0.0173$) with the extent of RC adduction on the antigen, independently of methods and types of aldehyde employed. The immune responses to RC-adducted antigens had a profound Th2 bias characterised by dominant IgG1, but minimal IgG2a/c and IgG3 isotypes, mirrored by production of Th2 cytokines including IL-4, IL-5 and IL-13, and an absence of IFN-γ. RC-induced immunogenicity was independent of TLR-induced signalling and was unrelated to mouse strain. More stable adducts such as hydroxyl ethyl lysine, carboxymethyl lysine, and pyridine ring derivatives, also formed by aldehyde modification, were consistently detected in the samples reduced to selectively eliminate RCs, but failed to prime any adaptive immune responses, underscoring the central immunomodulatory role of RCs. Together these data suggests that RCs are a common class of immune modulators in the context of oxidative stress, with potentially important implications for their engagement in health and disease.

WS/PP-005-06 *Artemisia khorassanica* sesquiterpene lactone fraction inhibits inducible nitric oxide synthase and cyclooxygenase-2 expression through the inactivation of NF-κB

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Members of the *Artemisia* genus (Astraceae) are important medicinal plants throughout the world. Here, we prepared a sesquiterpene lactone fraction from *Artemisia khorassanica* and evaluated its effect on inducible nitric oxide synthase and cyclooxygenase-2 expression and its action on NF-κB activity. The effects of sesquiterpene lactone fraction from *Artemisia khorassanica* (SLAK) on lipopolysaccharide (LPS)-induced nitric oxide (NO), prostaglandin E_2 (PGE_2), tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) production was evaluated in mouse macrophage J774A.1 cells. Moreover, we evaluated SLAK modulation of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) enzyme expression by western blot analysis. Our data revealed that SLAK (10-100 μg/mL) in a dose-dependent manner, inhibits NO, PGE_2, TNF-α and IL-1β production induced by LPS in the J774A.1 cells. These data were consistent with the modulation of iNOS and COX-2 expressions. We also showed that SLAK suppresses the iNOS and COX-2 enzyme expression through the inhibition of NF-κB activity. In this study, we demonstrated that SLAK inhibits the production of NO, PGE_2, TNF-α and IL-1β in LPS-stimulated macrophages. This anti-inflammatory effect possibly occurs by inhibiting iNOS and COX-2 expression via the inactivation of NF-κB pathway.

PP-005 NO and ROS in immune responses

PP-005-07 High-throughput flow cytometric assay system of reactive oxygen species in blood cells

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Even after sixty years have passed, exposure to atomic-bomb (A-bomb) radiation continues to have long-term effects on the health of A-bomb survivors, specifically enhanced risks of certain inflammatory diseases. Among a cohort of Hiroshima A-bomb survivors, we observed with aging and increased radiation dose decreased percentages of CD4 T-cells and elevated levels of plasma inflammatory markers including IL-6, TNF-α, IL-10, CRP, ESR, and total Igs. With the aim of finding a link between inflammation and various diseases, we recently developed an intracellular reactive oxygen species (ROS) assay system. This assay system can measure production levels of ROS in different types of circulating blood cells, in relation to inflammatory status. Intracellular levels of both H_2O_2 (using 5-(and-6)-chloromethyl-2′,7′-dichlorodihydro fluorescein diacetate, CM-H_2DCFDA) and O_2- (using hydroethidine, HE) were measured by flow cytometry for granulocytes, monocytes, and lymphocyte subsets (naïve CD4, memory CD4, naïve CD8, and memory CD8 T cells) in blood samples obtained from 240 A-bomb survivors. We found that intracellular H_2O_2 and O_2- levels were higher in monocytes than in granulocytes, followed by those levels in lymphocytes. With regard to lymphocyte subsets, intracellular H_2O_2 and O_2- levels in memory CD4 T cells were higher than in naïve CD4 T cells. These results indicate that this assay system is a useful tool for assessment of intracellular ROS level differences among various blood cell subsets. Analysis on association between intracellular ROS levels and inflammation is now underway.

PP-005-08 Inducible nitric oxide downregulates NF-κB activity in human chondrocytes: implications in osteoarthritis

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NF-κB plays a crucial role in osteoarthritis (OA), mediating important chondrocyte inflammatory and catabolic responses that ultimately lead to cartilage destruction. The mechanisms that regulate NF-κB activity in chondrocytes are incompletely understood. This work aimed at elucidating the role of endogenous inducible NO on the regulation of NF-κB activity in human chondrocytes. For this, we compared the protein levels of the neuronal (nNOS) and inducible (iNOS) NO synthase isoforms by western blot and NF-κB activity by ELISA in normal and OA human chondrocytes. Then, we evaluated the effect of inhibiting iNOS on the ability of interleukin-1β (IL-1) to induce NF-κB. Chondrocytes were isolated from human knee cartilage obtained from normal multi-organ donors or OA patients undergoing total knee replacement surgery. The results showed that nNOS was more frequently expressed in normal than OA chondrocytes, whereas the opposite was found for iNOS. Although IκB-α was present in all the normal samples and in the majority of the OA samples, NF-κB activity in OA chondrocytes was approximately twofold higher than in normal ones. Addition of a NOS inhibitor after induction of iNOS expression, induced IκB-α degradation and potenciated the effect of IL-1. These findings favor an inhibitory role of inducible NO on the regulation of NF-κB activity in human chondrocytes that contributes to sustain over time a moderate level of NF-κB activity and NF-κB-dependent gene expression. The downregulatory role of NO on NF-κB activation warrants caution as to the proposed utilization of NO inhibitors in the therapy of OA. Supported by FCT-PTDC/SAU-OSM/67936/2006

PP-005-09 Zinc deficiency in β-thalassemia major: the impact of antioxidant therapy

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Zinc deficiency is thought to be one of the major pathogenetic mechanisms of immune abnormalities in β-thalassemia. This study was performed to determine the possible relationship between immunological defects and zinc deficiency in Iranian patients with β-thalassemia major. Regarding antioxidant and iron chelating activities of silymarin, a flavonolignan complex isolated from *Silybum marianum*, a 3-month randomized double-blind clinical trial was conducted in 70 β-thalassemia major patients in order to investigate the beneficial effect of silymarin to restore zinc deficiency in β-thalassemia major patients under conventional iron chelation therapy by desferrioxamine. Patients were randomized to receive a silymarin (Legalon®, 140 mg) tablet 3 times a day plus conventional desferrioxamine therapy. The second group received the same therapy but a placebo tablet instead of silymarin. Plasma samples were deproteinized by trichloroacetic acid and the levels of zinc were measured using colorimetric kit. Result indicated decreased plasma zinc levels in thalassemia patients compared to controls. However, plasma and 24 h urinary zinc levels showed no significant change in β-thalassemia patients who were treated by silymarin compared to placebo. This study showed that combination therapy of silymarin with desferrioxamine could not recover urinary zinc excretion caused by desferrioxamine therapy in β-thalassemia major.

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PP-005-10 Phenolic acid phenethyl urea compounds with anti-oxidant activity exert anti-inflammatory activity as inhibiting lipopolysaccharide-induced production of nitric oxide and pro-inflammatory cytokines

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Acteoside is present in herbal medicinal plant and known to have a strong anti-oxidant activity without prominent cellular toxicity. In addition, acteoside is dissolved well in water. Consequently, acteoside is considered as a good material for anti-oxidant therapy. One of the problems to use acteoside practically is that the compound is hard to purify and, consequently, hard to obtain the compound in a large scale. In this study, we synthesized various phenolic acid phenethyl urea compounds based on the chemical structure of acteoside using the Curtius rearrangement and demonstrated their beneficial anti-oxidant, anti-cancer, and anti-inflammatory effects. In addition, effects of one of the synthesized compounds on NO production, iNOS expression, and cytokine secretion in LPS-stimulated RAW 264.7 cells were further analyzed.

PP-005-11 Tim-4 suppresses LPS and ploy(I:C) induced NO production by regulating NF-κB activation in RAW 264.7 macrophages

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T cell immunoglobulin- and mucin-domain-containing molecule-4 (Tim-4, also known as Timd4) is a member of TIM family which is a relatively newly described group of molecules and receives much attention as potential regulators of the immune system. Tim-4 is specifically expressed on macrophages and dendritic cells, but not on T cells or others immunocytes. Tim-4, as one natural ligand of Tim-1, shows bimodal regulation on T cell-mediated immune responses by interaction with Tim-1, which is selectively expressed on Th2 cells. However, littler is known about the role of Tim-4 in macrophage modulation. In this study, we evaluated the effect of Tim-4 on NO production in LPS and poly(I:C) induced RAW264.7 macrophages. The results showed that NO production and iNOS expression in T4-RAW cells (RAW264.7 cells stably transfected with Tim-4 expressing plasmid) were significantly lower than those in control cells induced by LPS, while Tim-4 blockade promoted LPS induced NO production and iNOS expression in Raw264.7 macrophages. Tim-4 blocking up-regulated poly(I:C) initiated NO secretion as well. LPS-induced NF-kappaB (NF-κB) p65 phosphorylation was markedly decreased in T4-RAW cells compared with control cells. On the contrary, LPS-initiated NF-κB P65 phosphorylation was increased by blocking Tim-4. Furthermore, up-regulation of NO induced by Tim-4 blockade was reversed by NF-κB inhibitory ligand in both LPS and poly(I:C) stimulated macrophages activation. Taken together, these results demonstrate that Tim-4 is involved in regulation on NO production from activated macrophages, suggesting the possible role of Tim-4 in immune diseases.

PP-005-12 Anti-inflammatory effects of HSPL isolated from *Streptomyces sp.* by suppressing TRIF-dependent pathway on LPS-stimulated RAW264.7 cells

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HSPL isolated from marine microbe *Streptomyces sp.* was designated as a new antiangiogenic agent. Nitric oxide (NO) is recognized as a mediator and regulator of inflammatory responses. We found that HSPL has a strong inhibitory effect on the production of NO, pro-inflammatory cytokines such as IL-1β, IL-6 and PGE_2. HSPL also inhibited gene expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) at LPS stimulated RAW264,7 cells. In order to explore the mechanisms responsible for the inhibition of iNOS gene expression by HSPL, we investigated its effect on down-regulation at TRIF-dependent signal pathway.

Our data suggested that HSPL attenuates the inflammation through the inhibition of NO, PGE_2 production and iNOS, COX-2 expression by regulation of STAT1 and STAT3 phosphorylation in LPS-stimulated RAW264.7 cells. These results suggest that HSPL inhibits the production of NO, PGE2 and pro-inflammatory cytokines via suppression of TRIF-dependent signal pathway.

PP-005-13 Cell death in immune system

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I have cell death of immune system of four ways

Primarily there is normal death about the death that duration of life is simply it, and is dismantled with spleen.

The duration of life is usually said with from 8 days to 10 days

Second when when viruses invaded the body, leucocyte does mycophagy and necrotizes as antigen presenting cell afterwards.

Thirdly,virulent death by immunosuppressive agent such as antipyretics analgesic and antibiotics or anticancer drug is given.

Death of an immune system cell by the humoral oxidation is nominated for the fourth.

I confirmed the blood which lived of the patients more than 1,000 people with an image in 12 years.

This problem is associated with the process when a tumor matures into.

In addition, the immune cell which necrotized adheres to vascular wall and blood capillary.

This problem is associated with the process that lesion tissue produces.

Blood capillary is jam-packed with the immune cell which necrotized.

Therefore energy metabolism is disordered and becomes depressed body temperature

As a result, an enzyme becomes inert, and metabolism is disordered, and lesion tissue is made.

Therefore, you must change it into herbal medicine from chemical agents to prevent cell death of immune system.

In addition, it is very important that we neutralize the humoral oxidation to relieve stress.

PP-005-14 7,8-dihydro-8-oxo-2′-deoxyguanosine is a strong scavenger of hydroxyl radicals, peroxynitrite and singlet oxygen

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In the present study, an attempt was made to test the anti-oxidant activity of 7,8-dihydro-8-oxo-2′-deoxyguanosine (8-oxo-dG). We report that 8-oxo-dG abolished the 5,5-dimethylpyrroline-*N*-oxide (DMPO)-OH signal completely as shown by electron spin resonance spectroscopy and inhibited HO·-induced oxidation of 2,7-dichlorodihydrofluorescein (DCHF). 8-oxo-dG also inhibited DCHF oxidations by peroxynitrite and low density lipoprotein (LDL) oxidation by $^1O_2$. In all oxidation systems used, 8-oxo-dG showed the strongest inhibition among the anti-oxidants tested, which included Trolox, N-acetylcysteine, ascorbate, β-carotene, (+-)-catechin hydrate, quercetin dihydrate, α-lipoic acid, β-estradiol, α-ketoglutaric acid, guanosine, L-carnosine, billirubin, melatonin and uric acid.

Also, we tested the anti-oxidant capacity of 8-oxo-dG *in vivo* using UVB irradiated mice skins. In this report, 8-oxo-dG significantly decreased oxidative protein modification, pathologic alteration, ERK and p38 phosphorylation, resulting in downregulation of matrix-metalloproteinase (MMP)-9 and MMP-13 expression. These effects were strong than other antioxidants including Trolox, β-carotene, *N*-acetylcystein and retinoic acid. These results suggest that 8-oxo-dG could be used as a potential tool to prevent the skin from photoaging.

PP-005-15 Molecular basis of anti-inflammatory effects by ketoconazole: A novel therapeutic approach for oxidative stress

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Oxidative stress caused by reactive oxygen species (ROS) is involved in wide variety of pathogenic condition. Ketoconazole (KCZ) is a major anti-fungal drug with a potent anti-inflammatory effect. However, molecular basis of its action has been poorly understood. Aryl hydrocarbon receptor (AhR), known as a dioxin receptor, has been shown to be a sensor of redox system against oxidative stress and to regulate nuclear factor-erythroid 2-related factor-2 (Nrf2), a master switch of redox machinery. Thus, we addressed whether KCZ modulates AhR-Nrf2 function leading to redox system activation.

We treated human keratinocytes with KCZ, since skin is the outermost organ of the body exposed to a variety source of oxidative stress including ultraviolet light and environmental dioxins such as benzo(a)pyrene. Confocal microscopic analysis revealed that KCZ induced nuclear translocation of AhR from cytoplasm, resulting in up-regulation of CYP1A1 mRNA and protein expression. Furthermore, KCZ actively switched on nuclear translocation of Nrf2 as well as expressions of Nrf2 and quinone oxidoreductase 1. TNF-α- and benzo(a)pyrene-induced ROS generation including IL-6 and IL-8 production were effectively inhibited by KCZ. Knockdown of either AhR or Nrf2 turned out to abolish the inhibitory capacity of KCZ on ROS, IL-6 and IL-8 production. In addition, KCZ-induced Nrf2 activation was canceled by AhR knockdown.

In conclusion, engagement of AhR by KCZ exhibits the cytoprotective effect mediated by Nrf2 redox system which potently down-regulates either dioxin-induced (AhR-dependent) or cytokine-induced (AhR-independent) oxidative stress. To our knowledge, these findings provide the first molecular basis of the anti-inflammatory effect of KCZ.

PP-005-16 Endothelial NOS is essential for NO generation and survival in FcεRI-induced mast cells

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Nitric oxide (NO) is known to suppress mast cell activation but its role in mast cell survival is unclear. We have previously reported that activation of mast cells through the high-affinity IgE receptor (FcεRI) resuls in NO production within a few minutes. This NO production is largely dependent on NO synthase (NOS) activity and extracellular Ca^{2+}. The NO production requires aggregation of FcεRI and is accompanied with increased phosphorylation of endothelial NOS (eNOS) at Ser1177 and Akt at Ser473. The phosphorylation of eNOS and Akt and production of NO are abolished by the phosphatidylinositol-3-kinase (PI-3K) inhibitor wortmannin. When NOS-dependant NO production is blocked, mast cell activation through FcεRI causes mitochondrial membrane potential collapse, cytochrome c release, caspase-3/7 activation and apoptosis. In the present study, we determined which type of NOS isoform was involved in the FcεRI-induced NO generation and survival. RT-PCR analysis revealed substantial expression of eNOS with lower expression of iNOS, while expression of nNOS was not observed in the cells. Knockdown of eNOS expression using small interfering RNA abolished FcεRI-induced Ca^{2+}-dependent NO production and NOS activity. In addition, activation of mast cells through FcεRI caused considerable apoptosis, mitochondrial cytochrome c release, caspase-3/7 activation, and of mitochondrial membrane potential collapse in the eNOS-knockdown cells. These findings suggest that eNOS plays key roles in NO production and survival in FcεRI-activated mast cells.

PP-005-17 Aspirin regulates Ca^{2+} influx in mast cells by modulating mitochondrial Ca^{2+} and reactive oxygen species signals

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Aspirin and its analogs are among the most widely used nonsteroidal anti-inflammatory drugs worldwide but can cause adverse immunological reactions known as aspirin intolerance. Aspirin intolerance is a disorder that induces urticaria, asthma and anaphylaxis in response to oral administration of the drug. Aspirin intolerance is accompanied by increased leukotriene (LT) synthesis and secretion. We have previously reported that aspirin and salicylates modulate IgE-mediated LTC_4 secretion in mast cells by modulating a dihydropyridine-sensitive Ca^{2+} channels most likely L-type Ca^{2+} channels (LTCCs). Therapeutic levels ($\leq$0.3 mM) of aspirin augmented Ca^{2+} influx whereas at concentrations of $\geq$1 mM reduced it. On the other hand, aspirin at concentrations of $\geq$0.3 mM dose-dependently reduced Ca^{2+} release-activated Ca^{2+} (CRAC) channel activity. siRNA-mediated gene knockdown of $Ca_v1.2$ LTCC completely abolished the aspirin enhancement of Ca^{2+} influx, although it enhanced CRAC channel activity, thereby indicating that aspirin modulates Ca^{2+} influx via $Ca_v1.2$ LTCC. Aspirin at concentrations of $\leq$0.3 mM also caused mitochondrial hyperpolarization and superoxide generation, while at higher concentrations it evoked mitochondrial depolarization. Subsequent studies revealed that mitochondrial superoxide generation was involved in the maintenance of mitochondrial Ca^{2+} and full activation of LTCC. Since a growing body of evidence suggests that LTCCs play key roles in mediating LTC_4 secretion, Th2 cytokine production and cell survival in mast cell and T cell, the aspirin modulation of LTCC may play a role in the exacerbation of allergic reactions including aspirin intolerance.

PP-005-18 Quercetin prevents hepatic fibrosis via decreased of inflammation and oxidative stress in experimental cirrhosis in rats

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Liver cirrhosis is characterized by a distortion of normal tissue architecture which occurs when liver is chronically damaged. The initial damage involves oxidative stress with free radical production followed by inflammation with activation of kupffer and stellate cells (HSC). HSC synthesize collagen setting cirrhosis. On the other hand, quercetin, a natural flavonoid and a potent antioxidant is a free radical scavenger and inhibitor of oxidative enzymes such as NADPH oxidase and nitric oxide synthase.

Aim: to elucidate the effect of quercetin on the inflammation and the development of fibrosis in an experimental model of cirrhosis.

Methods: male wistar rats were chronically intoxicated with carbon tetrachloride and concomitantly treated with quercetin for the same time and sacrificed at 3, 5 and 8 weeks of treatment. Liver samples were taken for histology, enzimatic activity, gene expression of antioxidants, inflammatory and anti-inflammatory proteins and serum for functional hepatic tests.

Results: treatment with Quercetin decreased significantly gene expression of inflammatory cytokines (TNF-α and IL-1β) and increase gene expression of antioxidants enzymes (CAT, SOD, GpX) and anti-inflammatory cytokines (IL-4, IL-10) which is proportional to the time of treatment being greater at eight weeks. These results correlate with fibrosis index, state of inflammation and hepatic function determined by histology and biochemical test. Respectively. Our results suggest that quercetin prevents liver injury and fibrosis via reduced oxidative stress and inflammation.

PP-005-19 ROS production and mitochondrial activity induced by halomethanes on peripheral blood mononuclear cells of *Cyprinus carpio*

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Introduction: Halomethanes (HM) are frequent contaminants of chlorine treated waters. Dichloromethane (DCM) is a potent carcinogen for humans and bromodichloromethane (BDCM) is immunotoxic in mouse. There is little information about the toxicity of these compounds in freshwater fish.

Objective: To evaluate the generation of ROS (O_2^- and H_2O_2) and mitochondrial activity (MA) induced by HM in PBMC of *Cyprinus carpio*.

Methods: Pre-adult specimens were obtained from a fish farm and kept in water tanks in the laboratory for 3 months before exposure to HM. DCM or BDCM in corn oil were administered IP at different doses. Recombinant 60kDa HSP form *S. typhi* and LPS from *K. pneumoniae* were used as positive controls and corn oil as negative control. Blood was obtained by cardiac puncture 96 h after injections. PBMC were purified by density gradient and adjusted to 300,000 cells per well. Cells were incubated at RT (20-22°C). *Ex vivo*, O_2^- production was determined at 30 min and H_2O_2 at 120 min, by validated spectrophotometry, and MA at 4 h by MTT. Data was analyzed by ANOVA, followed by Dunnett multiple comparison test .

Results: DCM induced ROS production higher than negative controls ($p < 0.001$) and MA similar to positive controls. BDCM induced significant ROS production higher than negative controls and MA was similar to positive controls, in both cases inversely proportional to concentration of BDCM.

Conclusions: HM are modulators of innate immunity in *Cyprinus carpio*.

PP-005-20 Carnosine does not inhibit nitric oxide production in LPS-activated RAW 264.7 macrophages

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Carnosine (ß-alanyl-L-histidine) is an endogenously synthesized dipeptide, widely distributed in brain, muscle, kidney, stomach tissues and in large amounts in skeletal muscle. Carnosine has been demonstrated to have various biological roles including an anti-inflammatory agent, free radical scavenger and protein glycosylation inhibitor (1,2,3,4,5). It has been suggested that carnosine inhibits nitric oxide synthesis in lipopolysaccharide (LPS)-treated microglial cells (6) and iNOS expression in LPS and IFN-gamma induced astroglial cells (7). When activated, macrophages transcriptionally express iNOS (inducible nitric oxide synthase) which is responsible for long time and extensive NO production. Abnormal release of NO leads to inflammation and tissue injury (8). Therefore, pharmacological interventions that aim to control potentially harmful pro-inflammatory activity of macrophages present promising treatment options. In this study the effect of l-carnosine on nitrite production in LPS activated RAW 264.7 macrophages was tested. After 1 hour of incubation with different concentrations of l-carnosine ranging between 1 mM and 20mM, cells were activated with LPS (1 μg/ml) for 24 hours. After this incubation period, nitrite levels in the medium was measured spectrophotometrically. Our results suggest that l-carnosine does not inhibit nitrite production of macrophages for all the doses tested ($p < 0,05$) and effects attributed to carnosine may be cell type specific.

WS-006 CD1d/NKT cells

Chairpersons: Ken-ichiro Seino, Dale Godfrey

WS/PP-006-01 Early divergence of NKT and conventional T cell lineages

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CD1d is believed to mediate positive selection of NKT cells in a similar way classical MHC molecules mediate the selection of $CD8^+$ and $CD4^+$ αβ T cells. However, whether these selection events are imposed on a pool of equivalent DP precursors and lineage choice depends solely on TCR interactions, or whether a NKT cell committed precursor exists is under debate. We compared TCRγ rearrangements in thymic αβNKT and conventional αβ T cells and found that, while conventional αβ T cells are selected against in-frame TCRγ rearrangements, there is no such selection among αβ NKT cells. Moreover, αβ NKT cells express functional TCRγ chains and can display them on their surface if TCRδ is provided by retroviral transduction. Since most DP thymocytes do not have functional TCRγ chains, these data indicate that NKT cells are derived from a distinct subset of DP thymocytes and suggest an early divergence of NKT and conventional T cell lineages.

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