Ahmad et al., J Glycomics Lipidomics 2015, 5:4
DOI: 10.4172/2153-0637.1000134

Journal of Glycomics & Lipidomics

Research Article Open Access

Relationship of IL-5 with Th1 and Th2 Cytokines in Individuals with or without Type-2 Diabetes

Rasheed Ahmad, Areej Al-Roub, Merin Koshy, Sardar Sindhu* and Kazem Behbehani

Immunology and Innovative Cell Therapy Unit: Dasman Diabetes Institute (DDI), P.O. Box 1180, Dasman 15462, Kuwait

Abstract

Purpose: Changes in plasma levels of T-cell cytokines may result in inflammatory disorders, including metabolic disease. The changes in circulatory IL-5 levels in obesity and type-2 diabetes (T2D) and their relationship with major Th1 and Th2 cytokines are poorly understood. The aim of this study was to determine obesity/T2D-associated perturbation in plasma IL-5 levels and investigate its association with Th1/Th2 cytokine levels in the circulation.

Experiments: Plasma samples were collected from 43 diabetic and 22 non-diabetic individuals selected over a wide range of body mass index (BMI), and further classified as obese (BMI=31-40 kg/cm^2), overweight (BMI=26-30 kg/cm^2), and lean (BMI=18-25 kg/cm^2). Clinical metabolic parameters were determined using commercial kits. IL-5 and Th1/Th2 cytokines were measured using Luminex X-MAP® technology. The data were compared using unpaired t-test and dependence between two variables was assessed by Pearson's correlation coefficient (r).

Results: In the diabetic cohort, circulatory IL-5 levels were significantly lower as compared to non-diabetic counterparts (Diabetic: 1.55 ± 0.23 pg/ml; Non diabetic: 3.31 ± 0.49 pg/ml; P=0.0004). Furthermore, we found that in diabetic individuals, plasma IL-5 levels were found to be significantly higher (P=0.036) in obese group (1.488 ± 0.21 pg/ml) as compared with lean+overweight group (1.03 ± 0.13 pg/ml). In diabetic individuals, IL-5 levels correlated positively with Th1/Th2 cytokines including IL-12 (r=0.68, P=0.002), IL-3 (r=0.97, p=0.001) and G-CSF (r=0.57, p=0.0001). While in non-diabetic individuals, IL-5 levels correlated positively with IL-2 (r=0.83, P=0.0005), IL-12 (r=0.66, P=0.0014), IL-3 (r=0.82, P=0.0054), IL-6 (r=0.802, P=0.009), IL-9 (r=0.88, P=0.0075), IL-10 (r=0.787, P=0.008), IL-13 (r=0.84, P=0.0002), and G-CSF (r=0.82, P=0.0001). Moreover, plasma IL-5 levels in diabetic individuals associated positively with clinical metabolic indicators including BMI (r=0.54, P=0.0001), fasting blood glucose (r=0.29, P=0.05) and glycated hemoglobin (r=0.32, P=0.034).

Conclusion: The changes in circulatory IL-5 levels show differential association with Th1/Th2 cytokines in diabetic and non-diabetic individuals which may have immunometabolic significance.

Keywords: IL-5; Th1/Th2 cytokines; Obesity; Type-2 diabetes

Introduction

Obesity is linked to metabolic syndrome including insulin resistance, type-2 diabetes (T2D), and cardiovascular disease. Persistent low-grade inflammation is associated with metabolic disorders. Changes in plasma cytokines have been reported in obesity and T2D [1]. Functionally polarized CD4+ T cells are classified as Th1, Th2, Th17, and Treg subsets depending on the pattern of their cytokine production [2,3]. Th1 cytokines, such as interleukin (IL)-2 and interferon (IFN)-γ activate macrophages and are involved in inflammatory immune responses whereas Th2 cytokines, such as IL-4, IL-5, IL-10, and IL-13 have anti-inflammatory properties and are involved in antibody production, eosinophil activation, and suppression of macrophage functions [4-6]. Th1/Th2 cytokine imbalance has been reported in chronic disease progression [3,5-7] and in metabolic syndrome [8]. IL-2 is a pro-inflammatory cytokine that promotes synthesis of tumor necrosis factor (TNF)-α and IFN-γ from natural killer cells (NK) cells and is associated with atherogenesis [7,8] and T2D [9,10]. IFN-γ is related with the production of macrophage mediators, chemokines, induction of leukocyte adhesion molecules and class II major histocompatibility antigens, and potentiates the antigen presenting cell functioning [9-11]. IL-4 which is secreted by activated Th2 cells, basophils, and mast cells has pleiotropic functions including Th2 differentiation, B-cell proliferation and immunoglobulin class switching [12]. IL-10 is an anti-inflammatory cytokine which attenuates inflammation induced by IL-1, IL-6, and TNF-α while it also promotes the release of anti-inflammatory IL-1RA [13].

IL-5 is an important T cell-derived cytokine that regulates the expression of diverse genes involved in proliferation, cell survival, as well as maturation and effector functioning of B cells and eosinophils [14]. IL-5 plays a pivotal role in both the innate and adaptive immune responses and the biologic effects of IL-5 are best characterized for eosinophils in humans. It is not clear whether plasma IL-5 levels are modulated and also relate with the Th1/Th2 cytokine profile in metabolic disorders such as obesity and T2D. The aim of the study was, therefore, to determine the circulatory IL-5 levels in diabetic and non-diabetic individuals and evaluate the relationship of IL-5 levels with Th1/Th2 cytokine profile in these two populations. Here, we show that plasma IL-5 levels were significantly lower in diabetic individuals and these changes correlated with Th1/Th2 cytokines and clinical metabolic markers differentially between diabetics and non-diabetics.

Materials and Methods

Study population

This study included 43 diabetic and 22 non-diabetic adult individuals classified as obese (BMI=31-40 kg/cm^2), overweight (BMI=26-30 kg/cm^2), and lean (BMI=18-25 kg/cm^2). The study

***Corresponding author:** Dr. Sardar Sindhu, Immunology and Innovative Cell Therapy Unit, Dasman Diabetes Institute (DDI), P.O. Box 1180, Dasman 15462, Kuwait, Tel: +965 2224 2999 Ext. 4332; Fax: +965 2249 2406; E-mail: sardar.sindhu@dasmaninstitute.org

Received: October 07, 2015; **Accepted:** November 03, 2015; **Published:** November 10, 2015

Citation: Ahmad R, Al-Roub A, Koshy M, Sindhu S, Behbehani K (2015) Relationship of Il-5 with Th1 and Th2 Cytokines in Individuals with or without Type-2 Diabetes. J Glycomics Lipidomics 5: 134. doi:10.4172/2153-0637.1000134

participants were recruited through outpatient clinics of Dasman Diabetes Institute, Kuwait. Recruiting the non-diabetic individuals with clinico-demographic characteristics comparable to those of diabetics within 3 BMI subgroups was challenging and, therefore, less number of non-diabetic individuals could be recruited as compared with diabetics. The clinico-demographic data of the study participants are summarized in Table 1. All participants gave written informed consent and study was approved by Ethical Review Committee of Dasman Diabetes Institute. The diagnosis of T2D was performed by designated physician based on results of fasting blood glucose (FBG), oral glucose tolerance test (OGTT), and glycated hemoglobin (HbA1c) test. FBG levels of ≥ 126 mg/dL (≥ 7 mmol/L), 2 h-OGTT values of >200 mg/dL (11.1 mmol/L), and/or HbA1C levels of ≥ 6.5% on two separate tests were diagnosed as T2D. Anthropometric and physical measurements included body weight, height, waist circumference as well as systolic and diastolic blood pressure. Height and weight were measured with barefoot participants wearing light indoor clothing using calibrated portable electronic weighing scales and portable inflexible height measuring bars; the waist circumference at the highest point of the iliac crest and the mid-axillary line was measured using constant tension tape at the end of a normal expiration with arms relaxed at the sides. The waist-to-hip ratios were calculated, and the whole body composition including percentage of body fat, soft lean mass and total body water were measured by the use of IOI 353 Body Composition Analyzer (Jawon Medical, South Korea). Blood pressure was measured by using Omron HEM-907XL digital automatic sphygmomanometer (Omron Healthcare Inc. IL, USA). An average of the 3 blood pressure readings, with 5-10 min rest between each, was obtained. BMI was calculated using standard BMI formula i.e. body weight (kg)/height (m^2). Regarding clinical laboratory measurements, peripheral blood was collected by phlebotomist through venipuncture from overnight-fasting (minimum 10 h) individuals and samples were analyzed for FBG, HbA1c, and lipid profile. Glucose and lipid profiles were measured using Siemens dimension RXL chemistry analyzer (Diamond Diagnostics, Holliston, MA, USA) and HbA1c was measured by using Variant device (BioRad, Hercules, CA, USA). All assays were carried out following instructions as recommended by the manufacturers.

Determination of plasma cytokines

A total of 41 cytokines and chemokines were measured using panel MILLIPLEX MAP Human Cytokine/Chemokine Magnetic Bead Panel - Premixed 41 Plex - Immunology Multiplex Assay (Milliplex map kit, HCYTMAG-60K-PX41; Millipore, USA) following the manufacturer's instructions. Data from the reactions were acquired using Luminex, Milliplex analyzer, while a digital processor managed data output and the Milliplex analyst software was used to determine mean fluorescence intensity (MFI) and analyte concentration (pg/mL).

Statistical analysis

The data obtained were expressed as mean ± SD values; group means were compared using unpaired t-test and the linear dependence between two variables was assessed by Pearson's correlation coefficient (r). GraphPad Prism software (version 6.05; San Diego, CA, USA) was used for statistical analysis and graphical representation of data. All P-values ≤ 0.05 were considered statistical significant.

Results

Decreased IL-5 levels in diabetic individuals

IL-5 is an important Th2 cytokine and its role in metabolic disorders is not well understood. Since not much work has been done regarding changes in IL-5 expression and their relationship with Th1/Th2 cytokines in obesity and T2D, we therefore determined levels of IL-5 and Th1/Th2 cytokines in plasma samples both from diabetic and non-diabetic individuals. The data show that IL-5 levels in diabetics (1.55 ± 0.23 pg/ml) were lower (P=0.0004) than in non-diabetics (3.31 ± 0.49 pg/ml) (Figure 1A and 1B).

Increased IL-5 levels in diabetic individuals with obesity

Next, we asked if obesity could modulate IL-5 expression in diabetic and non-diabetic individuals. To this end, our data show that in diabetic patients, IL-5 levels were significantly higher in obese (BMI=33.96 ± 1.744 kg/cm^2) group (1.488 ± 0.21 pg/ml) as compared with lean+overweight (BMI=25.89 ± 2.548 kg/cm^2) group (1.03 ± 0.13 pg/ml) (P=0.036) (Figure 2A and 2B). In non-diabetic individuals, mean IL-5 levels in obese (BMI=34.09 ± 2.805 kg/cm^2) group (3.91 ± 0.71 pg/ml) were also relatively higher than in lean+overweight (BMI=23.60 ± 2.640 kg/cm^2) group (2.57 ± 0.59 pg/ml) but the difference between two groups did not reach statistical significance (P=0.17) (Figure 2C and 2D).

Association between IL-5 and Th1/Th2 cytokines in diabetic and non-diabetic individuals

As our data show that IL-5 levels were lower in diabetic patients, we further wanted to know how the IL-5 expression changes related with signature Th1/Th2 cytokines both in diabetic and non-diabetic subjects. To this effect, we found a positive/significant correlation

Table 1: Patients characteristics and clinical data.

Parameters	Non-Diabetic (Mean ± SD)	Diabetic (Mean ± SD)
Number (N)	22	43
Age (yrs)	35.70 ± 8.498	49.53 ± 8.610
BMI (kg/m^2)	29.86 ± 6.385	31.63 ± 4.715
Fasting Blood Glucose (mmol/l)	5.146 ± 0.7636	7.939 ± 2.897
HDL cholesterol (mmol/l)	1.320 ± 0.7646	1.167 ± 0.3552
LDL cholesterol (mmol/l)	2.886 ± 0.9243	3.208 ± 0.9627
Triglycerides (mmol/l)	1.370 ± 1.719	1.490 ± 1.099
Cholesterol (mmol/l)	4.636 ± 0.8463	4.968 ± 1.037
HbA1C (%)	5.350 ± 0.4627	7.613 ± 2.041

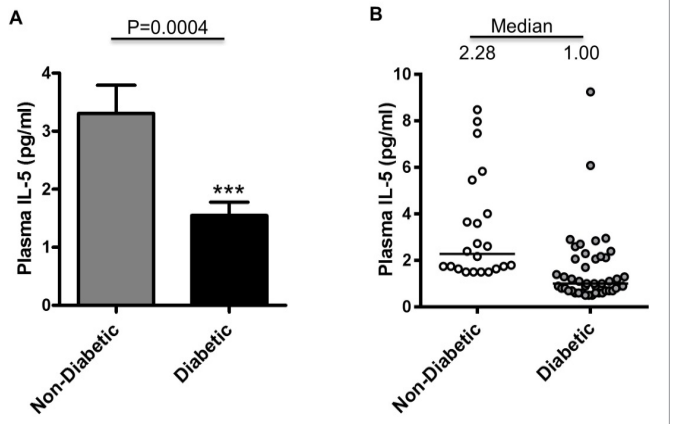

Figure 1: Plasma samples from 43 diabetic and 22 non-diabetic individuals were analyzed for IL-5 levels using Luminex magnetic bead assay. (A) IL-5 levels (mean±SD) are shown for diabetic and non-diabetic individuals. (B). Dot plot of IL-5 levels is shown for diabetic and non-diabetic subjects. Each dot represents the individual value of IL-5 and the lines represent median values in each group.

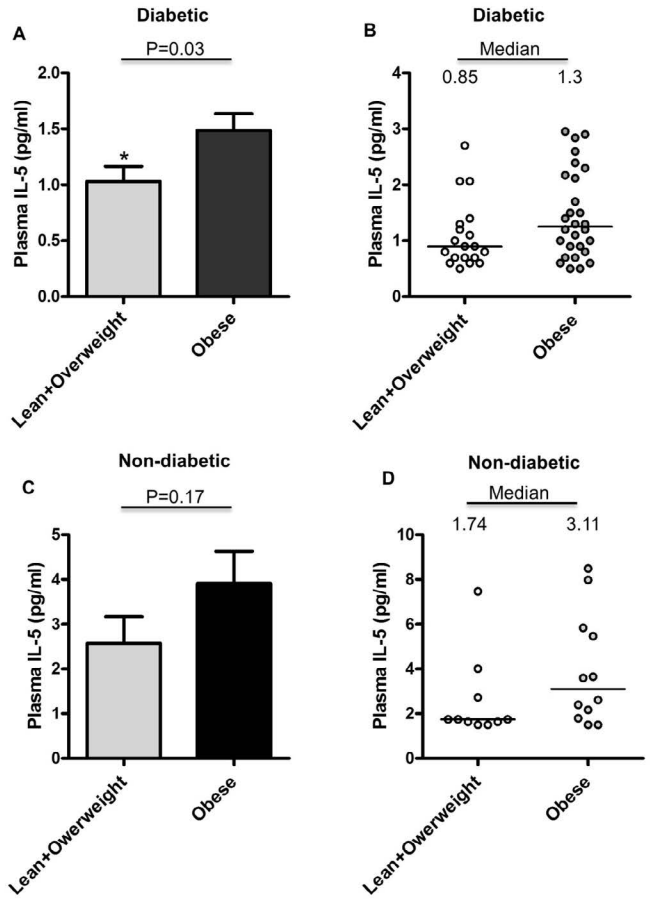

Figure 2: Plasma samples from 43 diabetic and 22 non-diabetic individuals were analyzed for the expression of IL-5 using Luminex magnetic bead assay. The diabetic and non-diabetic group, each, was classified on the basis of body mass index (BMI) as described in Materials and Methods. (A) IL-5 levels (mean±SD) are shown for obese diabetic and overweight/lean diabetic individuals. (B). Dot plot of IL-5 levels is shown for obese diabetic and overweight/lean diabetic subjects. Each dot represents the individual value of IL-5 and the lines represent median values of plasma IL-5 in each group. (C) IL-5 levels (mean±SD) are shown for obese non-diabetic and overweight/lean non-diabetic individuals. (D). Dot plot of IL-5 levels shown for obese non-diabetic and overweight/lean non-diabetic subjects. Each dot represents the individual value of IL-5 and the lines represent median values of plasma IL-5 in each group.

of IL-5 with Th1 cytokines (TNF-α, IL-2, and IL-12) as well as Th2 cytokines (IL-3, IL-6, IL-9, IL-10, IL-13, and G-CSF). Further, in this regard, IL-5 levels showed significant correlations ($P<0.05$) with IL-2 (r=0.83), IL-6 (r=0.80), IL-9 (r=0.89), IL-10 (r=0.79), and IL-13 (r=0.84) only in non-diabetic individuals. Whereas, both in non-diabetics and diabetics, IL-5 levels also correlated ($P<0.05$) with IL-12 ($r_{non\text{-}diabetic}=0.67$, $r_{diabetic}=0.68$), IL-3 ($r_{non\text{-}diabetic}=0.82$, $r_{diabetic}=0.97$), and G-CSF ($r_{non\text{-}diabetic}=0.82$, $r_{diabetic}=0.57$). However, the correlation between IL-5 and TNF-α did not approach the level of statistical significance in non-diabetic individuals (P=0.06). No association of IL-5 was observed with IL-2, IL-3, IL-6, IL-9, IL-10, and IL-13 in diabetic patients and with IFN-γ and IL-4 in both diabetic and non-diabetic individuals. The data are summarized in Table 2.

Association between IL-5 and clinical metabolic parameters in diabetic and non-diabetic subjects

We further investigated whether the modulated IL-5 expression had an association with clinico-metabolic parameters. To this end, serum levels of triglyceride, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, FBG, and HbA1c were also measured. Our data show that IL-5 levels correlated with FBG (r=0.29, P=0.05), HbA1c (r=0.32, P=0.03), as well as with BMI (r=0.54, P=0.0001) in diabetic subjects only. Whereas, TGL, HDL, LDL, and total cholesterol levels did not correlate with IL-5 in this population. In non-diabetics, IL-5 had no association with clinico-metabolic parameters (Table 3).

Discussion

Obesity and T2D are marked with a state of chronic low-grade inflammation and the expanding adipose tissue plays a dual role as an organ for excessive triglyceride storage as well as an endocrine organ which secretes a variety of adipokines and inflammatory cytokines/chemokines. Whereas, the roles of adipokines and macrophage-elicited cytokines/chemokines in metabolic disease are well elucidated, little is known about the perturbation in Th2-cell cytokine IL-5 and its relationship with other Th1/Th2 cytokines in metabolic disease. Th1/Th2 cytokine balance is critical to the execution of normal immune response and perturbations in these cytokines may sway the balance from protective to deleterious consequences. The association of Th1 cytokines with metabolic disease was already reported in humans and animals [15,16]. Whereas, IL-5 is a Th2 cell-derived cytokine which is involved in diverse biological functions such as cellular proliferation, survival, maturation, as well as effector functioning of eosinophils and B cells. In this study, we show that plasma IL-5 levels were significantly lower in diabetic individuals as compared with non-diabetic counterparts. In agreement with our finding, another study also showed the suppression of Th2 serum cytokines in subjects with diabetic coronary artery disease [8]. As though the exact cause(s) for lower Th2 cytokine levels in metabolic disease is/are currently unknown, a shift in Th1 to Th2 ratio toward Th1 dominance has been earlier reported [17]. Interestingly, our data further show that in obese diabetic population, IL-5 levels were significantly higher than overweight/lean diabetic individuals. It is not clear whether obesity

Table 2: Correlation of plasma IL-5 levels with Th1/Th2 cytokines in diabetic and non-diabetic individuals.

		Non-Diabetic		Diabetic	
	Th1 Cytokines	**Pearson r**	**P**	**Pearson r**	**P**
Plasma IL-5	TNF-α	0.51	0.06	-0.185	0.227
	IL-2	0.826	0.0005***	-0.316	0.488
	IL-12	0.665	0.0014**	0.684	0.002**
	Th2 Cytokines	**Pearson r**	**P**	**Pearson r**	**P**
	IL-3	0.82	0.0054***	0.973	0.001**
	IL-6	0.802	0.009**	-0.135	0.509
	IL-9	0.888	0.0075**	-0.163	0.987
	IL-10	0.787	0.008**	-0.116	0.546
	IL-13	0.839	0.0002***	-0.089	0.833
	G-CSF	0.816	0.0001***	0.568	0.0001**

Table 3: Correlation between plasma IL-5 levels and metabolic parameters.

		Non-Diabetic		Diabetic	
	Metabolic Parameters	**Pearson r**	**P**	**Pearson r**	**P**
Plasma IL-5	Body mass index (BMI) (kg/cm^2)	0.165	0.445	0.536	0.0001***
	Fasting Blood Glucose (mmol/l)	0.257	0.249	0.2908	0.051
	HbA1C (%)	-0.036	0.871	0.315	0.034*
	HDL cholesterol (mmol/l)	-0.218	0.328	0.182	0.229
	LDL cholesterol (mmol/l)	0.077	0.740	0.042	0.781
	Total cholesterol (mmol/l)	0.006	0.916	0.105	0.492

was a major player in upregulating IL-5 expression in diabetic patients; however, obesity associated with enhanced eosinophil numbers and IL-5 levels in a murine model of allergic asthma [18].

The data further show that IL-5 correlated positively with IL-2, IL-6, IL-9, IL-10, and IL-13 only in non-diabetic subjects while it associated with IL-12, IL-3, and G-CSF in both non-diabetic and diabetic individuals. It implies that IL-5 has a broader relationship with both the Th1 and Th2 cytokines which is expressed differentially in the presence or absence of T2D. Herein, we found that IL-5 associated with IL-12, IL-3, and G-CSF whether or not diabetes was a morbid cofactor in the population studied whereas it did not associate with IL-2, IL-6, IL-9, IL-10, and IL-13 if diabetes was present as a comorbidity. It is not clear if the regulatory functions of IL-12, IL-3, and G-CSF are well preserved in obesity/T2D. IL-3 and CSF interact to promote CD11c+ IL10-producing macrophages [19]. IL-3 stimulates the proliferation of monocytes, granulocytes and dendritic cells. G-CSF is a cytokine and a hormone that acts as a colony stimulating factor for granulocytes, stem cells, and also promotes the proliferation and differentiation of neutrophils. Elevated serum levels of IL-12 were reported in overweight and obese adult individuals that showed a strong relationship with markers of low-grade inflammation and obesity [20]. IL-12 helps in differentiation of naïve T cells into Th1 cells; it stimulates the production of IFN-γ and TNF-α and also plays a critical role in the activation of T cells and NK cells [21]. We further show that IL-5 associates with clinical metabolic markers including BMI, HbA1C and FBG in diabetic subjects which points to its clinical relevance as an immune marker in T2D. Overall, the peripheral IL-5 levels were found to be associated differentially with Th1 and Th2 cytokines in diabetic and non-diabetic individuals. Further studies involving larger cohorts will be required to verify these preliminary data as well as study the relationship of IL-5 with cytokines and chemokines produced by other immune effector cells such as monocytes/macrophages, dendritic cells, B-cells, NK cells, and adipocytes to enhance our understanding of the significant role of IL-5 in metabolic disease.

In conclusion, our data show that plasma IL-5 levels were significantly lower in diabetic as compared with non-diabetic individuals; whereas in diabetic cohort, IL-5 levels were higher in obese as compared with overweight/lean subjects. IL-5 associated differentially with Th1/Th2 cytokines in diabetic and non-diabetic individuals and also related with clinical disease markers.

Acknowledgments

This work was supported by Kuwait Foundation for Advancement of Sciences (KFAS) (Grant # RA-2011-015). The authors thank staff of Pancreatic Islet Biology and Transplantation unit for help with Luminex assay.

References

1. Gregor MF, Hotamisligil GS (2011) Inflammatory mechanisms in obesity. Annu Rev Immunol 29: 415-445.
2. Sallusto F, Lanzavecchia A (2009) Heterogeneity of CD4+ memory T cells: functional modules for tailored immunity. Eur J Immunol 39: 2076-2082.
3. Murphy KM, Reiner SL (2002) The lineage decisions of helper T cells. Nat Rev Immunol 2: 933-944.
4. Kawashima N, Stashenko P (1999) Expression of bone-resorptive and regulatory cytokines in murine periapical inflammation. Arch Oral Biol 44: 55-66.
5. Jankovic D, Liu Z, Gause WC (2001) Th1- and Th2-cell commitment during infectious disease: asymmetry in divergent pathways. Trends Immunol 22: 450-457.
6. Lappin DF, MacLeod CP, Kerr A, Mitchell T, Kinane DF (2001) Anti-inflammatory cytokine IL-10 and T cell cytokine profile in periodontitis granulation tissue. Clin Exp Immunol 123: 294-300.
7. Gemmell E, Yamazaki K, Seymour GJ (2007) The role of T cells in periodontal disease: homeostasis and autoimmunity. Periodontol 2000 43: 14-40.
8. Madhumitha H, Mohan V, Deepa M, Babu S, Aravindhan V (2014) Increased Th1 and suppressed Th2 serum cytokine levels in subjects with diabetic coronary artery disease. Cardiovasc Diabetol 13: 1.
9. Geng YJ, Hansson GK (1992) Interferon-gamma inhibits scavenger receptor expression and foam cell formation in human monocyte-derived macrophages. J Clin Invest 89: 1322-1330.
10. Hansson GK, Jonasson L, Holm J, Clowes MM, Clowes AW (1988) Gamma-interferon regulates vascular smooth muscle proliferation and Ia antigen expression *in vivo* and *in vitro*. Circ Res 63: 712-719.
11. Tellides G, Tereb DA, Kirkiles-Smith NC, Kim RW, Wilson JH, et al. (2000) Interferon-gamma elicits arteriosclerosis in the absence of leukocytes. Nature 403: 207-211.
12. Nelms K, Keegan AD, Zamorano J, Ryan JJ, Paul WE (1999) The IL-4 receptor: signaling mechanisms and biologic functions. Annu Rev Immunol 17: 701-738.
13. Juge-Aubry CE, Somm E, Pernin A, Alizadeh N, Giusti V, et al. (2005) Adipose tissue is a regulated source of interleukin-10. Cytokine 29: 270-274.
14. Kouro T, Takatsu K (2009) IL-5- and eosinophil-mediated inflammation: from discovery to therapy. Int Immunol 21: 1303-1309.
15. Rocha VZ, Folco EJ, Sukhova G, Shimizu K, Gotsman I, et al. (2008) Interferon-gamma, a Th1 cytokine, regulates fat inflammation: a role for adaptive immunity in obesity. Circ Res 103: 467-476.
16. Pacifico L, Di Renzo L, Anania C, Osborn JF, Ippoliti F, et al. (2006) Increased T-helper interferon-gamma-secreting cells in obese children. Eur J Endocrinol 154: 691-697.
17. Szodoray P, Timar O, Veres K, Der H, Szomjak E, et al (2006) TH1/TH2 imbalance, measured by circulating and intracytoplasmic inflammatory cytokines-immunological alterations in acute coronary syndrome and stable coronary artery disease. Scand J Immuno l 64: 336-344.
18. Calixto MC, Lintomen L, Schenka A, Saad MJ, Zanesco A, et al. (2010) Obesity enhances eosinophilic inflammation in a murine model of allergic asthma. Br J Pharmacol 159: 617-625.
19. Sheng KC, Herrero LJ, Taylor A, Hapel AJ, Mahalingam S (2014) IL-3 and CSF-1 interact to promote generation of CD11c+IL-10-producing macrophages. PLoS One 9: e95208.
20. 20.Suarez-Alvarez K, Solis-Lozano L, Leon-Cabrera S, Gonzalez-Chavez A, Gomez-Hernandez G, et al (2013) Serum IL-12 is increased in Mexican obese subjects and associated with low-grade inflammation and obesity-related parameters. Mediators Inflamm 2013: 967067.
21. Kaiko GE, Horvat JC, Beagley KW, Hansbro PM (2008) Immunological decision-making: how does the immune system decide to mount a helper T-cell response? Immunology 123: 326-338.