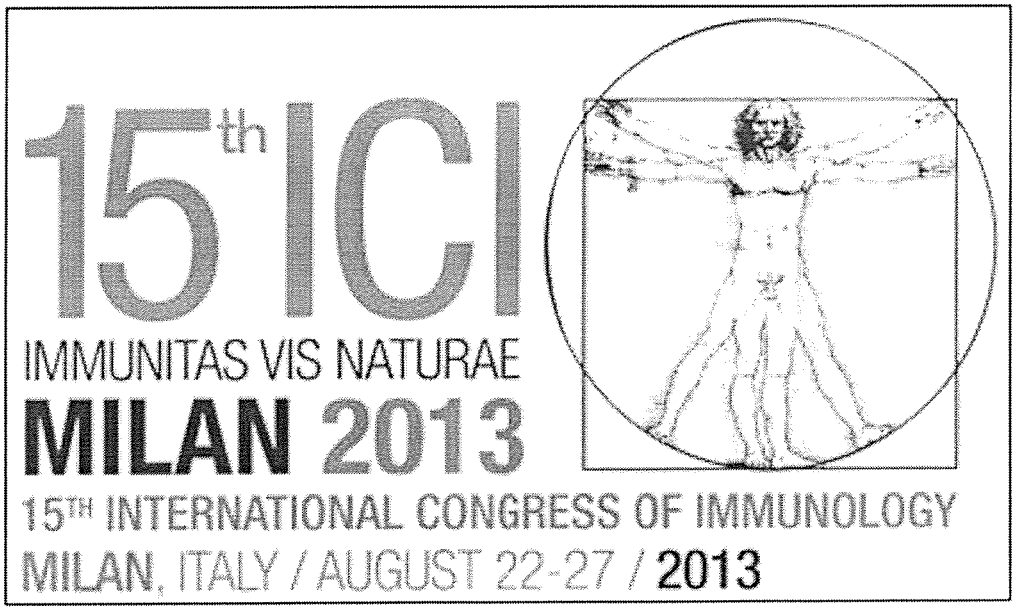
BOOK OF ABSTRACTS

Co-Editors: Luciano Adorini, Massimo Locati



ANNOTATIONS

In the following we are publishing the abstracts as submitted by the authors.

Missing session numbers represent sessions with no abstracts associated.
Missing presentation numbers represent talks with no abstracts received as per date of production. Bold presentation numbers indicate the presenting author.

The sessions are in numerical order.

Keys and Abbreviations:

IL1.01.01	Invited Lecture
LB.1	Late Breaking Session 01
LL.1	Lunchtime Lecture
P1.01	Poster Presentation
PL.1	Plenary Lecture
PS.1	Lecture: Perspectives in Immunology
S.1	Symposium
SS.1	Sponsored Session
W1.01	Workshop

The Editors

P6.02.08
Activation markers show greater expression on adipose tissue resident T-lymphocytes with increased adiposity

*R. Travers[1], **A. C. Motta**[2], J. Betts[1], D. Thompson[1];*
[1]University of Bath, Bath, United Kingdom, [2]Unilever R&D, Vlaardingen, Netherlands.

The presence of T-lymphocytes in human adipose tissue has only recently been demonstrated and relatively little is known of their potential relevance in the development of obesity-related diseases. We aimed to further characterise these cells and investigate how they vary with increased adiposity and other markers of metabolic health. Subcutaneous adipose tissue samples were obtained from 17 'healthy' male subjects with waist circumferences ranging from 80.9 to 117.2 cm. Cells comprising the stromovascular fraction were obtained by collagenase digestion of adipose tissue and analysed by flow cytometry. CD4+ and CD8+ T-lymphocyte populations together with macrophages were identified and T-lymphocytes were further characterised by their expression of activation markers CD25 and CD69.
Although the overall proportions of CD4+ and CD8+ T-lymphocytes as a percentage of total cells within the SVF were not correlated with measures of adiposity, there were significant correlations between waist circumference and expression of activation marker CD69 on CD4+ ($R=0.775$, $p<0.001$) and CD8+ cells ($R=0.618$, $p<0.01$) and CD25 on CD4+ ($R=0.602$, $p<0.01$) and CD8+ cells ($R=0.478$, $p<0.05$). In addition, the proportion of macrophages correlated with waist circumference ($R=0.638$, $p<0.005$) and other measures of adiposity. The increased T-lymphocyte activation and proportion of macrophages further correlated with measures of adipocyte size and serum leptin. Our results suggest that T-lymphocyte populations in the SVF are more activated with increased adiposity and we propose that leptin may be important in their regulation as part of metabolic and immune system cross-talk within adipose tissue.

P6.02.09
Galectin-3 deficiency accelerates high-fat diet induced obesity and diabetes by amplifying metaflammation

***N. Pejnovic**[1], J. Pantic[1], I. Jovanovic[1], G. Radosavljevic[1], M. Milovanovic[1], I. Nikolic[2], N. Zdravkovic[1], A. Djukic[3], N. Arsenijevic[1], M. Lukic[1];*
[1]Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia, [2]Institute for Biological Research 'Sinisa Stankovic', University of Belgrade, Beograd, Serbia, [3]Center for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center Kragujevac, Kragujevac, Serbia.

Obesity-induced diabetes is associated with low-grade inflammation in adipose tissue and infiltration of macrophages in pancreatic islets. Galectin-3 (Gal-3), a galactoside-binding lectin, has a role in inflammation, uptake and removal of metabolic compounds. We show that ablation of Gal-3 accelerates high-fat diet-induced obesity and diabetes. Wild-type and $LGALS3^{-/-}$ mice on a C57BL/6J background were fed either high-fat (60% fat) or a low-fat diet (3% fat) for 11 or 18 weeks. The increased body weight, amount of total visceral adipose tissue (VAT), fasting blood glucose and insulin levels, homeostasis model assessment of insulin resistance and systemic inflammation were observed in high-fat diet-fed $LGALS3^{-/-}$ mice compared to diet-matched WT animals. Obese $LGALS3^{-/-}$ mice had increased incidence of Type-1 T and NKT lymphocytes and pro-inflammatory $CD11c^{+}CD11b^{+}$ macrophages and decreased $CD4^{+}CD25^{+}FoxP3^{+}$ Tregs and M2 macrophages in VAT. The severe insulitis, increased expression of NLRP3 inflammasome and IL-1ß in macrophages and increased accumulation of advanced glycation endproducts (AGE) and receptor for AGE (RAGE) expression in pancreatic islets of obese $LGALS3^{-/-}$ animals were associated with elevated expression of phospho-NFκB p65 and mature Caspase-1 protein in pancreata and VAT. $LGALS3^{-/-}$ peritoneal macrophages stimulated with lypopolysaccharide (LPS) and saturated fatty acid palmitate *in vitro* produced increased Caspase-1 dependent IL-1β and had increased expression of NLRP3 inflammasome and phospho-NFκB p65 compared to WT macrophages. Transfection of $LGALS3^{-/-}$ macrophages with NLRP3 inflammasome siRNA attenuated IL-1β production in response to palmitate and LPS plus palmitate. Obtained results suggest important protective roles for Gal-3 in obesity-induced inflammation and diabetes.

P6.02.10
P2X7 receptor expression and potential role in T cells in Type 1 Diabetes

***L. Perruzza**, F. Grassi;*
Institute for Research in Biomedicine IRB, Bellinzona, Switzerland.

The P2X7 receptor is an ATP-gated ion channel expressed in a variety of cell types. In the immune system, the function of P2X7 has been mostly studied in macrophages and T cells. ATP-mediated P2X7 activation facilitates macrophage maturation and IL-1β secretion. Moreover P2X7 stimulation by high concentration of ATP induces T cell apoptosis.
Although *p2rx7* has been proposed as a type 1 diabetes (T1D) susceptibility gene in NOD mice, its potential pathogenic role has not been directly determined. To test this possibility we investigated *p2rx7* expression in various T cells subsets namely $CD4^{+}CD62L^{high}CD44^{low}$ naive and $CD4^{+}CD62L^{low}CD44^{high}$ effector from pancreatic lymph nodes of healthy , prediabetic and overtly diabetic NOD mice. *p2rx7* expression significantly increases in $CD4^{+}$ T effector cells of prediabetic NOD mice but dramatically decreases in NOD mice with overt disease. Since *p2rx7* is silenced by cognate antigen stimulation these observations underscore the relevance of pancreatic epitope spreading in the development of T1D in NOD mice. Down regulation of *p2rx7* would render effector T cells resistant to apoptosis induction by extracellular ATP generated by inflammatory tissue damage, thereby propagating and sustaining tissue destruction. The role of P2X7 activity in limiting the T cell diabetogenic potential was supported by T1D induction with low-dose of streptozotocin in *p2rx7* knock-out mice, which developed a significantly more severe disease than the wild-type counterpart. Our study suggests that P2X7 could constitute a therapeutic target in the early phases of T1D by promoting apoptosis of potentially diabetogenic effector T cells.

P6.02.11
Insulin resistant obese individuals have increased frequency of CD14++CD16+ monocytes, what is modulated by a bout of aerobic exercise

***E. Rocha-Vieira**, M. Matos, T. Duarte, V. Ottone, K. Costa, G. Brito-Melo, F. Amorim;*
Federal University of Jequitinhonha and Mucuri Valleys, Diamantina, Brazil.

The expansion of the CD16+ monocytes has been suggested to occur in human obesity, a low-grade chronic inflammation condition. In this study the frequency of different monocytes subpopulations in obese insulin-sensitive (OB, n=9) (BMI 33.5 ± 2.8 kg/m2, HOMA-IR 0.5 ± 2 mmol.μU/L²) and insulin-resistant individuals (OBR, n=9) (BMI 34.8 ± 2.7 kg/m2, HOMA-IR 4.0 ± 1.0 mmol.μU/L²), before and after a session of aerobic exercise (AE) (3 sets of 20 minutes, at 60% of VO2 peak, in cycle ergometer) was determined. Control eutrophic individuals (CTRL, n=9) (BMI 22.7 ± 2 kg/m2, HOMA-IR 1.0 ± 0.3 mmol.μU/L²) were also enrolled in the study. At baseline, the frequency of intermediate monocytes was higher in the OBR (22.26 ± 12.26%) than in CTRL (7.67 ± 5.37%) ($P = 0.013$, two-way Anova), and AE reduced the frequency of these cells ($P = 0.003$), with a tendency of time versus condition interaction ($P = 0.060$). Additionally, reduced values ($P = 0.051$) were found for OBR (-7.8 ± 8.72%) compared to CTRL (-1.54 ± 1.92%) considering the effect of exercise on the frequency of intermediate monocytes (delta of variation). For classical and nonclassical monocytes, no differences were observed among the groups nor there was effect of exercise. A positive correlation between the frequency of intermediate monocytes and the percentage of body fat, BMI and HOMA1-IR was observed. These data demonstrate that obese insulin resistant individuals, but not insulin sensitive ones, have increased frequency of intermediate monocytes, what is modulated by a single session of exercise.