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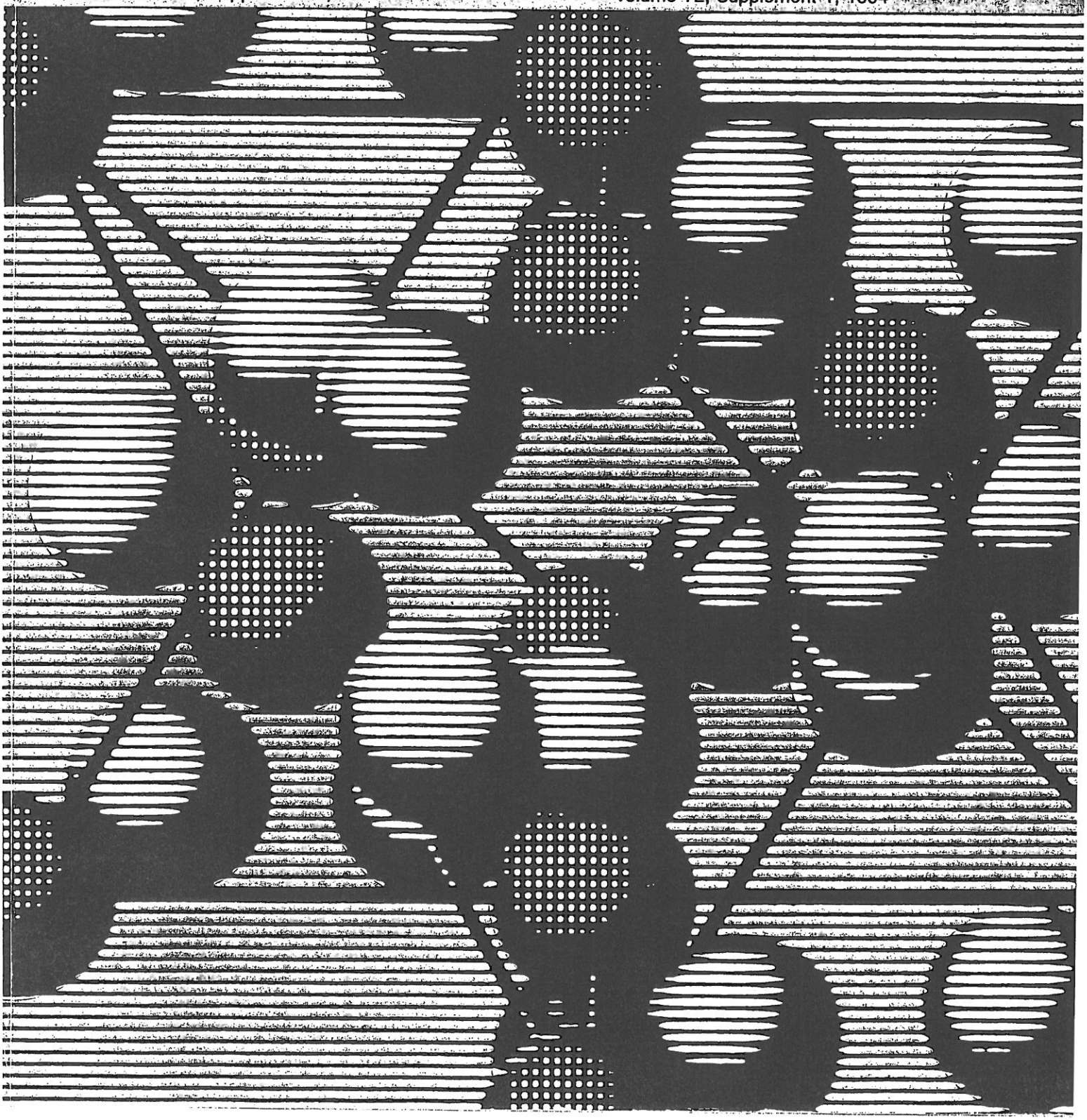

MONTRÉAL

IUPHAR 1994

XIIth International Congress of Pharmacology
XIIe Congrès international de pharmacologie

July / juillet 24 – 29, 1994, Montréal, Québec, Canada

April 5, 1994

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Dear Colleague:

We are pleased to inform you that your abstract has been accepted for a poster presentation at the XIIth International Congress of Pharmacology to be held on July 24-29, 1994 in Montréal, Québec.

Your abstract has been assigned to the poster session as follows:

Title:	EFFECT OF BIO-NORMALIZER ON MACROPHAGE CHEMOTAXIS IN NATURALLY OCCURRING GINGIVITIS RAT, M. Shinohara[1], Y. Morikawa[1], K. Ogata[1], A.J. Osato[2], K. Ohura[1], [1]Osaka Dental University, Osaka and [2]Osato Research Institute, Gifu, Japan
Abstract No:	P10.5.003
Date of presentation:	WEDNESDAY, July 27, 1994

Your poster board number will appear in the Final Program which you will receive at the registration desk.

The poster sessions will take place in the Exhibit Hall of the Palais des Congrès between 12:00 and 14:00 hours and the provided poster boards are approximately 1 m high and 1.5 m wide (please see preliminary program for details).

P10.5.1

GENERATION OF LEUKOTRIENE C4 [illegible]AMINE RELEASE WITH PHOSPHATIDIC ACID VIA CALCIUM INFLUX IN MASTOCYTOMA CELL LINE.

Y. Moriya and H. Teshigawara. Department of pharmacology, Nihon University School of Dentistry at Matsudo, Matsudo,Chiba, Japan.

Mechanisms of phosphatidic acid (PA)-induced histamine release from mastocytoma P-815 cells were studied. Extracellular PA(1-100 μ M) induced histamine release and LTC4 accumulation inside cells in dose dependent manner, but other phospholipids were not released histamine or released only slightly. LTC4 accumulation was not significantly increased with addition of other phospholipids. When intracellular leukotriene C4 (LTC4) increased with addition of extracellular LTC4, the release of histamine was observed. LTC4-induced histamine release was inhibited with removal of extracellular Ca^{2+}. Treatment with 5 μ M p-bromophenacyl bromide as a PLA2 inhibitor significantly suppressed the increase of intracellular LTC4 and PA-induced histamine release in dose dependent manner, even in the presence of PA. PA-induced histamine release and LTC4 accumulation were inhibited with inorganic and organic Ca^{2+} channel blockers. Removal of extracellular Ca^{2+} also suppressed both LTC4 accumulation and histamine release. When cells were incubated with high K^+ solution(50mM), LTC4 accumulation and histamine release were induced.
Our results indicated that intracellular LTC4 was increased with PA via PLA2 activation induced by Ca^{2+} influx and histamine release was elicited . Furthermore, Ca^{2+} channels on mastocytoma cells were regulated with PA. Ca^{2+} influx was required for the increase of intracellular LTC4 and LTC4-induced histamine release, respectively. There may be at least two pathways for PA-induced histamine release; it is known that PA provokes histamine release via diacylglycerol as a PA metabolite and a second messenger, another pathway is that PA elicits histamine release via the increase of intracellular LTC4.

P10.5.2

EFFECT OF LPS AND INDOMETHACIN ON SHORT TERM FEVER RESPONSE AND HYPOTHALAMIC PGE_2 PRODUCTION IN MICE

L. Abramovich, V. Fraifeld, D. Shemi and J. Kaplanski. Department of Clinical Pharmacology, Ben Gurion University of the Negev, Beer Sheva, Israel.

Bacterial endotoxin (lipopolysaccharide, LPS) is a pyrogen that causes fever in a variety of animals. In our previous study we have demonstrated that in mice rectal temperature (RT) significantly decreased ($p<0.01$) during 6 hr after LPS injection, then followed recovery of RT to the control level up to 24 hr. In spite of the lack of hyperthermic phase, ex-vivo HT PGE_2 production, measured 24 hr after LPS injection, was two-fold greater as compared with controls. The present investigation was undertaken to correlate the effect of LPS and INDO on RT and HT PGE_2 production in the hypothermic phase. Adult male mice in control room (22±1 °C) were injected with LPS (E. coli, 50 µg/mice), saline and INDO (50 mg/kg) immediatly after LPS. Significant decrease ($p < 0.01$) in RT was found after LPS injection (3 hr, -1.5 °C), without changes in HT PGE_2 production. Effect of INDO+LPS on RT did not differ from that of LPS. However, in contrast to LPS, INDO significantly ($p<0.01$) decreased HT PGE_2 production in LPS-treated mice (control 91± 3.8, LPS 94±6.0, INDO+LPS 34±2.7 pg/mg tissue/hr). Our data indicate, that no correllation occurs between HT PGE_2 production and changes in RT during initial hypothalamic phase. In conclusion, it seems that changes in RT of LPS-treated mice in the initial phase are not PGE_2-dependent.

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P10.5.3

EFFECT OF BIO-NORMALIZER ON MACROPHAGE CHEMOTAXIS IN NATURALLY OCCURRING GINGIVITIS RAT.

M. Shinohara, Y. Morikawa, K. Ogata, A.J. Osato* and K. Ohura.
Department of Pharmacology, Osaka Dental University, Osaka 540, *Osato Research Institute, Gifu 500, Japan.

Bio-catalyzer (Bio-normalizer: BN, Sun-O International Inc., Japan) is a white, sweet, multiple plant enzyme granules produced by fermentation of Carica papaya and tropical herbal plants with fermentative cereals from tropical and Japanese traditional food. BN is a free radical scavenger, which inhibits bacterial growth, and the action of toxohormone-L. In this study, we examined its effect on chemotaxis of macrophages (MΦs) in naturally occurring gingivitis rat (ODUS/Odu). ODUS/Odu were given 2% BN for 2 months. Rat MΦs were collected 4 days after intraperitoneal injection of 1% oyster glycogen solution in saline. MΦ chemotaxis was measured by the membrane filter method using 48-well microchemotaxis chambers, using zymosan-activated serum as the chemoattractant. MΦ chemotaxis was significantly lower in the BN-treated group than in the control group. This suggests that BN plays an immunological role in host defence.

P10.5.4

EFFECT OF STREPTOZOTOCIN-INDUCED DIABETES ON LEUKOCYTE FUNCTIONS IN RATS WITH NATURALLY OCCURRING GINGIVITIS.

K. Ohura, K. Ogata and M. Shinohara. Department of Pharmacology, Osaka Dental University, Osaka 540 Japan.

Many studies have shown that periodontal lesions in diabetic patients progress rapidly and resist treatment. To elucidate the effect of diabetes on periodontal lesions, chemotaxis, phagocytosis and superoxide anion (O_2^-) production of leukocytes were studied in rats with naturally occurring gingivitis (ODUS/Odu) treated with streptozotocin to induce diabetes. Rat macrophages (MΦs) were obtained 72 hours after intraperitoneal injection of mineral oil. MΦ chemotaxis was measured by the membrane filter method. Phagocytosis was measured using opsonized zymosan and fetal bovine serum. O_2^- production was measured by the reduction of cytochrome c. . Three functions of MΦs from diabetic ODUS/Odu were significantly less than those of MΦs from non-diabetic ODUS/Odu, diabetic or non-diabetic control rats. These suggest that diabetes strongly affects the leukocyte function of MΦ, thereby weakening the host defense mechanism, and leading to production of severe periodontal lesions. (Supported by a Grant-in-Aid for Scientific Research No.04671147)

P10.5.5

EFFECT OF LPS ON BODY TEMPERATURE AND HYPOTHALAMIC PGE_2 PRODUCTION IN YOUNG AND OLD RATS

J. Kaplanski, V. Fraifeld and L. Abramovich. Department of Clinical Pharmacology, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

Pyrogen-induced elevation of hypothalamic (HT) PGE_2 production is considered to play a major role in changing the thermoregulatory "set point" to a new level, that is the characteristic feature of fever. Aging is associated with attenuated febrile response. It was the aim of the present study to compare the effects of bacterial endotoxin (E. coli LPS, 50 µg per animal, i. p.) on rectal temperature (RT) and ex-vivo HT PGE_2 production in young adult (4- 6-mo-old) and old (24-mo-old) female Wistar rats. Animals were kept at 22±1 °C, 12L:12D, water and food ad libitum. RT was measured before and at different post-injection time periods. 24 h later, hypothalamus was excised and incubated in Krebs buffer solution for 3 h. The incubation medium was replaced each hour for PGE_2 assay by RIA. As compared with young adults, LPS-treated old rats displayed delayed febrile response, however no age-related differences in maximum RT amplitude were found (+RT, 6 h, 0.8 and 0, $p<0.05$; 24 h, 0.7 and 0.6 °C, young adults and olds, respectively). Both in young adult and old rats, LPS induced about two-fold elevation in HT PGE_2 production, as compared with control rats ($p< 0.05$). Regardless of the lack of age-related differences in RT and HT PGE_2 production, measured 24 h post LPS injection, in young adult rats, in contrast with olds, correlation between RT changes and HT PGE_2 production was observed ($p<0.05$). The data obtained point toward probable disregulation between central and peripheral thermoregulatory mechanisms of fever in aging.

P10.5.6

THE POSSIBLE CONTRIBUTION OF NEUTROPHILS, BUT NOT T LYMPHOCYTES, TO MDP-LYS(L18)-INDUCED ARTHRITIS IN RATS.

T. SUGAWARA, S. TAKADA, M. MIYAMOTO and M. KATO.
Drug Safety Research Center, Developmental Research Laboratories, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan.

When MDP-Lys(L18), an analogue of muramyl dipeptide, was subcutaneously administered to rats, swelling of the tarsal joints was seen from 1 week later. We speculate that MDP-Lys(L18)-induced arthritis (MIA) is different from Freund's complete adjuvant-induced arthritis (AIA). In the present study, we investigated the contribution of T lymphocytes to the development of MIA and AIA. AIA was not induced in athymic nude rats, and spleen cells obtained from Lewis rats with AIA transferred the arthritis to normal recipients. In contrast, MIA was induced in nude rats and was not transferred by spleen cells. We also examined the contribution of neutrophils to MIA because neutrophil infiltration was the earliest change observed in synovial membrane. MDP-Lys(L18) stimulated the production of neutrophil chemotactic factor(s) by rats peritoneal macrophages *in vitro*, but did not by those of mouse which never showed MIA. These data suggest that neutrophils recruited by chemoattractants released from MDP-Lys(L18)-activated macrophages may have an important role in MIA.

EFFECT OF BIO-NORMALIZER ON MACROPHAGE CHEMOTAXIS IN NATURALLY OCCURING GINGIVITIS RAT

M. Shinohara, Y. Morikawa, K. Ogata, J. A. Osato[1] and K. Ohura

Osaka Dental University, Osaka, Japan and [1]Osato Research Institute, Gifu, Japan

(Poster paper presented at the 12th International Congress of Pharmacology, 24 ~ 29 July 1994, Montreal,Canada)

This study examined the effect of two- month administration of Bio-normalizer (BN) on the chemotaxis of macrophages in naturally occuring gingivitis rat (ODUS/Odu) injected with 1% oyster glycogen solution. BN significantly decreased the macrophage chemotaxis as compared to the control group of rats suggesting that BN may play an immunological role in host defense.

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XII^{e} Congrès international de pharmacologie

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XII[th] International Congress of Pharmacology

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P10.4.34 (369) SYNERGISTIC EFFECT OF VASOACTIVE AMINES ACCOUNTS FOR ANTIGEN-INDUCED PLEURAL LEAKAGE IN ACTIVELY IMMUNIZED RATS, **M.C.R. Lima**, M.S.S. Chagas, P.M.R. e Silva, H.C. Castro-Faria-Neto, R.S.B. Cordeiro, M.A. Martins, *Oswaldo Cruz Institute, Rio de Janeiro, Brazil*

P10.4.35 (370) DIFFERENTIAL CELLULAR ACCUMULATION TRIGGERED BY PAF IN THE PERITONEAL CAVITY OF SENSITISED MICE, **C. Zuany-Amorim**[1], D.C. Deslandes[1], A.P. Hofer[1], R.S.B. Cordeiro[1], M. Pretolani[1], B.B. Vargaftig[2], [1]*IOC/FIOCRUZ, Rio de Janiero, Brazil;* [2]*Institut Pasteur, Paris, France*

P10.4.36 (371) COMPARISON OF NON-PEPTIDE NK-1 RECEPTOR ANTAGONISTS AND CALCIUM CHANNEL ANTAGONISTS ON THE INHIBITION OF THE PLASMA EXTRAVASATION INDUCED BY THERMAL INJURY IN RATS, **G.M. Pitcher**, J.L. Henry, T.J. Coderre, *Clinical Research Institute of Montréal and McGill University, Montréal, QC, Canada*

P10.4.37 (372) CONTROL OF RAT MAST CELL ACTIVITY THROUGH HISTAMINE H_3-RECEPTOR, **V. Dimitriadou**[1], M. Garbarg[2], A. Rouleau[2], M. Dam Trung Tuong[2], G. Newlands[3], J.-C. Schwartz[1], [1]*Université de Paris V, Paris and* [2]*INSERM U-109, Paris, France;* [3]*Moredun Institute, Edinburgh, UK*

P10.4.38 (373) THE ROLE OF NEUROPEPTIDES IN THE PATHOGENESIS OF CUMULATIVE TRAUMA DISORDERS, **R. Kijowski**, D. Hoppensteadt, M. Chinthagada, G. Chejfec, J. Fareed, S. Blair, *Loyola University, Maywood, IL, USA*

P10.4.39 (374) GASTRODUODENAL MUCOSA PAF LEVELS BEFORE AND AFTER TREATMENT OF HELICOBACTER PYLORI INFECTION, **V.D. Pasechnikov**, N.V. Zhurbina, I.V. Kuznetsova, *Stavropol Medical Institute, Stavropol, Russia*

Inflammation: Other — P10.5 — Autres inflammation

P10.5.1 (375) GENERATION OF LEUKOTRIENE C4 AND HISTAMINE RELEASE WITH PHOSPHATIDIC ACID VIA CALCIUM INFLUX IN MASTOCYTOMA CELL LINE, **Y. Moriya**, H. Teshigawara, *Nihon University School of Dentistry at Matsudo, Chiba, Japan*

P10.5.2 (376) EFFECTS OF LPS AND INDOMETHACIN ON SHORT TERM FEVER RESPONSE AND HYPOTHALAMIC PGE_2 PRODUCTION IN MICE, **L. Abramovich**, V. Fraifeld, D. Shemi, J. Kaplanski, *Ben Gurion University of the Negev, Beer Sheva, Israel*

P10.5.3 (377) EFFECT OF BIO-NORMALIZER ON MACROPHAGE CHEMOTAXIS IN NATURALLY OCCURRING GINGIVITIS RAT, **M. Shinohara**[1], Y. Morikawa[1], K. Ogata[1], A.J. Osato[2], K. Ohura[1], [1]*Osaka Dental University, Osaka and* [2]*Osato Research Institute, Gifu, Japan*