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THE EFFECT OF INTERLEUKIN-2 ON SOME FUNCTIONS OF POLYMORPHNEUCLEAR NEUTROPHILS

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ABSTRACT

Polymorphonuclear neutrophils (PMN) were originally described as short lived and terminally differentiated phagocytes that contribute only to the innate immune response. Recent evidence of PMN cytokine production and expression of numerous cell surface proteins has suggested that PMN are likely to influence adaptive responses and may satisfy the criteria of antigen presenting cells.

There are three types of IL-2R (α, β and γ). Only IL-2R α and γ were detected in stimulated PMN. In this study IL-2Rβ chain was detected on PMN using flow cytometry. This prompted us to define IL-2 participation in some biological properties of PMN. It had been previously shown that normal human PMN contain cytoplasmic stores of molecules. These were found to translocate to the cell surface with different stimuli.

In this study, IL-2 *in vitro* activation of PMN had acquired, important costimulatory molecules required for T-cell signaling (CD83), LPS receptor (CD14) and IgG Fc receptor (CD64) on the surface and at the gene level by reverse transcriptase polymerase chain reaction.

Keywords: IL-2, PMN, CD14, CD64, CD83.

INTRODUCTION

Polymorphnuclear neutrophils (PMN) functional history: PMN possess a very short half-life in the circulation because they constitutively undergo apoptosis [**Gasmi, *et al.*, (1996); Stringer, *et al.*, (1996) and Moulding, *et aL*, (1998)**]. Under certain conditions PMN play an important role in the effector arm of host immune defense through the clearance of immune complexes, phagocytosis of opsonized particles, and the release of inflammatory mediators [**Shen, *et al.*, (1987); Petroni *et aL*, (1988); and Lloyd and Oppenheim, (1992)**]. During the recent years the image of PMN has changed considerably. Traditionally considered to be the first line defense against bacterial infection. It became increasingly clear that PMN also participate in chronic inflammation disease and regulation of the immune response when appropriately activated [**Iking-konert, *et al.*,(2001)**].

Effects of cytokines on PMN: PMN function and recruitment to the site of inflammation have been shown to be upregulated by various cytokines, including interleukin (IL)-1, IL-8, tumor necrosis factor (TNF-α), interferon-γ (IFN-γ), and granulocyte macrophage-colony stimulating factor (GM-CSF) [**Steinbeck , Roth, (1989)** and , **Lloyd and Oppenheim, (1992)**]. A foreign stimulus, particularly cell components of bacteria and fungi, can readily attract PMN, and a local inflammatory reaction results in the production of cytokines that further mobilize and activate incoming PMN. Moreover, CD64 is up-regulated, as major histocompatibility complex (MHC) class II antigens [**Gosselin, *et al.*, (1993) and Gericke *et al.*, (1995)**]. Cytokines, such as GM-CSF, IFN-γ, IL-1β, and IL-2, which are produced by activated T-cells and monocytes, can delay neutrophil apoptosis and extend the functional life span of neutrophils to several days [**Brach, *et al.*, (1992)**; **Colotta, *et al.*, (1992)**; **Lee, *et al.*, (1993) and Pericle, *et al.*, (1994)**]. PMN activated with TNF-α, IFN-γ, and GM-CSF express HLA-DR and CD83 [**Shigeo *et al.*, (2000)**].

Effects of IL-2 on PMN: Classically, IL-2 has been considered to be a lymphocyte-activating and growth-promoting factor, and has been widely studied on T cells and NK cells [**Smith, (1984) and Waldmann, (1989)**]. Recently, monocytes have been reported to express IL-2Rβ and to be activated by IL-2 for tumoricidal activity [**Espinoza-Delgado, *et al.*, (1990)**]. The direct effect of IL-2 on PMN, especially the mechanisms involved in the activation of PMN, is unknown, although the ability of other immune cells to respond to IL-2 is well studied. Preliminary studies have shown that PMN have the capacity to respond to IL-2 with increased antifungal activity [**Djeu, *et al.*, (1993)**]; more importantly they have identified, also that PMN express surface receptors for IL-2, but only IL-2Rβ and not IL-2R is present.

Purpose of the study: In the present work we found that PMN cultured with IL-2 acquired CD83, important costimulatory molecules required for T-cell signaling, LPS receptor CD14 and IgG Fc receptor CD64. In addition, we also demonstrated mRNA specific for CD83, CD14 and CD64 within PMN.

MATERIALS AND METHODS

Donors: Blood samples were taken by venous puncture using 7·5ml heparin-coated tubes (Sarstedt; Nümbrecht, Germany) and were analysed within 2 hours.

PMN purification, cultivation and stimulation: PMN were separated from heparinized blood of healthy donors by Polymorphprep (Nycomed; Oslo, Norway). The PMN were further purified by adsorption to CD15 microbeads using magnetic activated cell sorter, MACS (MiltenyBiotech; Bergisch-Gladbach, Germany). Purified PMN (1×10^6 /ml) were cultivated in AIM V (Gibco; Eggenstein, Germany) with 2·5% autologous normal human serum (inactivated at 56°C for 30 minutes). Highly purified PMN were placed into 24-well plate and incubated for about 48 hours in the presence or absence of the activator rhIL-2, 10ng/ml (Sigma; St Louis, MO, USA) at 37°C with 5% CO_2 in air.

Cytoflourocytometry: IL-2R was detected on PMN by direct and indirect extracellular fluorescence-activated cell sorter (FACS). In direct sets of experiments cells in whole blood were stained with 2μg anti-CD122-FITC and 2μg anti-CD25 (Serotic; Oxford, UK) as a markers for IL-2Rβ chain and IL-2Rα chain. Primary an unlabeled antibody for IL-2Rβ chain was added to cells before staining with anti-CD122-FITC. Anti-mouse IgG-FITC and anti-CD66-FITC (Immunotech.; Marseille, France) were used as a negative and a positive control, respectively.
Viability of PMN was determined by propidium iodide (10ng/ml) which is a membrane-impermeant dye for living cells, but intercalates into DNA and RNA when the membrane becomes permeable. Propodium Iodide was purchased from Sigma (München, Germany). PMN were isolated by polymorphprep and CD15 microbeads. Those PMN excluded the dye and are found in M1 when analyzed by cytofluorometry. Samples were analyzed by FACS within 2 hours after incubation for 5 minutes at room temperature in dark place.

For double labeling, fluorescein isothiocyanate (FITC) and phycoerythrin (PE)-labeled murine MoAbs were used. Highly purified PMN were double labeled with 2μg anti-CD66b-FITC (Immunotech.; Marseille, France) as a PMN marker and 2μg PE-labeled antibodies to CD14, CD64 and CD83 (Immunotech.; Marseilles, France). Cells were analyzed by FACSCalibur and CellQuest software (Becton-Dickinson; Heidelberg, Germany). Results are expressed as percentage of positive cells in the respective gate or quadrant.

RNA isolation and reverse transcription-polymerase chain reaction (RT-PCR): Total RNA was isolated from 1 x 10^7 PMN after 6 hours of culture with IL-2. RNA isolation was performed using a RN Aeasy kit (Quiagen; Hilden, Germany) following the instructions of the manufacturer exactly. RNA was transcribed using a GIBCO RT Superscript II kit (GIBCO Life Technologies; Karlsruhe, Germany). To detect mRNA the following primers were used: CD83-specific primers (sense: 5;-GCC ATG TCG CGC GGC CTC CAG CTT-3' and antisense 5′-GGA CAA TCT CCG CTC TGT ATT TC-3′) yielded a 445-bp fragment. CD14 primers (sense: 5'-TGACATCCCAGG ATTACAGTCG ATAA-3' and antisense: 5'-CCTACACTCACCATGGT CGATAA-3'), CD64 primers (sense 5′-ATG TGG TTC TTG ACA ACT CTG-3′ and antisense 5′-CCA GTG GAA AAA CTT AAA GGC-3′). For quantitative PCR a primer for β-actin, kindly provided by Dr Giese (Institute for Immunology; Heidelberg, Germany) yielded a 450-bp PCR product. The primers were synthesized by ARK Scientific Biosystems (Darmstadt, Germany). PCR was performed in a Hybaid PCR express thermocycler as follows: 2 min at 95°C once; 30 min at 95°C; 30 min at 66°C; 30 min at 72°C 10 times; 30 min at 95°C; 30 min at 56°C; 45 min at 72°C 25 times and finally 7 min at 72°C. To 2 mg of RT-product 1 U of Taq-DNA polymerase (Boehringer), 5 ml 10 buffer with Mg2 , 25 mM of sense- and antisense-primer, 10 mM of dNTPs (GIBCO) was given and filled with DEPC water (final volume 50 ml). The PCR products were separated by a 1% agarose gel, stained with SybrGreen (Molecular Probes; Leiden, Netherlands) and analyzed by FLA2000 (Fuji, Japan) using Image Gauge V3·0 (Fuji) as software. We used a Boehringer DNA Marker VI (range 154–2176 bp) at a concentration of 30 mg/ml.

RESULTS

1. Direct immunofluorescence analysis of IL-2R:

In order to investigate constitutive expression of IL-2R, we tested the presence of the two IL-2R chains (IL-2α and IL-2β) on the PMN cell surface by FACS. In line with previous data by others, the α chain (CD25) could not be detected (< 1 % positive cells), while PMN expressed CD122, though rather small amounts **Fig. (1)**.

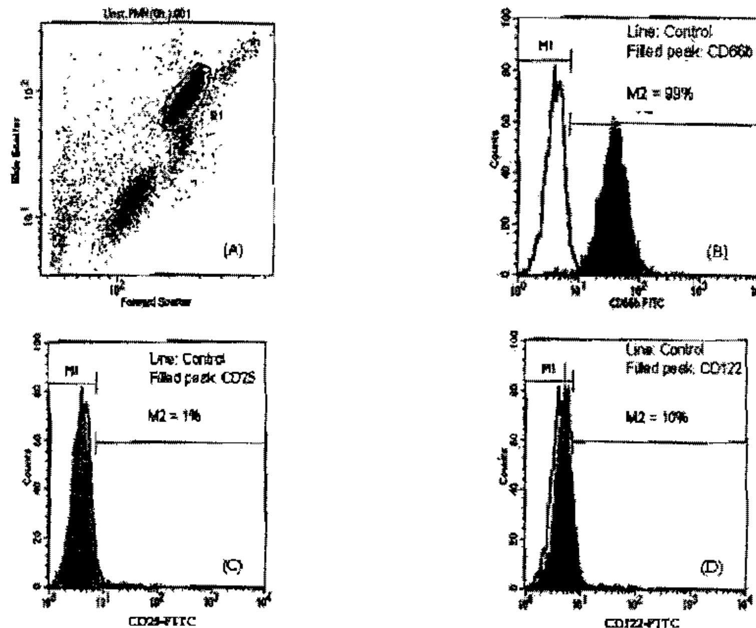

Fig. (1) : Detection of IL-2R on PMN: (A) Forward-scatter (FSC) versus side-scatter (SSC) of whole blood flow cytometry showed different populations of leukocytes. R1 was set for PMN identified by expression of CD66b (B) filled peak. PMN expressed only IL-2Rβ chain (D), while IL-2Rα chain was absent (C) (filled peaks: antibody; line isotype control).

When comparing cells of different donors, the mean fluorescence intensity varied (summary of 6 donors is shown in **Table (1)**).

No. of tested donors	mean fluoresence intensity
1-	**10**
2-	**22**
3-	**16**
4-	**14**
5-	**32**
6-	**25**

Table (1) : Expression IL-2Rβ chain (CD122) on PMN of different donors.

2. Indirect immunofluorescence for the IL-2Rβ chain:

By indirect labeling, using first an unlabeled antibody to IL-2Rβ, followed by a FITC-labeled antibody to mouse IgG, the signal for the IL-2Rβ chain could be amplified. That nearly all cells were positive **Fig. (2)**.

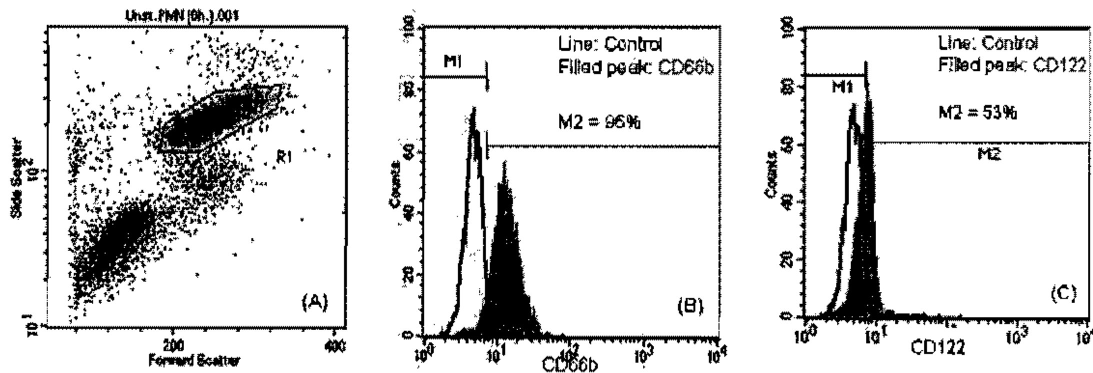

Fig. (2) : Indirect extracellular detection of IL-2Rβ chain: (A) the forward-side scatter analysis of whole blood flow cytometry showed different populations of leukocytes. PMN were identified in R1. (B) M2 is the percentage of CD66b–positive cells (filled peak). (C) PMN expressed IL-2Rβ chain as detected by anti-CD122 (filled peak); the line is the negative control using mouse IgG in place of anti-CD122.

3. Effect of IL-2 on the viability of PMN:

Viability was measured using propidium iodide and analyzed by cytofluorometry. After 24 hours and 48 hours in culture two more populations of cells were identified (M2, M3). In both, unstimulated and IL-2 stimulated PMN, more than 70 % of PMN were still viable after 24 hours; by 48 hours cells death increased and there was now a difference with the IL-2 treated cells showing a better survival **Fig. (3)**.

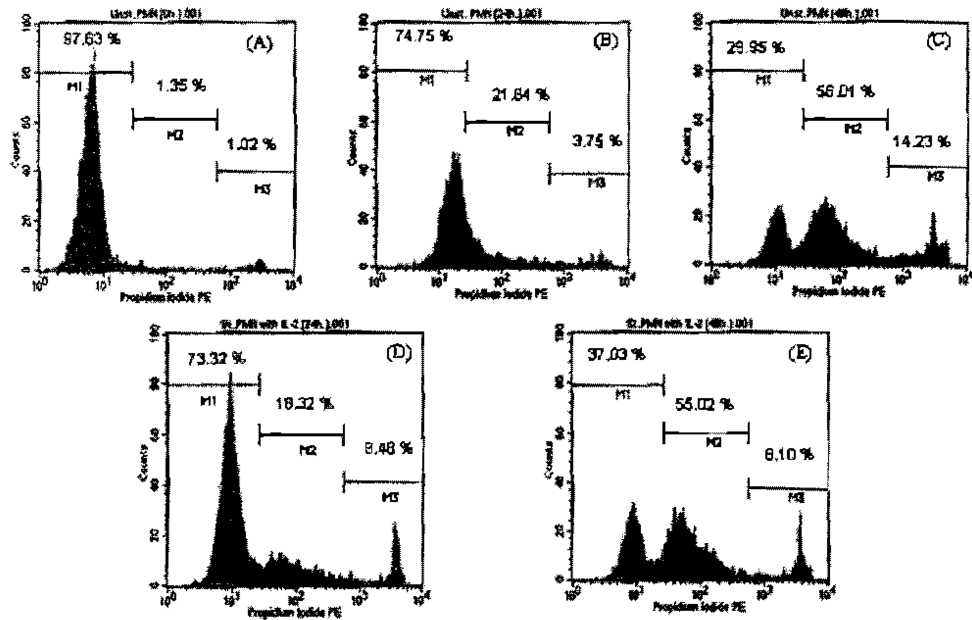

Fig. (3) : The viability was measured using propidium iodide: The unstimulated PMN can be seen in A, B and C quadrants. The stimulated with IL-2 can be also seen in D and E quadrants. The percentage of the positive cells is depicted in each quadrant; viable cells are in MI; dead and dying cells are expected in M2 and M3.

4. Up-regulation of CD14 on PMN:

To test effects of IL-2 on CD14 up-regulation, CD14 in highly purified PMN 48 hours cultured with IL-2 increased recording 55 % **Fig. (4c)**. Freshly isolated PMN had 45 % **Fig. (4a)**. PMN cultured with medium alone for 48 hours had 15 % CD14 **Fig. (4b)**.

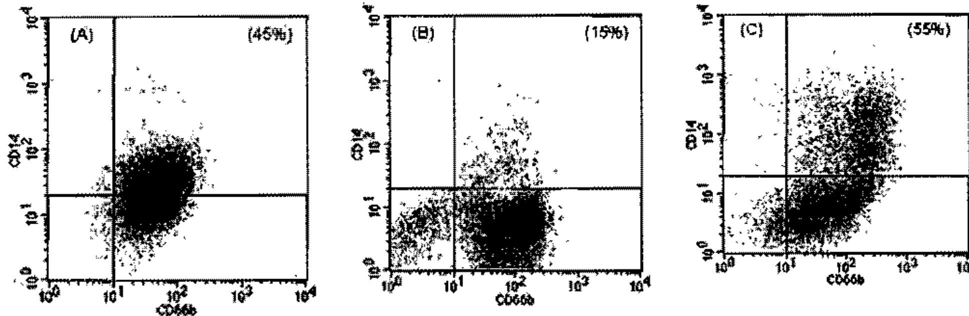

Fig.(4) : Direct flow cytometry of the CD14 induction in highly purified PMN: A) Unstimulated PMN (0 hour). B) Unstimulated PMN (48 hours). C) Stimulated PMN with IL-2 (48 hours).

When the values were corrected for the input of the PCR-product by using β-actin as a housekeeping gene **Fig. (5a)** and when calculating the mean of three independent experiments, it was seen that the increase in abundance of CD14 RNA increased when PMN were cultivated for 6 hours about 3.4 folds. The increase was more pronounced in the presence of IL-2 and was 4.8 folds **Fig. (5b)**.

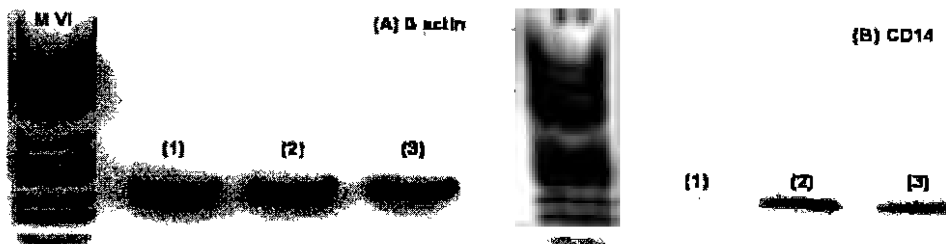

Fig. (5) : RT-PCR detection of CD14 mRNA in PMN activated with IL-2: PMN were incubated with IL-2 (10 ng / ml) for 6 hours. The M VI was the used marker (154-2176 bp). Freshly isolated PMN were in Lane (1). Lane (2) showed the stimulated PMN after 6 hours, while the unstimulated PMN after 6 hours was in lane (3).

5. Up-regulation of CD64 on PMN:

The results showed that highly purified PMN stimulated with IL-2 also expressed CD64 after 48 hours **Fig.**(6).

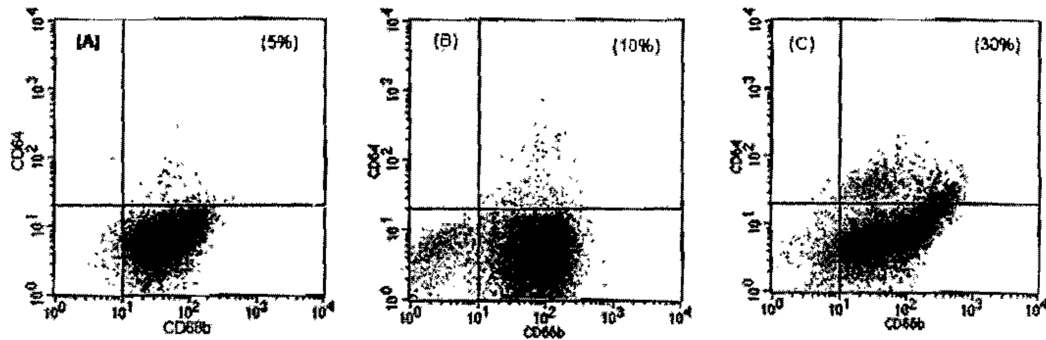

Fig. (6) : Direct flow cytometry of the CD64 induction in highly purified PMN: A) Unstimulated PMN (0 hour). B) Unstimulated PMN (48 hours). C) Stimulated PMN with IL-2 (48 hours).

Again, as described for CD14, direct effects of IL-2 on CD64 RNA were tested. PMN were highly purified and cultured with IL-2 for 6 hours or, for comparison, without a stimulus added. As seen from **Fig.** (7a), CD64 specific RNA was found in all PMN; when corrected for the input, i.e. related to β-actin, there was no considerable difference between unstimulated or IL-2 stimulated PMN at 6 hours **Fig.**(7b).

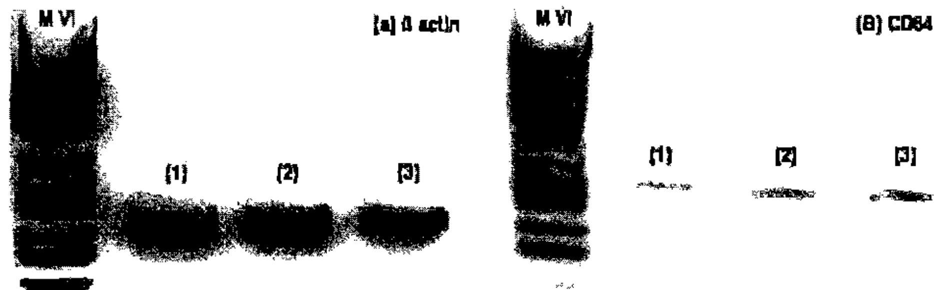

Fig. (7) : RT-PCR detection of CD64 mRNA in PMN activated with IL-2: PMN were incubated with IL-2 (10 ng / ml) for 6 hours. The M VI was the used marker (154-2176 bp). Freshly isolated PMN were in Lane (1). Lane (2) showed the stimulated PMN after 6 hours, while the unstimulated PMN after 6 hours was in lane (3).

6. Up-regulation of CD83 on PMN:

From 5 experiments using PMN of different donors, IL-2 could also affect the CD83 expression, when highly purified PMN were used. In line with the data seen for CD14 antigens, a rather distinct subpopulation of PMN acquired CD83 **Fig. (8)**.

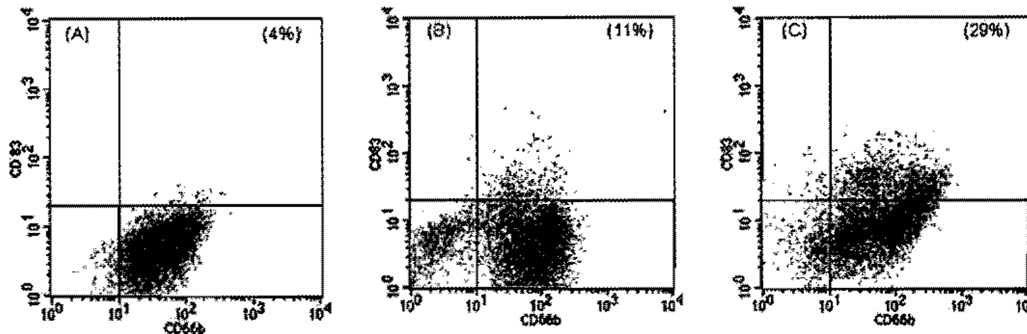

Fig. (8) : FACS for CD83 surface expression in highly purified PMN: A) Unstimulated PMN (0 hour). B) Unstimulated PMN (48 hours). C) Stimulated PMN with IL-2 (48 hours).

The mRNA of CD83 was detected by using CD83 primer. As shown in **Fig. (9)**, freshly isolated PMN did not express CD83 mRNA (lane1), while it was detected after 6 hours culture with either medium or medium with IL-2 (lane 3 and 2, respectively).

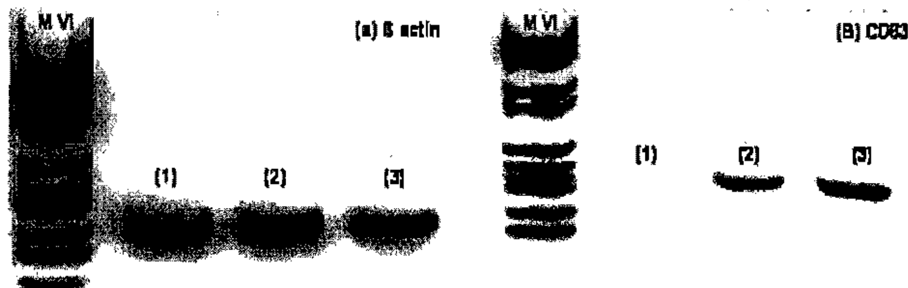

Fig. (9) : RT-PCR detection of CD83 mRNA in PMN activated with IL-2: PMN were incubated with IL-2 (10 ng / ml) for 6 hours. The MVI was the used marker (154-2176 bp). Freshly isolated PMN were in lane (1). Lane (2) showed the stimulated PMN after 6 hours, while the unstimulated PMN after 6 hours was in lane (3).

DISCUSSION

In this study, I asked the question whether T-cells-derived cytokine, IL-2, would activate PMN to involve in immune response? Previous data by **[Bahaa, (2009)]** suggested that PMN express a receptor for IL-2. We know could confirm these data and provide evidence that PMN express constitutively IL-2R. As shown for monocytes and NK cells only the IL-2Rβ chain is expressed, but not IL-Rα **[Sharon *et al.*, (1988); Espinoza-Delgado *et al.*, (1990)]**. The density of IL-2Rβ expression varied among different donors; in all, however, intracellular protein was found.

IL-2 has been known primarily for its critical role in activation and clonal expansion of lymphocytes and NK cells **[Smith, (1984); Waldmann, (1989)]**. In this study, the effects of IL-2 on PMN was analyzed. **[Julie *et al.*, (1993)]** had described that IL-2 increased the antimicrobial activity of PMN. Confirming finding by **[Wagner *et al.* (2003) and Fujimoto *et al.* (2002)]**, we demonstrated that normal human PMN stimulated with IL-2 expressed CD83, and increased the expression of CD14 and CD64. For CD83 we could demonstrate *de novo* protein synthesis in response to IL-2.

Constitutive expression of CD83 is limited to dendritic cells and thymic epithelial cells; its expression on monocytes can be induced by cultivating these cells in cytokines. **[Zhou *et al.*, (1992); Zhou and Tedder (1996); Pickl *et al.*, (1996); Palucka *et al.*, (1998); Fujimoto *et al.*, (2002)]**. CD83, however, can also be induced on PMN precursor cells **[Oehler *et al.*, (1998)]** and even in mature PMN can acquire CD83 in response to INF-γ, TNF-α **[Iking-Konert *et al.*, (2001); Yamashiro *et al.*, (2000)]**, and as we showed now, to IL-2.

While CD83 expression is entirely dependent on protein *de novo* synthesis, PMN contain a pool of preformed CD14, which can be released upon degranulation. There is, however, evidence also for *de novo* synthesis of CD14, indicating that expression of CD14 is regulated by different means, and also by various cytokines **[Wagner *et al.*, (2003); Eberhard *et al.*, (2001); Rodeberg *et al.*, (1997); Detmers *et al.*, (1995)]**. As CD14 also CD64 is regulated by various means, but particularly INF-γ **[Perussia, *et al.*, (1983)]** but not by G-CSF **[Erbe *et al.*, (1990)]**, although a synergistic effect of the two cytokines was noted **[Gurye *et al.*, (1990)]**. Our data imply *de novo* synthesis in response to IL-2.

The functional consequences of the receptor modulation of PMN are still a matter of speculation. So far, CD14 and CD64 have been associated with recognition and elimination of bacteria.

PMN stimulated with IL-2 also acquired CD83. Its expression is limited to antigen presenting cells and therefore further supports our notion of a transdifferentiation of PMN to cells with characteristics of dendritic cells **[Iking-Konert, *et al.*,(2001)]**.

In conclusion, Detection of IL-2Rβ chain on PMN prompted us to use IL-2 as a stimulator. CD14 and CD64 detection on PMN increase the PMN phagocytosis activity, where CD14 and CD64 act as LPS receptors and Fcγ receptor, respectivly. Expression

of CD83 on PMN provide further evidence for a crosstalk between PMN and T-cell, where CD83 is specific for the main APCs or dendretic cells.

REFERENCES

Brach M.A., deVos S., Gruss H.J., F. Hermann. (1992): **Prolongation of survival of human polymorphonuclear neutrophils by granulocyte-macrophage colony stimulating factor is caused by inhibition of programmed cell death.** *Blood* 80:2920-2924.

Colotta F., Re F., Polentarutti N., Sozanni S., Mantovani A. (1992): **Modulation of granulocyte survival and programmed cell death by cytokines and bacterial products.** *Blood* **80:2012-2020.**

Detmers P.A., Zhou D., Powell D., Lichtenstein H., Pironkova R. (1995): **Endotoxins receptors (CD14) are found with CD16 (FcγRIII) in an intracellular compartment of neutrophils that contains alkaline phosphatase.** *Journal of Immunology* 155: 2085-2095.

Djeu J.Y., Liu J.H., Wei S., Rui H., Pearson C.A., Leonard W. J., Blanchard D.K. (1993): **Function associated with IL-2 receptor β on human neutrophils: mechanism of activation of antifungal activity against *Candida albicans* by IL-2.** *Journal Immunology.* 150:960-970.

Eberhard B., Guenther F., Elisabeth M.S, Jochen W., Michael G., Manfred W. (2001): **Differences in the expression of CD64 and mCD14 on polymorphonuclear cells and on monocytes in patients with septic shock.** *Cytokine.* 14: 299-302.

Erbe D.V., Collins J.E., Shen L., Graziano R.F., Fanger M.W. (1990): **The effect of cytokines on the expression and function of Fc receptors for IgG on human myeloid cells.** Molecular Immunology 27: 57-67.

Espinoza-Delgado I., Ortaldo J.R., Winkler-Pickett R., Sugamura K., Varesio L., Longo D.L. (1990): **Expression and role of p75 interleukin-2 receptor on human monocytes.** *The Journal of Experimental Medicine.* 171: 1821 1826.

Fujimoto Y., Tu L., Miller A.S., Bock C., Fujimoto M., Doyle C, Steeber D.A., Tedder T.F. (2002): **CD83 expression influences CD4 (+) T-cell development in the thymus.** *Cell.* 108: 755-767.

Gasmi L., McLennan A.G., Edwards S.W. (1996): **The diadenosine polyphosphates Ap3A and Ap4A and adenosine triphosphate interact with granulocyte-macrophage colony-stimulating factor to delay neutrophil apoptosis: implications for neutrophil-platelet interactions during inflammation.** *Blood* 87:3442–3449.

Gericke G.H., Ericson S.G., Pan L., Mills L.E., Guyre P.M., Ely P. (1995): **Mature polymorphonuclear leukocytes express high-affinity receptors for IgG (Fc gamma RI) after stimulation with granulocyte colony-stimulating factor (G-CSF).** *Journal of Leukocyte Biology* 57: 455-461.

Gosselin E.J., Wardwell K., Rigby W.F., Guyre P.M. (1993): **Induction of MHC class II on human polymorphonuclear neutrophils by granulocyte/ macrophage colony-stimulating factor, IFN-gamma, and IL-3.** *Journal of Immunology* 151:1482-1490.

Gurye P.M., Campbell A.S., Kniffin W.D., Fanger M.W. (1990): **Monocytes and polymorphonuclear neutrophils of patients with streptococcal pharyngitis express increased numbers of type I IgG Fc receptors.** *Journal of Clinical Investigation.* 86: 1892-1896.

Iking-Konert C., Csekö C., Wagner C., Stegmaier S., Andrassy K., Hänsch G.M. (2001): **Transdifferentiation of polymorphonuclear neutrophils: acquisition of CD83 and other functional characteristics of dendritic cells.** *Journal of Molecular Medicine.* 79: 464-474.

Julie Y.D., Jin H.L., Sheng W., Hallgeir R., Carolyn A.P., Warren J.L. and Blanchard D.K. (1993): **Function Associated with IL-2 Receptors-β on Human Neutrophils.** *Journal of Immunology.* 150: 960-970.

Lee A., Whyte M.K.B., Haslett C. (1993): **Inhibition of apoptosis and prolongation of neutrophil functional longevity by inflammatory mediators.** *Journal of Leukocyte Biology.* 54:283-289.

Lloyd A.R., Oppenheim J.J. (1992): **Poly's lament: The neglected role of the polymorphonuclear neutrophil in the afferent limb of the immune response.** Immunology Today. 13: 169-172.

Moulding D.A., Quayle J.A., Hart C.A., Edwards S.W. (1998): **Mcl-I expression in human neutrophils: regulation by cytokines and correlation with cell survival.** *Blood* 92:2495-2502.

Oehler L., Majdic O., Pickl W.F., Stöckl J., Riedl E., Drach J., Rappersberger K., Geissler K., Knapp W. (1998): **Neutrophil granulocyte-committed cells can be driven to acquire dendritic cell characteristics.** *The Journal of Experimental Medicine.* 187: 1019-1028.

Palucka K.A., Taquet N., Sanchez-Chapuis F., Gluckman C. (1998): **Dendritic cells as the terminal stage of monocyte differentiation.** *Journal of Immunology.* 160: 4587-4595.

Pericle F., Liu J.H., Diaz J.I., Blanchard D.K, Wei S., Forni G., Djeu J.Y.. (1994): **Interleukin-2 prevention of apoptosis in human neutrophils.** *European Journal of Immunology.* 24:440-444.

Perussia B., Dayton E.T., Lazarus R., Fanning V., Trinchieri G. (1983): **Immune interferon induces the receptor for monomeric IgGI on human monocytic and myeloid cells.** *The Journal of Experimental Medicine.* 158: 1092-1113.

Petroni K.C., Shen L., Guyre P.M. (1988): **Modulation of human polymorphonuclear leukocyte IgG Fc receptors and Fc receptor-mediated functions by IFN-γ and glucocorticoids.** *Journal of Immunology.* 140:3467-3472.

Pickl W.F., Majdic O., Kohl P., Stockl J., Riedl E., Scheinecker C., Bello-Fernandez C., Knapp W. (1996): **Molecular and functional characteristics of dendritic cells generated from highly purified CD14 peripheral blood monocytes.** *Journal of Immunology.* 157: 3850-3859.

Rodeberg D.A., Morris R.E., Babcock G.F. (1997): **Azurophilic granules of human neutrophils contain CD14.** *Infectious Immunology.* 65: 4747-4753.

Sharon M., Siegal J.P., Tosato G., Yodoi J., Gerrard T.L., Leonard W.J. (1988): **The human interleukin-2 receptor beta chain (p70). Direct identification, partial purification, and patterns of expression on peripheral blood mononuclear cells.** *The Journal of Experimental Medicine.* 167: 1265-1270.

Shen L., Guyre P.M., Fanger M.W. (1987): **Polymorphonuclear leukocyte function triggered through the high affinity Fc receptor for monomeric IgG.** *Journal of Immunology.* 139: 534-538.

Shigeo Y., Ji-Ming W., De Y., Wang-Hua G., Hidenobu K., Teizo Y. (2000): **Expression of CCR6 and CD83 by cytokine-activated human neutrophils.** *Blood* 96: 3958-3963.

Smith K.A. (1984): **Interleukin-2.** *Annual Review of Immunology.* 2: 319-333.

Steinbeck M.J., Roth J.A. (1989): **Neutrophil activation by recombinant cytokines.** *Review of Infectious Disease.* II: 549-568.

Stringer RE, Hart C.A., Edwards S.W. (1996): **Sodium butyrate delays neutrophil apoptosis: role of protein biosynthesis in neutrophil survival.** *British Journal of Hematology.* 92:169-175.

Wagner C., Deppische R., Denefleh B., Hug F., Andrassy K., Hänsch G.M. (2003): **Expression patterns of the lipopolysaccharide receptors CD14, and the FCγ receptors CD16 and CD64 on polymorphonuclear neutrophils: data from patients with severe bacterial infections and lipopolysaccharide - expressed cells.** *Shock.* 19: 5-12.

Waldmann T.A. (1989): **The multi-subunit interleukin-2 receptor.** *Annual Review of Biochemistry.* 58: 875-905.

Zhou L.J., Tedder T.F. (1996): **CD14 blood monocytes can differentiate into functionally mature CD83 dendritic cells.** *Proc Natl Acad Sci USA.*93: 2588-2592.

Zhou L.J., Schwarting R., Smith H.M., Teddler T.F. (1992): **A novel cell surface molecule expressed by human interdigitating reticulum cells, Langerhans cells and activated lymphocytes is a new member of the Ig superfamily.** *Journal of Immunology.* 149: 735-742.

الملخص العربى

تأثير انترلوكين-٢ على بعض وظائف الخلايا المتعادلة عديدة الأنوية

د. بهاء قناوى أبو الحسن عبد السلام- جيرالترود ماريا هاينش
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توصف الخلايا المتعادلة عديدة الأنوية أساسا كخلايا التهامية قصيرة الحياه و تتميز فى النهاية و تساهم فقط فى الإستجابة المناعية. و الإتجاهات الحديثة لهذه الخلايا هى إنتاج السيتوكين و التعبير عن عديد من بروتينات خلايا السطح ، و يمكن الاقتراح بأن الخلايا المتعادلة عديدة الأنوية تؤثر فى الاستجابة الملائمة و تلى بفكرة تولجد الإنتيجينات الممثلة للخلية ، يوجد ثلاثة أنواع من انترلـوكين-٢ (α- β - γ) اكتـشف منها ألفا و جاما فقط و هى تؤثر فى إثارة الخلايا المتعادلة عديدة الأنوية.

فى هذه الدراسة اكتشفت سلسلة انترلوكين-β على الخلايا المتعادلة عديدة الأنوية بإستخدام جهـاز المقياس الخلوى المتدفق (flow cytometry) . مما جعلنا تعرف مشاركة انترلوكين-٢ فى بعض الخـواص البيولوجية للخلايا المتعادلة عديدة الأنوية . سبق أن أوضحنا أن الخلايا المتعادلة عديدة الأنوية فـى الإنـسان تحتوى على مخزون سيتوبلازمى للجزيئات و هذه تنقل لسطح الخلية بإشارات مختلفة. فـى هـذه الدراسـة نوضح دور انترلوكين-٢ فى تنشيط الخلايا المتعادلة عديدة الأنوية خارج جسم الكـائن الحـى مـا يكـسبها جزيئات خاصة مطلوبة لخلايا T - المؤثرة (CD83) - مستقبلات LPS (CD14) و الجلوبيولين المنـاعى G المستقبل Fc (CD64) على السطح و على مستوى الجين الموصف العكسى لتفاعل البلمرة.