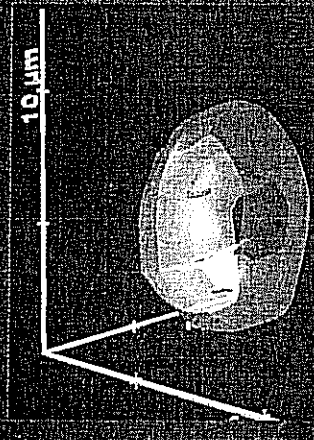
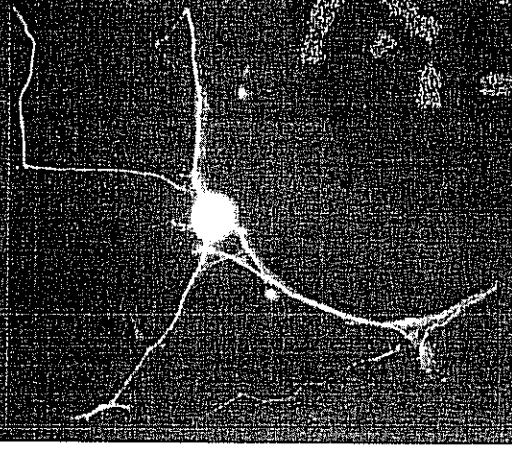
CELLULAR AND MOLECULAR BIOLOGY

3rd World-Congress on Cellular and Molecular Biology, 8-13 Oct 2000, Jena, Germany

An interdisciplinary conference on modern advances in microscopy and its applications in Biology, Biotechnology and Medicine hosted by the Society for Cellular and Molecular Biology





Local Organizers
K.-J. Halbhuber
G.F. Jirikowski
K. König

Institute for Anatomy II
Friedrich-Schiller-University
Teichgraben 7
07740 Jena
Germany
Phone +49 (0) 3641 938550
Fax +49 (0) 3641 938552
http://www.uni-jena.de/wccmb/

3rd World-Congress on Cell Mol Biology, 8-13 Oct 2000, Jena

109

REDUNDANCY OF LAMELLIPODIA IN LOCOMOTING WALKER CARCINOSARCOMA CELLS: WHAT ELSE DRIVES LOCOMOTION?

H.U. KELLER

Institute of Pathology, University of Bern, Murtenstrasse 31, CH-Bern, Switzerland
e-mail: kellerhu@patho.unibe.ch

Polarised locomoting Walker carcinosarcoma cells normally exhibit lamellipodia at the leading front. Following treatment with low concentrations (10^{-7} M) of latrunculin A, formation of lamellipodia is suppressed and the cells exhibit either no morphologically recognizable protrusions, or occasionally blebs. Cells without morphologically recognizable protrusions can migrate as fast or even faster than cells with lamellipodia. Blebbing cells as well as cells without morphologically show modifications of the actin cytoskeleton at the front, which include gap formation in the cortical actin layer. At higher concentrations of latrunculin A ($\geq 3x10^{-8}$ M), cortical contraction as manifested by uropod formation is also suppressed and this is associated with an arrest of locomotion. The modifications of the actin cytoskeleton have been related to the protrusive activity at the front, to suppression of tail contraction and to locomotor activity. First, a unifying hypothesis for the formation of different types of protrusions will be presented. Furthermore, the relative importance of actin polymerisation at the front vs cortical contraction by the actin/myosin system at the rear of the cells will be analysed. This will be discussed with respect to cortical flow and the relative role of pseudopodial motility, cell body motility and tail retraction in cell locomotion.

110

ELECTROPHYSIOLOGY AND THERMODYNAMICS OF MITOCHONDRIA

Reinhold KIEHL

Laboratory and Research for Molecular Medicine/Biology (RKI), Saliterweg 1, 93437 Furth im Wald, Germany
fax: +49 9973 801 057

The research performed during the last 20 years lead inevitably to the formulation of the mitochondrial F_OF_1-complex as coupled K^+/H_2O-pump (similar to the nAChR) with H^+/P_i-inducible ATPsynthase as well as to the respiratory chain substrate driven K^+/H^+-antiport system. These systems are linked together in anticyclic energy driven K^+/H_2O, H^+/P_i-movements and oscillations (swelling plus contraction of the mitochondrial matrix space by osmotically active K^+-ions), controlled by O_2 and the free Mg^{2+} and Ca^{2+} –concentrations in the cytosol of the cells.The systems is responsible for the thermoregulation of our body–. The cyclic hydrolysis/synthesis of ATP and the concomitantly cyclic release/binding of Mg^{2+} in the "steady state flow system" releases heat (q) and the temperature (ΔT) is permanently raised. The released heat is constantly distributed throughout the entire body by the oscillating mitochondria, as well as the pumping heart, and is used up by the normal body functions. Disturbances of this system are normally compensated for by lower/higher respiration rates. The essentially by iron and its state of oxidation dependent H^+/e^- displacements, current (i), lead to high local voltages (ΔV) over the membrane with corresponding magnetic fields (H). The entire system is dependent on oxidized and reduced glutathione.

European Journal of Cell Biology Abstracts

Supplement 49
(Vol. 78)
1999
ISSN 0171-9335

23. Annual Meeting of the

Deutsche Gesellschaft für Zellbiologie

Topics:

Cell adhesion and migration - Chemokine receptors - Prions - Phenotype conversion - Cell cycle, growth and apoptosis - Cells as Biosensors - Nuclear receptors - Transcription factors - G protein coupled receptors - Membranes - Chromosome architecture - Cytokine signaling - Environmental stress - Cells and tissues - Cytoskeleton - Intracellular trafficking and GFP

Rostock, March 14-18, 1999

EJCB

URBAN & FISCHER

246 **Interleukin signaling and metalloprotease expression in the wobbler neuropathy**

Silvia Rathke-Hartlieb, Uwe Schlomann, Harald Jockusch, Jörg W. Bartsch Developmental Biology /Molecular Pathology, University of Bielefeld, D-33615 Bielefeld, Tel.: +49 521-1065630; FAX: -1065654; joerg.bartsch@biologie.uni-bielefeld.de

The mouse mutant wobbler (WR) serves as an animal model for human spinal muscular atrophies. WR mice show neurodegeneration in brain stem and spinal cord from 14 p.n. onward. In reponse, reactive astrocytes and microglia activation can be observed throughout spinal cord and brain stem cross sections. The glial cell activation is not correlated with proliferation. Using RT-PCR and immunohistochemistry, we looked for cytokine levels in control and WR mice. Expression of transforming growth factor ß (TGF-ß), a presumed inhibitor of astrogliosis, was not elevated, thus permitting massive hypertrophy of astrocytes in brain stem and spinal cord. Furthermore, mRNA levels of interleukins IL-6 and IL-10 were not changed in WR mice, but tumor necrosis factor α (TNF-α) expression was elevated, both on the mRNA and protein levels. TNF-α was localized in reactive astrocytes, in oligodendrocytes and in distinct neurons. Activated microglia were grouped around degenerating neurons, forming a network structure. We adressed the question how microglia can remodel the extracellular matrix by studying the expression levels of membrane-typed metalloproteases, using RT-PCR homology screening for the zinc binding domain of metalloproteases and for the disintegrin binding domain of ADAM (A Disintegrin and Metalloprotease Domain) proteases. Whereas the expression levels of several ADAM proteases were not affected, ADAM 8 (CD 156) mRNA was elevated in WR mice and localized to activated microglia. This suggests that ADAM 8 plays a role in CNS diseases in which microglia activation occurs.

This work was supported by DFG, SFB 549/TP A4.

247 **CNS / Psyche - Blood / Immune system / Cells - Acupuncture / Drugs - Electrophysiology and Thermodynamics: The redox potential / electron transfer is responsible for stress protein or O_2^- - synthesis / transport and proliferation**

Reinhold Kiehl, Laboratory and Research for Molecular Medicine/Biology, Saliterweg 1, D-93437 Furth i. Wald,Germany, Fax: 0049-9973-801057.

The plasma membrane NADPH oxidase is a rather complicated electron transfer system, which resembles probably the most important crossover-, end- and starting point of various signal transduction pathways: Ca^{2+}/Mg^{2+}-sensitive phosphorylation and dephosphorylation (incl. JAK-STAT-g-protein-pathway) of the complex regulates the electron transfer (incl. thiol / disulfid-interchange-FeS-protein) between mitochondria / plasma and nucleus / ER (NADH / ATP-NADPH / K^+-O_2 / O_2^- - DNA / IgE). Another control is played for instance by arachidonic acid (delivered by PLA_2): The NADPH oxidase belongs then to enzyme systems like insulinR, nAcChR, adenylate cyclase, mitochondrial K^+ ATPase / ATP-synthase presenting a universal principle of nature: The connecting logistics between CNS (adrenal cortex) and blood / immune system / cells is played by electron transfer or redox potential and may be visualized by the successful treatment of various diseases and psychological disorders with acupuncture / homeopathy / relaxation therapy or drugs. We try to connect natural sciences in order to get involved into this logistic for prediction of effective new treatments, which includes the modeling of interfering drugs for instance. Literature: Kiehl R (1976) Dissertation, MPI for Med. Res. Heidelberg; Kiehl R and Hanstein WG (1984) 3. EBEC, 323; Kiehl R et al. (1987) BBRC 147, 1251; Kiehl R (1993) Dear Colleague, New in dermatology 2(2), 4; Kiehl R (1994) Int. Alk-Ciba Corning Joint Symp, Benzheim; Kiehl R (1995/1996) Habilthesis LMU Munich Med. Fak.; Kiehl R (1997) Bioforum 12, 686; Amino Acids 13, 50; Kiehl R (1998) Proc., 17th Int. Symp., Electrolyte / Blood Gas, Intercontinental Working Group on the Confluence of Crit. Care Analysis and Near Patient Testing, Nice; Biotechnology Int., Universal Med Press Inc; 2nd Joint Meeting, Signal Transduction: Receptors, Mediators and Genes, Langen.

2nd INTERNATIONAL SYMPOSIUM ON MINIMAL RESIDUAL CANCER

Detection, Significance and Clinical Implications

September 19th - 22nd, 1998
Universitäts Klinikum
Charité, Campus Virchow
Berlin, Germany

Poster Abstracts

Organisation Committee

Klaus Pantel · Gert Riethmüller
University of Munich, Institute of Immunology
Goethestr. 31 · 80336 Munich, Germany

Hans Joachim Gath · Jürgen Bier
University Hospital Virchow, Department of. Oral-Maxillo-Facial Surgery
Augustenburger Platz 1 · 13353 Berlin, Germany

LINEAGE-ASSOCIATED ANTIGENS AS MARKERS FOR IMMUNOCYTOCHEMICAL DETECTION OF MELANOMA CELLS IN BLOOD: EXPERIMENTAL MODEL.

M. Valladares, M.T. Yebra [1], E. Rendal[2], G. Alonso, L Calvo, S. Antolín. L. Antón [3], C. Andión [2]. Medical Oncology Unit. [1] Pathology Dept. [2] Criobiology Unit. "Juan Canalejo" Hospital. La Coruña. [3] Medicine Dept. University of La Coruña. Spain.

Introduction and objetive: Melanomas are tumours that express differents lineage specific proteins. Several monoclonal antibodies (mAbs) have been described with high specificity for detecting these melanoma-associated antigens (MAA). We have used an immunocytochemical assay using mAbs against MAA in order to detect occult melanoma cells in blood in a model system.

Material and Methods: mAbs HMB-45 against gp100and Melan-A (clon A103) were used. Human tumour cell lines A375 and FEM (melanoma) and H146 (small-cell lung cancer) were used to asses the sensitivity and especificity of immunocytochemical procedure. The antigen-mAb reaction was developed with the avidin biotin complex-alkaline phosphatase system. Smears and cytospins of fine-neddle aspirations of metastatic lesions from melanoma patients (pt)were stained by the same method. Modelsystem based on dilution of cells from melanoma cell line into peripheral blood (PB) and bone marrow (BM) mononuclear cells (MNC) from healthy donors and lymphoma pt were performed. Cell suspension was placed on poly-L-lysine coated slides, stained and visualized at optical microscopy.

Results: Diffuse cytoplasmic staining with HMB-45 and A103 mAbs in FEM cells were homogeneously present. A375 cell line shown heterogeneous expression for Melan-A by A103 mAb. It was negative for HMB-45 reactivity. No staining were present for these MAA in H146cells, PB- and BM- MNC. Expression of MAA in smears and cytospins of fine-neddle aspirations of metastatic lesions from melanoma ptwere heterogeneous. Preliminary dilution experiments with FEM cells into PB and BM-MNC detect efficiently tumour cells with 22,5 % detection rate.

Conclusions: Antigenic profiles are heterogeneous in human melanomacell lines and in metastatic melanoma. This suggest that multimarker immunocytochemical assay using specific mAbs against MAA may be more efficient for detecting occult melanoma cells in blood.

P I. 11

REGULATION OF STRESS PROTEIN IGE SYNTHESIS/PROLIFERATION: gIFN, INTERLEUKINS, ROS, TOTAL IgE AND NO

R. Kiehl, Laboratory and research for Molecular Medicine/Biology, Saliterweg 1, 93437 Furth i. Wald/FRG, faxnumber: 0049/9973/801057

We could show [1] that circulating immune complexes and IgE in the blood of atopic eczema patients activates the congulation system with elevation of platelet aggregation and histamine release with further enhancement of aggregation (thrombosis). This process could be related to significantly lowered diamine oxidase activities of platelets. We now conclude that this process starts with rising IgE concentrations in the circulating blood or affected skin areas (activation of the contact system by surfactants etc; contact allergy). Platelets aggregation results presumably in a changed energy metabolism in these particles with buildup of vitamin K H_2 and H_2O_2/Reactive Oxygen Species (ROS), inhibition of diamine-oxidase by ROS (H_2O_2) with elevation of histamine, inactivation of α_2-macroglobulin and activation of metalloproteases by ROS/H_2O_2. ROS may also be produced by prolonged exposure of skin cells to UV-light and responsible for development of skin carcinomas [2]. Nitric oxid (NO) seems not to be a physiologic regulator of the cardiovascular system. However, abnormalities of the L-arginine: NO pathway could contribute to the pathophysiology of diseases like thrombosis [3]. gIFN-molecules were significantly degraded by activated leucocyte collagenase under in vivo conditions, although our in vitro assay showed no such behavior [2]. Degradation of two plasma components namely C1-inhibitor and α_1-proteinase inhibitor, by metalloprotease has already been demonstrated [4, 5]. The implication for metalloprotease regulation is evident, and the impact of the changing active gIFN- and IL-4-concentrations on the IgE-levels/atopic eczema and leukemia, HIV-infection, immune complexes/thrombosis (arteriosclerosis) [2, 6, 7] will be shown.

[1] Kiehl R and Ionescu G. Med. of Inflammations 1993: 2: 403-406. - [2] Kiehl R. Habilthesis, University Munich, Med. Fak. 1996. - [3] Allister RJ and Vallance P. JIFCC 1996: 8: 152. - [4] Knäuper V, Reinke H and Tschesche H. FEBS Letters 1990: 263: 355-357. - [5] Knäuper V, Triebel S, Reinke H and Tschesche H FEBS Letters 1991: 290: 99-102. - [6] Kiehl R. InCom '97, Düsseldorf, Abstr. p. 15 and p. 383; MEDLAB 12th IFCC, Basel, Abstr. p. 105, A54 DGKC Joint Congress with the GSLM, Münster, Abstr. p. 105, p. 112. - [7] Kiehl R. BIOforum, GIT-Verlag 1997: 12: 686-690; and IFCC, Proc. of the 17th Int. Symp. on the Confl. of Crit. Care Anal. and Near Patient Testing, Nice, June 4-7, 1998.

P I. 12

Anwendung der Durchflußzytometrie in der Klinischen Zelldiagnostik

– Abstracts –

• • • • • • • • • • • • • • •

19./20. März 1998

XII. Arbeitstagung

Institut für Klinische Chemie und
Laboratoriumsmedizin
– Zentrallaboratorium und Blutbank –
Universität Regensburg

Regulation of stress protein IgE synthesis/proliferation: gIFN, interleukins, ROS, total IgE and NO

R. Kiehl, Laboratory and research for Molecular Medicine/Biology
Saliterweg 1, 93437 Furth i. Wald/FRG, faxnumber: 0049/9973/801057

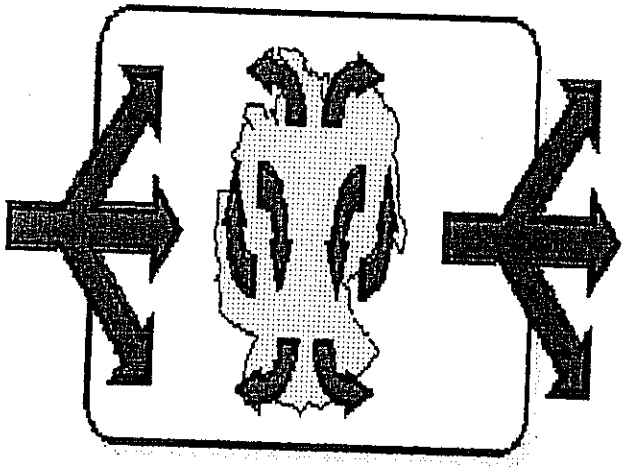
We could show [1] that circulating immune complexes and IgE in the blood of atopic eczema patients activates the coagulation system with elevation of platelet aggregation and histamine release with further enhancement of aggregation (thrombosis). This process could be related to significantly lowered diamine oxidase activities of platelets. We now conclude that this process starts with rising IgE concentrations in the circulating blood or affected skin areas (activation of the contact system by surfactants etc; contact allergy). Platelets aggregation results presumably in a changed energy metabolism in these particles with buildup of vitamin K•H_2 and H_2O_2/Reactive Oxygen Species (ROS), inhibition of diamine-oxidase by ROS (H_2O_2) with elevation of histamine, inactivation of α_2-macroglobulin and activation of metalloproteases by ROS/ H_2O_2. ROS may also be produced by prolonged exposure of skin cells to UV-light and responsible for develop-ment of skin carcinomas [2]. Nitric oxid (NO) seems not to be a physiologic regulator of the cardiovascular system. However, abnormalities of the L-arginine: NO pathway could contribute to the pathophysiology of diseases like thrombosis [3]. gIFN - molecules were significantly degraded by activated leucocyte collagenase under in vivo conditions, although our in vitro assay showed no such behavior [2]. Degradation of two plasma components namely C1-inhibitor and α_1-proteinase inhibitor, by metalloprotease has already been demonstrated [4, 5]. The implication for metalloprotease regulation is evident, and the impact of the changing active gIFN- and IL-4/concentrations on the IgE-levels/atopic eczema and leukemia, HIV-infection, immune complexes/thrombosis (arteriosclerosis) [2, 6, 7] will be discussed.

[1] Kiehl R. and Ionescu G. Med. of Inflammations 1993:2:403-406. - [2] Kiehl R. Habilthesis, University Munich, Med. Fak. 1996. - [3] Allister RJ and Vallance P. JIFCC 1996:8:152 - [4] Knäuper V, Reinke H and Tschesche H. FEBS Letters 1990:263:355-357. - [5] Knäuper V, Triebel S, Reinke H and Tschesche H. FEBS Letters 1991:290:99-102. - [6] Kiehl R. InCom '97, Düsseldorf, Abstr.p.15 and p.383; MEDLAB 12th IFCC, Basel, Abstr.p.105, A54 DGKC Joint Congress with the GSLM, Münster, Abstr.p.105, p.112. - [7] Kiehl R. BIOforum, GIT-Verlag 1997: 12:686-690 and BIOSCOPE, TH Guur-Verlag in press

1. Joint Meeting
der Signaltransduktions-Arbeitskreise der DGfI und der DGZ
sowie der Studiengruppe Gentechnik/Biotechnologie der GBM

Intracellular Signal Transduction:

Receptors, Mediators and Genes



Paul-Ehrlich-Institut, Langen
20. - 22. November 1997

organizers:

Ottmar Janssen (Langen)
Ralf Hass (Berlin)
Karlheinz Friedrich (Würzburg)

P16

STRESS PROTEIN IgE, CIRCULATING IMMUNE COMPLEXES AND THROMBOSIS

R. Kiehl
Laboratory and research for Molecular Medicine/Biology
Saliterweg 1, 93437 Furth i. Wald/FRG, faxnumber: 004999973801057

We could show [1] that circulating immune complexes and IgE in the blood of atopic eczema patients activates the coagulation system with elevation of platelet aggregation and histamine release with further enhancement of aggregation (thrombosis). This process could be related to significantly lowered diamine-oxidase activities of platelets. We now conclude that this process starts with rising IgE concentrations in the circulating blood or affected skin areas (activation of the contact system by surfactants, etc; contact allergy). Platelets aggregation results presumably in a changed energy metabolism in these particles with build-up of vitamin K•H_2 and H_2O_2 / Reactive Oxygen Species (ROS), inhibition of diamine-oxidase by ROS (H_2O_2) with elevation of histamine, inactivation of α_2-macroglobulin and activation of metalloproteases by ROS/H_2O_2. ROS may also be produced by prolonged exposure of skin cells to UV-light and responsible for development of skin carcinomas [2]. Nitric oxid (NO) seems not to be a physiologic regulator of the cardiovascular system. However, abnormalities of the L-arginine: NO pathway could contribute to the pathophysiology of diseases like thrombosis [3].- gIFN - molecules were significantly degraded by activated leucocyte collagenase under in vivo conditions, although our in vitro assay showed no such behavior [2]. Degradation of two plasma components, namely C1-inhibitor and α_1-proteinase inhibitor, by metalloprotease has already been demonstrated [4,5]. The implication for metalloprotease regulation is evident, and the impact of the changing active gIFN-concentrations on the IgE-levels, immune complexes and thrombosis (arteriosclerosis) [2,6,7] will be discussed.

[1] Kiehl R and Ionescu G. Med. of Inflammations 1993;2:403-406
[2] Kiehl R. Habilthesis, University Munich, Med. Fak. 1996
[3] Allister RJ and Vallance P.JIFCC 1996:8:152
[4] Knäuper V, Reinke H and Tschesche H. FEBS Letters 1990:263:355-357
[5] Knäuper V, Triebel S, Reinke H and Tschesche H. FEBS Letters 1991:290:99-102
[6] Kiehl R. InCom'97, Heinrich-Heine-Universität, Abstr.p.15 and p.383; 12th IFCC, Basel, August 17-22, 1997, DGKC Joint Congress with the GSLM Münster, Sept 30-Oct 2,1997
[7] Kiehl R. BIOSCOPE, TH Guur-Verlag 1997, in press and Ann.Clin.Lab. Science 1997, accepted

JOINT CONGRESS

DGKC

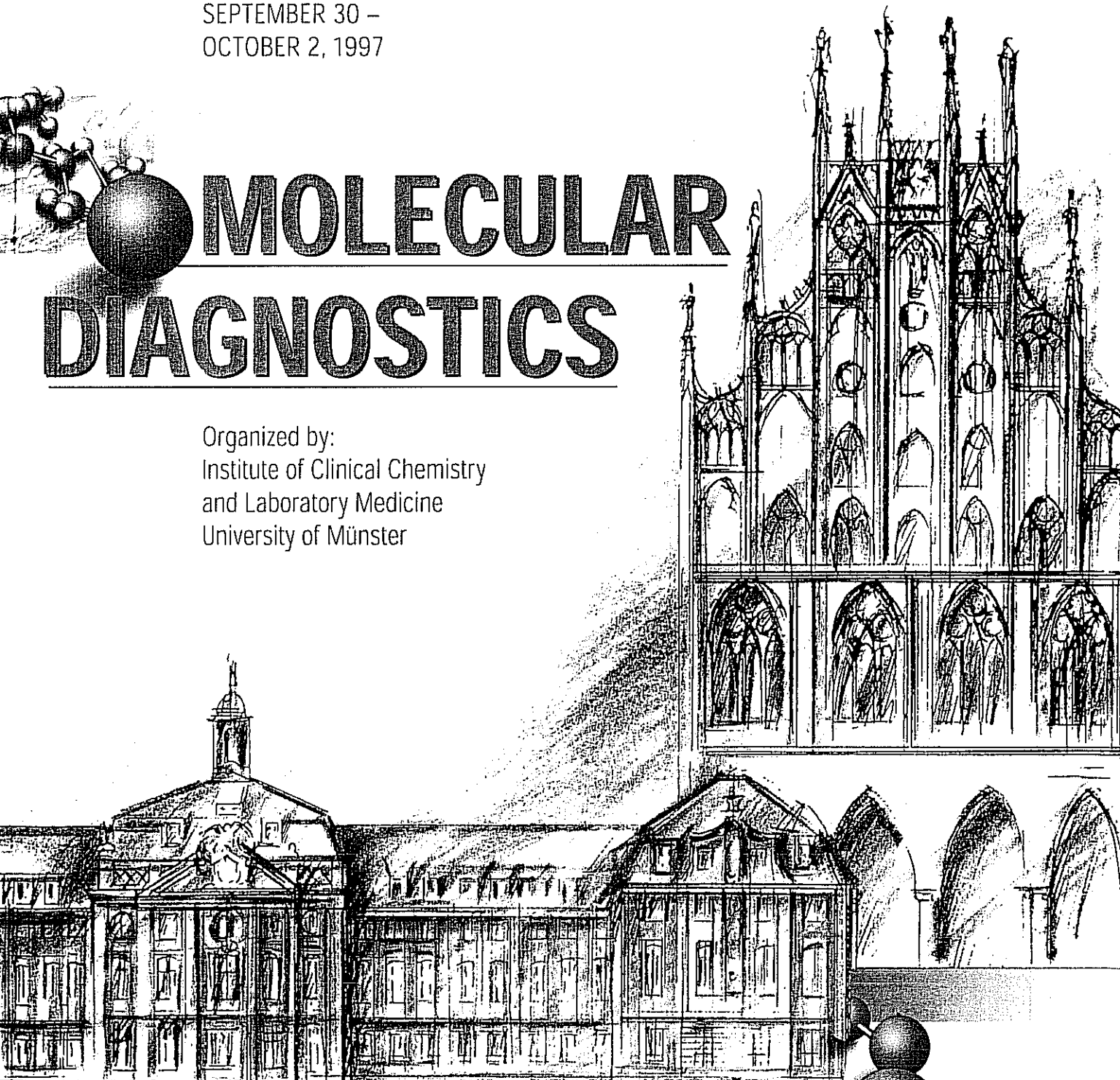
German Society of Clinical Chemistry
and
German Society of Laboratory Medicine

MÜNSTER, GERMANY

SEPTEMBER 30 –
OCTOBER 2, 1997

MOLECULAR DIAGNOSTICS

Organized by:
Institute of Clinical Chemistry
and Laboratory Medicine
University of Münster



Abstracts

Kiehl R.

Regulation of stress protein IgE-synthesis/ proliferation: gInterferon, interleukins, reactiv oxygen species and total IgE as monitoring/ response tools to therapy

Reinhold Kiehl Institute for Molecular Medicine/ Biology, Saliterweg 1, 93437 Furth im Wald/FRG, faxnumber: 0049 9973 801057

Toxic Hg or ROS seem to be not responsible for changes in the IgE-levels of AE-patients but for activation of metalloproteases and associated glucocorticoid sensitive inflammations of the skin. ROS may be obtained by prolonged exposure of skin cells to sunlight and also responsible for development of skin carcinomas. Metalloproteases degrade gIFN. Especially the course of capillary leucocytes collagenase/gelatinase activity out of the skin is opposite to gIFN conc and in correlation with the lactoferrin activity from the same lesion (collagenase/ gelatinase/lactoferrin = 8 to 140/288 to 2699/75 to 601 ng/ml vs gIFN = 100 to 0 %). Skin Prick-tests and skin Epicutaneous-tests do not match either with the total/ specific IgE-measurements. It is concluded, that the adaption of cells to stress conditions includes the gIFN and Il-4 controlled synthesis of IgE antibodies by B-cells and that stress protein IgE is the early warning signal for our body. Environmental pollutants reacting irreversibly with the involved essential dithiol/disulfide redox state (and a coupled unknown membrane bound factor: possibly a FeS-protein, Rieske(?), but not glutathione) or CO, by binding to the NADPH oxidase, are shifting the redox state to the reduced form with enhanced probability for stress protein IgE synthesis (low for O_2^-) and development of AE or hyper-IgE syndrome. The oxidized form ist not able to synthesize IgE but O_2^- and the risk for mitogen stimulated proliferations, buildup of leukemia, carcinomas and CGD is extremely high. The first expression of, for instance, food- or inhalative allergen specific IgE and the allergical triggering of AE may purely be incidental and relate to autoimmune diseases. The pathogenesis of AE and concomitantly of leukemia relates to the development of AIDS. All factors influencing mitochondrial energy formation, are influencing IgE and O_2^--level. A pharmacological treatment of HIV-infection by nucleotide analogs should take care of this fact. The implication for metalloprotease regulation by changing active gIFN conc is evident, and the impact of these gIFN variations on IgE levels, immune complexes and thrombosis (arteriosclerosis) will be shown.

Lehmitz, R. [1], T.O. Kleine [2]

Evaluation of Cellular and Humoral Immune Reactions in Cerebrospinal Fluid (CSF) in Patients with Optic Neuritis and Multiple Sclerosis

[1] Laboratory for CSF Diagnosis, Centre for Nervous Diseases, University, D-18147 Rostock, Germany
[2] Centre of Nervous Diseases, FB Neurochemie, University, D-35033 Marburg, Germany

Optic neuritis and multiple sclerosis both indicate chronic inflammation reactions in CSF concomitant with various clinical and other findings. To discriminate both diseases by clinical chemical investigations, diagnostic sensitivity of 11 cellular and humoral parameters of inflammations were evaluated in 24 patients with optic neuritis and in 36 to 46 patients with multiple sclerosis using immuno-cytological and immuno-chemical methods: manual and differential cell countings (coefficient of variation (CV): <35%) and immuno-cytochemistry of leukocytes; immuno-nephelometric and ELISA techniques (CV: <15%) for calculation of albumin (alb) and immunoglobulin (Ig) concentration ratios in CSF and serum samples, respectively antibody specific index (AI) for measles (M), rubella (R), varicella zoster (Z) to estimate local Ig production or local MRZ reaction (AI > 1.4 according to Reiber); isoelectric focusing (IEF) with immunofixation to detect oligoclonal IgG bands. Positive results are indicated as % of optic neuritis, respectively, % of multiple sclerosis cases for cellular parameters: leukocyte counts > 4 M/l: 58%, 57%; plasma cells: 71%, 74%; B lymphocytes activated for IgG: 75%, 85%; for IgM: 38%, 44%; for IgA: 38%, 56%; for humoral parameters: Qalb > 7: 12%, 20%; local immunglobulin production: IgG: 46%, 65%; IgM: 21%, 17%; IgA: 13%, 11%; oligoclonal IgG bands: 71%, 100%; MRZ reaction (AI > 1.4): 63%, 87%. - Our data indicate the 11 cellular and humoral parameters investigated here to be unable to discriminate between optic neuritis and multiple sclerosis; although some pathological data were found more frequently with multiple sclerosis and oligoclonal IgG bands were detected in all cases of multiple sclerosis. Moreover, our data point to relations of the pathomechanisms of multiple sclerosis and most cases of optic neuritis. However, some optic neuritis cases, clinically verified, expressed no inflammatory signs in CSF, suggesting different disease pathomechanisms, respectively subtypes.

1997: BASEL

AUGUST 17-22

MEDLAB

12TH IFCC EUROPEAN CONGRESS OF CLINICAL CHEMISTRY

THE OFFICIAL PUBLICATION OF MEDLAB 97 ABSTRACTS

A54

Kiehl R.
Laboratory and Research for Molecular Medicine/Biology
Saliterweg 1, 93437 Furth im Wald/FRG
Fax: 00499973801057

STRESS PROTEIN IGE, CIRCULATING IMMUNE COMPLEXES AND THROMBOSIS

We could show [1] that circulating immune complexes and IgE in the blood of atopic eczema patients activates the coagulation system with elevation of platelet aggregation and histamine release with further enhancement of aggregation (thrombosis). This process could be related to significantly lowered diamine-oxidase activities of platelets. We now conclude that this process starts with rising IgE concentrations in the circulating blood or affected skin areas (activation of the contact system by surfactants, etc; contact allergy). Platelets aggregation results presumably in a changed energy metabolism in these particles with build-up of vitamin K x H_2 and H_2O_2/ROS, inhibition of diamine-oxidase by ROS (H_2O_2) with elevation of histamine, inactivation of α_2-macroglobulin and activation of metalloproteases by ROS/H_2O_2. ROS may also be produced by prolonged exposure of skin cells to UV-light and responsible for development of skin carcinomas [2]. – IFN-molecules were significantly degraded by activated leucocyte collagenase under in vivo conditions, although our in vitro assay showed no such behavior [2]. Degradation of two plasma components, namely C1-inhibitor and α_1-proteinase inhibitor, by metalloproteases has already been demonstrated [3,4]. The implication for metalloprotease regulation is evident, and the impact of the changing active gIFN-concentrations on the IgE-levels, immune complexes and thrombosis (arteriosclerosis) [2,5,6] will be discused.

1 Kiehl R and Ionescu G. Med. of Inflammations 1993: 2: 403-406.
2 Kiehl R. Habilthesis, University Munich, Med.Fak. 1996.
3 Knäuper V, Reinke H and Tschesche H. FEBS Letters 1990: 263: 355-357.
4 Knäuper V, Triebel S, Reinke H and Tschesche H. FEBS Letters 1991: 290: 99-102.
5 Kiehl R. InCom' 97, Heinrich-Heine-UniversitÑt, Abstr.p.15 and p.383 and BIOSCOPE, TH Guur-Verlag 1997, in press.
6 Kiehl R. Pharmacia Allergy Research Foundation and Clin.Biochem.1997, submitted.

A55

Readio J., Lee C., Norton A., Swirski C.,
Freeman J., Hsu J.
Bayer Corporation, Business Group Diagnostics
511 Benedict Ave., Tarrytown,NY 10591, USA

AN AUTOMATED ENZYME IMMUNOASSAY FOR THE DIRECT QUANTITATION OF UNCONJUGATED ESTRIOL ON THE BAYER IMMUNO 1 SYSTEM

A competitive heterogeneous enzyme immunoassay has been developed for the quantitative determination of unconjugated estriol in serum using the Bayer Immuno 1 (Trade mark) System, a fully automated random access system. The assay consists of a fluoresceinated capture antibody an estriol labeled alkaline phosphatase conjugate and a magnetic particle solid phase. The enzyme produces para-nitrophenoxide which is measured at 405 nm. The assay requires a 50 µL sample with a time to first results of 38 minutes.
The assay analytical range is 0-104 nmol/L with a sensitivity of 0.11 nmol/L as defined by 2SD above the zero calibrator. The imprecision study was performed over 15 days with three commercial controls and three serum pools between 1.25-53.75 nmol/L. Within-run CVs of the serum pools and commercial controls ranged from 6.8 to 1.8 % and between-run CVs from 7.3 to 3.3%. Linearity studies gave 100 ± 5%, while spike recoveries and parallelism were 85-120% of the expected values.
Correlation studies between Bayer Immuno 1 Unconjugated Estriol assay, DPC Coat-A-Count Free Estriol assay and DSL Ultra-Sensitive Unconjugated Estriol assay (n=278, range 0-104 nmol/L) give the following regression statistics:

Bayer Immuno	1 uEstriol=0.84*DPC+1.2 nmol/L,	r=0.920, Syx=5.9
Bayer Immuno	1 uEstriol=1.48*DSL+2.0 nmol/L,	r=0.980, Syx=2.9

The assay is highly specific with <1% crossreactivity to estriol-3-sulfate, estriol-3ß-glucuronide, estriol-16α-glucuronide, 16-epiestriol, 17-epiestriol, estradiol, and 5% to 16α-hydroxyestrone. Crossreactivities to estriol-17ß-glucuronide, estrone, estrone-b-glucuronide, estrone-3-sulfate, cortisol, 11-deoxycortisol, 5α-dihydroxytestosterone and testosterone are non-detectable.
We conclude that the Bayer Immuno 1 Unconjugated Estriol assay is an accurate and reliable method to monitor unconjugated estriol levels in serum.

A56

Mack M., Markowitz G., Drahovsky M., Weiß A.
Byk-Sangtec Diagnostica
D-63128 Dietzenbach, Germany

LIAISON, FT3, A FULLY AUTOMATED CHEMILUMINESCENT IMMUNOASSAY BASED ON MAGNETIC PARTICLES

The new LIAISON® FT3 assay was developed for the determination of free triiodothyronine concentration in serum and is designed to run on the fully automated LIAISON® immunoanalyzer system. All LIAISON® assays are based on magnetic particles for bound/free separation of immune complexes. The competitive FT3 assay works according to the SPALT principle using labeled antibodies as tracer and covalently immobilized antigen. High affinity polyclonal antibody against T3 is labeled with activated isoluminol derivative. The light emission is generated by injection of two ready-to-use trigger solutions with a measuring time of 3 s. The assay protocol follows a sequential incubation of reagents. First the 100 µl sample is incubated with labeled antibody solution and then with antigen-coated magnetic particles. Each incubation step takes 10 min. The time to first results is less than 25 min. The assay shows excellent within-assay precision below 4% and between-assay precision below 5% over the full concentration range. The maximum value of the standard curve is 25 pg/ml, the minimum detectable dose is 0.2 pg/ml defined as the intercept of three standard deviations of zerobinding from standardcurve. In contrast to analogue assay systems for FT3 the LIAISON® tracer does not bind to endogenous albumin or TBG from samples. Spiking of samples with albumin and TBG solutions revealed the expected decrease of patient values due to lowering of the free T3 concentration in serum by binding proteins. Predilution of samples up to 1:2.5 has only minimal effects on the results. Addition of oleic acid increases the free fraction of hormone due to blocking of endogenous binding proteins. The LIAISON® FT3 fulfills all demands for a convenient and fast determination of free T3 concentrations in human serum.

Instrumentalized Analytical Chemistry and Computer Technology 1997

Tagungsband

Species-relates external „in vivo" test systems to screen for the biological profile of drugs

R. KIEHL

EUR CHEM
Dipl. Ing. (FH) Dr. R. Kiehl VDI
Registered Eco-Audit Specialist
Dr. Kiehl Labor und Forschung
Saliterweg 1t
93437 Furth im Wald
Tel.: 0049 (0) 9973 801056
Fax.: 0049 (0) 9973 801057

SCOPE OF ACTIVITIES:
Research for Molekular Medicine/Biology, Biotechnology/Med. Technics-Bioenergy, Consulations/Certifications (Beratung und Gutachten)

KEY WORDS:
gInterferon, cytokines, reactive oxygen species, stress protein IgE, electron transfer chain, redox potentials, metalloproteases, immune diseases, inflammation

The systems presently in use to diagnose ill persons are in some cases far away from reality. Therefore an „in vivo" test system for analyzing blood of these persons has been developed on atopic eczema (AE) patients [1-3]. This system can be used for detection of almost every blood parameter. The system is fast an comparable to „live" conditions, thus artificial, „in vitro" cell culture systems are spared.
This fact is most important for research on AIDS patients where robots or automated devices have to be used for analysis of HIV-contaminated samples. Pharmacologists are thus able to do „in vivo" experiments without the use of experimental animals. The results are obtained in a very short time and the pharmacological profile of a substance is easy to perform. It is possible to evaluate the toxic limits of substances, as well as the combinatorial chemistry and molecularbiology (molecular biology) for the development of new drugs can be fully explored. Simulation of the most likely conditions presumably leading to various diseases, including cancer, and consequently treatment of these induced diseases by the new discovered drugs will be possible. As a result, bonemarrow transplants would likely become unnecessary in the future. Diseases like atopic eczema, leukemia and AIDS would be able to be controlled in a very short time and, therefore, the cost of medical treatment would be lowered [4,5].

[1] R. Kiehl, Int. Alk-Ciba Corning Joint Symposium, Benzheim, 1994, manuscript, Abstr. book and BIOTEC MEDICA, Düsseldorf, 1994, Abstr. P846.
[2] R. Kiehl, Int. Conf. New Appl. Emerg. Mol. Diagn. for Inf. Diseases, Cambridge Healthtech. Inst., London, 1995, Abstr. PII and WASOG Joint Meeting with the BSACI, London, 1995, Proc. p. 54, P/119.
[3] R. Kiehl, Analytica Conference, München, 1996, Abstr. p. 144 and BSACI, Manchester, 1996, Abstr. p. 25, P55.
[4] R. Kiehl, Habilitationsschrift, Universität München, Med. Fakultät, 1996.
[5] R. Kiehl, BIOSCOPE, TH Guur-Verlag, 1997, in press.

Regulation of stress protein IgE-synthesis/proliferation: γ-interferon, interleukins, reactive oxygen species and total IgE as monitoring/response tools to therapy

R. KIEHL

EUR CHEM
Dipl. Ing. (FH) Dr. R. Kiehl VDI
Registered Eco-Audit Specialist
Dr. Kiehl Labor und Forschung
Salterweg 1t
93437 Furth im Wald
Tel.: 0049 (0) 9973 801056
Fax.: 0049 (0) 9973 801057

SCOPE OF ACTIVITIES:
Research for Molekular Medicine/Biology, Biotechnology/Med. Technics-Bioenergy, Consulations/Certifications (Beratung und Gutachten)

KEY WORDS:
γinterferon, cytokines, reactive oxygen species, stress protein IgE, electron transfer chain, redox potentials, metalloproteases, immune diseases, inflammation

Toxic Hg or ROS seem to be not responsible for changes in the IgE-levels of AE-patients but for activation of metalloproteases and associated glucocorticoid sensitive inflammations of the skin. ROS may be obtained by prolonged exposure of skin cells to sunlight and also responsible for development of skin carcinomas. Metalloproteases degrade gIFN. Especially the course of capillary leucocytes collagenase/gelatinase activity out of the skin is opposite to gIFN conc and in correlation with the lactoferrin activity from the same lesion. Skin Prick-tests and skin Epicutaneous-tests do not match either with the total/specific IgE-measurements. Environmental pollutants reacting irreversibly with the involved essential dithiol/disulfide redox state (and a coupled unknown membrane bound factor: possibly a FeS-pro-tein, Rieske(?), but not glutathione) or CO, by binding to the NADPH oxidase, are shifting the redox state to the reduced form with enhanced probability for stress protein IgE synthesis (low for O_2^-) and development of AE or hyper-IgE syndrome. The oxidized form is not able to synthesize IgE but O_2^- and the risk for mitogen stimulated proliferations, buildup of leukemia, carcinomas and CGD is extremely high. The first expression of, for instance, food- or inhalative allergen specific IgE and the allergical triggering of AE may purely be incidental and relate to autoimmune diseases. The pathogenesis of AE and concomitantly of leukemia relates to the development of AIDS.

All factors influencing mitochondrial energy formation, are influencing IgE and O_2^--level. A pharmacological treatment of HIV-infection by nucleotide analogs should take care of this fact.

[1] R. Kiehl, Int. Alk-Ciba Corning Joint Symposium, Benzheim, 1994, manuscript, Abstr. book and BIOTEC MEDICA, Düsseldorf, 1994, Abstr. P846.

[2] R. Kiehl, Int. Conf. New Appl. Emerg. Mol. Diagn. for Inf. Diseases, Cambridge Healthtech. Inst., London, 1995, Abstr. P11, WASOG Joint Meeting with the BSACI, London, 1995, Proc. p. 54, P/119 and Amino Acids 1995, 9(1) p.20.

[3] R. Kiehl, Analytica Conference, München, 1996, Abstr. p. 144 and BSACI, Manchester, 1996, Abstr. p. 25, P55.

[4] R. Kiehl, Habilitationsschrift, Universität München, Med. Fakultät, 1996.

[5] R. Kiehl, BIOSCOPE, TH Guur-Verlag, 1997, in press.

BRITISH SOCIETY FOR ALLERGY AND CLINICAL IMMUNOLOGY

ANNUAL MEETING

4 – 6 September 1996

University of Manchester

BOOK OF ABSTRACTS

P/53

EFFECT OF REPORTED MATERNAL SMOKING ON HISTAMINE RELEASE FROM CORD BLOOD BASOPHILS

M.E.M. Thompson[1], J. Nelson[1,2], M.C. Stewart[2], M.D. Shields[2] & M. Ennis[1]

Departments of Clinical Biochemistry[1], and Child Health[2], The Queen's University of Belfast, Northern Ireland, UK

Prenatal maternal smoking has been reported to increase the incidence of atopy and asthma, as well as reducing lung function. The aim of this study was to investigate the effect of reported maternal smoking on cord blood basophil releasability.
Cord blood samples (n=75) were obtained from 30 mothers who reported smoking during pregnancy and 45 who did not. Spontaneous histamine release was determined, as well as after challenge with anti-human IgE, *N*-formyl Met-Leu-Phe and the calcium ionophore A23187.
Spontaneous histamine release was not significantly different in the 2 groups (mean±SEM, maternal smokers 7.9±0.6%; maternal non-smokers 9.5±0.5%). The response to stimuli was also similar in both groups for example: anti-human IgE 200 fold dilution 15.5±7.5% maternal non-smokers and 15.8±9.4% maternal smokers; *N*-formyl Met-Leu-Phe 1 µM 23.3±8.5% and 27.9±11.2%; A23187 1 µM 38.1±8.4% and 37.9±10.7%. However, there was considerable variation between subjects as demonstrated by the SEM values. Reported maternal smoking did not influence basophil releasability in this study population. This may be due to false reporting by the mothers. Further studies will therefore examine the effect of cord blood serum cotinine concentrations and cord blood IgE concentrations on basophil releasability.

Supported by the Department of Health and Social Services and the Northern Ireland Mother and Baby Appeal

P/54

SUBSTANCE P AND HISTAMINE INDUCE OXYGEN FREE RADICAL PRODUCTION BY EOSINOPHILS FROM HORSES WITH ALLERGIC SKIN DISEASE

A.P. Foster and F.M. Cunningham

Department of Veterinary Basic Sciences, The Royal Veterinary College, North Mymms, Hatfield, Hertfordshire, UK.

Sweet itch (SI) is a seasonal pruritic allergic skin disease of horses characterised by eosinophil accumulation. Eosinophils from SI horses show altered chemotactic responses during the active, but not inactive, season (Foster & Cunningham, 1995). In the first of a two part study, the effect of mediators on oxygen free radical (OFR) production by eosinophils from SI horses during the inactive season was compared with that of cells from normal (N) horses.
Eosinophils (5 x 10^5) were incubated in the presence of cytochrome C for 30 min at 37°C with either substance P (SP), histamine (H) or the positive control, PMA. OFR generation was calculated as nmol of reduced cytochrome C/10^6 cells and dose-response curves were compared using three-way analysis of variance.
SP ($1x10^{-5}$-$3x10^{-4}$M) caused a dose-related increase in OFR generation by SI eosinophils ($p<0.01$;n=6). Although the differences between eosinophils from SI and N horses were not significant, the maximal responses of cells from 5 of 6 SI animals were greater (SI:71±5&N:49±9 nmol/10^6cells at $3x10^{-4}$M). H (10^{-8}-10^{-3}M) and PMA (10^{-14}-10^{-7}M) also induced dose-related increases in OFR generation by SI eosinophils ($p<0.01$; n=7), which were of similar magnitude to those of N cells. Maximal responses were seen at 10^{-4}M H (SI:12±2&N:15±1 nmol/10^6cells) and 10^{-8}M PMA (SI:346±9&N:335±7 nmol/10^6cells).
Thus, antigen-induced SP and H release could activate eosinophils in SI lesions. The lack of significant differences between cells from N and SI horses during the inactive season agrees with our earlier study of eosinophil chemotaxis and suggests that OFR production is not inherently greater in SI animals.
Foster & Cunningham, 1995. Agents Actions 41, C258-C259.

P/55

IGE-REGULATION, PROLIFERATION AND DEVELOPMENT OF AIDS: G.INTERFERON, INTERLEUKINS, REACTIVE OXYGEN SPECIES AND TOTAL IGE AS MONITORING/RESPONSE TOOLS TO THERAPY.

R Kiehl

Laboratory and research for Molecular Medicine/Biology, 93437 Furth, FRG

Toxic Hg or ROS seem to be not responsible for changes in the IgE-levels of AE-patients but for activation of me-proteases and associated glucocorticoid sensitive inflammations of the skin. ROS may be obtained by prolonged exposure of skin cells to sunlight and also responsible for development of skin carcinomas. Me-proteases degrade gIFN. Especially the course of capillary leucocytes collagenase/gelatinase activity out of the skin is opposite to gIFN conc and in correlation with the lactoferrin activity from the same lesion. Skin Prick-tests and skin Epicutaneous-tests do not match either with the total/specific IgE-measurements. Environmental pollutants reacting irreversibly with the involved essential dithiol/disulfide redox state (and a coupled unknown membrane bound factor: possibly a FeS-protein but not glutathione) or CO, by binding to the NADPH oxidase, are shifting the redox state to the reduced form with enhanced probability for stress protein IgE synthesis (low for O_2^-) and development of AE or hyper-IgE syndrome. The oxidized form ist not able to synthesize IgE but O_2^- and the risk for mitogen stimulated proliferations, buildup of leukemia, carcinomas and CGD is extremely high. The first expression of, for instance, food- or inhalative allergen specific IgE and the allergical triggering of AE may purely be incidental and relate to autoimmune diseases. The pathogenesis of AE and concomitantly of leukemia relates to the development of AIDS. All factors influencing mitochondrial energy formation, are influencing IgE and O_2^--level. A pharmacological treatment of HIV-infection by nucleotide analogs should take care of this fact.
Kiehl R (1994) Int Alk-Ciba Corn J Symp, Benzheim, manuskript, Abstr book; (1995) Amino Acids 9 (1), 20; (1996) Analytica Conf, München, Abstr book, p.498, P144; Habilthesis, Uni Regensburg, and Clin and Diagn Virology, subm

P/56

THE ROLE OF CD8$^+$ T CELLS IN THE REGULATION OF MURINE IgE ANTIBODY RESPONSES *IN VIVO*

MJ Thomas, PA MacAry, BJ Holmes & DM Kemeny.

Department of Immunology, King's College School of Medicine and Dentistry, London, UK.

Studies in our laboratory, and elsewhere, have shown that CD8$^+$ T cells are involved in the regulation of IgE responses to non-relicating antigens in rats. In order to investigate the mechanism(s) of CD8$^+$ T-cell mediated IgE regulation, a similar model was set up in mice. BALB/c mice were immunized intraperitonally (ip) with concentrations of OVA ranging from 1000 to 1 µg/animal and boosted with up to 100 µg of OVA on day 14. Serum samples were collected on days 0, 7, 14, 21 & 28. IgE levels rose in proportion to the amount of antigen given to maximum of 20 ng/ml. Levels OVA-specific IgE antibody were measured by passive cutaneous anaphylaxis (PCA) and rose correspondingly to a maximum titer of 1:2,048. Spleen and lymph node (LN) T cells cultured for 6 days with 100 µg/ml OVA proliferated to a peak on day 21 in the spleen and day 14 in the LN. 10 µg of OVA gave the maximal LN, and 1000 µg of OVA the maximal splenic, proliferative response. To determine the effect of CD8$^+$ T cells on the IgE response, mice were immunized ip with either 100 µg or 1000 µg of OVA, and boosted with 100 µg of OVA on days 14 and 21. CD8$^+$ T cells were depleted by injection of 100 µg of anti-Ly2 Mab on days 11, 16 and 42 (removed >90% of CD8$^+$ T cells). No difference in IgE was seen between CD8-depleted and undepleted animals until day 49 when the IgE response started to drop in normal but not in CD8-depleted animals. These data show that CD8-depletion prolongs the IgE response in mice as well as rats and confirm the importance CD8$^+$T cells in IgE regulation.

ANALYTICA Do 96

Abdruck des Poster-Textes (maximal 1.800 Zeichen):

SPECIES-RELATED EXTERNAL "IN VIVO" TEST SYSTEMS TO SCREEN FOR THE BIOLOGICAL PROFILE OF DRUGS

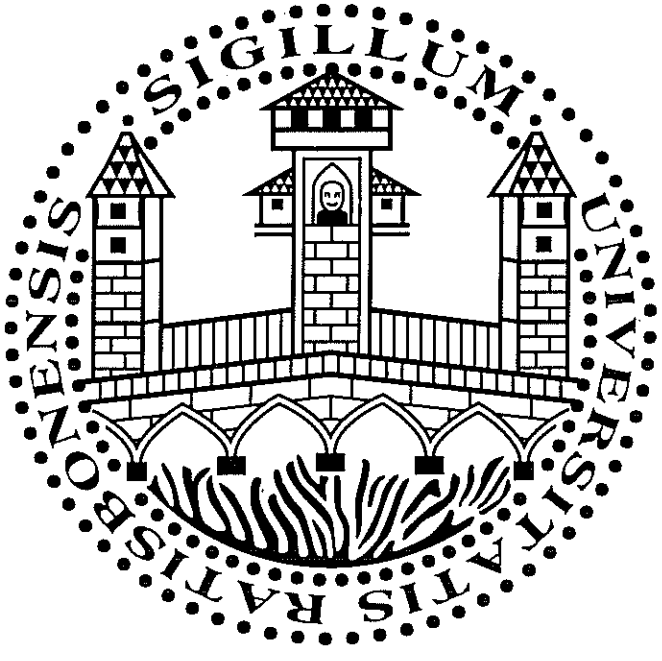
R. Kiehl
- Registered Eco-Audit Specialist -
Laboratory and Research for Molecular Medicine/Biology,
93437 Furth im Wald, Germany.

The systems presently in use to diagnose ill persons are in some cases for away from reality. Therefore an "in vivo" test system for analyzing blood of these persons has been developed on atopic eczema (AE) patients [1-3]. This system can be used for detection of almost every blood parameter. The system is fast and comparable to "live" conditions, thus artificial, "in vitro" cell culture systems are spared. This fact is most important for research on AIDS patients where robots or automated devices have to be used for analysis of HIV-contaminated samples. Pharmacologists are thus able to do "in vivo" experiments without the use of experimental animals. The results are obtained in a very short time and the pharmacological screening for the biological profile of a substance is easy to perform. It is possible to evaluate the toxic limits of substances, as well as the combinatorial chemistry and molecularbiology (molecular biology) for the development of new drugs can be fully explored. Simulation of the most likely conditions presumably leading to various diseases, including cancer, and consequently treatment of these induced diseases by the new discovered drugs will be possible. As a result, bone-marrow transplants would likely become unnecessary in the future. Diseases like atopic eczema, leukemia and AIDS would be able to be controlled in a very short time and, therefore, the cost of medical treatment would be lowered [4,5].

[1] R.Kiehl, Int.Alk-Ciba Corning Joint Symposium, Benzheim, 1994, manuscript, Abstr.book
[2] R.Kiehl, WASOG Joint Meeting with the BSACI, London, 1995, Proc.p.54,P/119
[3] R.Kiehl, Analytica Conference, München, 1996, Abstr.book p.144
[4] R.Kiehl, Habilitationsschrift, Universität Regensburg, Med.Fakultät, 1996
[5] R.Kiehl, Clin.Chem., 1996, and Clin.and Diagn.Virology, 1996, submitted.

Anwendung der Durchflußzytometrie in der Klinischen Zelldiagnostik

– X. Arbeitstagung –
21./22. März 1996



Institut für Klinische Chemie und
Laboratoriumsmedizin
– Zentrallaboratorium und Blutbank –
Universität Regensburg

Durchflußzytometrie zur Therapie-Überwachung von psychisch Erkrankten

Reinhold Kiehl
Laboratory and Research for Mol.Medicine/Biology, 93437 Furth im Wald, FRG

Die durchflußzytometrische Lymphozytendiagnostik, ursprünglich als Meßmethode zur Erforschung der AIDS-Erkrankung entwickelt, wird heute allgemein zur Beurteilung sehr vieler Krankheitsbilder eingesetzt. Obwohl inzwischen der Stellenwert dieser teuren Meßmethode relativiert ist und erkannt wurde, daß sie zur Zeit für die Routine-Diagnostik im klinischen Labor nicht zu gebrauchen ist, steht ihr hoher Wert für Forschungszwecke außer Frage.

Der Einsatz der Lymphozyten-Typisierung, z.B. zur Bestimmung der absoluten Zellzahlen von T-, B-, T4(Helfer)-, T8(Suppresor)-, NK-Zellen sowie der T4/T8-Verhältnisse bei Patienten (Kinder plus Erwachsene) mit dermatologischen Problemen (eingeschlossen Atopisches Ekzem, Psoriasis Vulgaris) zeigt keine Notwendigkeit einer allgemeinen Anwendung der Methode zur Diagnose dieser Patientengruppe [1,2, Erfahrungswerte].

Zur Kontrolle von Therapie-Maßnahmen ist die Durchflußzytometrie allerdings eine erste Methode der Wahl: Mit entsprechenden Antikörpern sollte es in Zukunft möglich sein, fast alle Therapien zu überwachen. Ein Beispiel für zukünftige Entwicklungen wäre die Kontrolle der Therapie von psychisch bedingten Erkrankungen: Psychischer Streß ist in unserer heutigen Gesellschaft allgegenwärtig [3]. Eine Vermessung der β-Rezeptorendichte auf den Lymphozyten dieser Patienten sollte sehr schnelle Therapie-Erfolge bringen und dadurch Behandlungskosten ersparen helfen.

1. Manuel P (1992) Dissertation, Naturwissenschaftliche Medizin der Ruhr-Universität Bochum, Institut für Physiologische Chemie und Spezialklinik Neukirchen. 2. Kiehl R et al (1994) H+G Band 69, 42-48. 3. Kiehl R (1996) Habilitationsschrift, Med.Fakultät der Universität Regensburg, eingereicht.