favor of proinflammatory cytokine expression. These data suggest suggests that epidermal LC are important targets for the polarization of immune responses to chemical allergens.

1362 CHEMICAL RESPIRATORY ALLERGENS UP-REGULATE GRANZYME B GENE EXPRESSION.

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Selective T helper (Th) 1 and Th2 type responses are induced following repeated topical exposure of BALB/c strain mice to chemical contact and respiratory allergens, respectively. In previous experiments, gene expression profiles following exposure of mice to the chemical respiratory allergen trimellitic anhydride (TMA) have been analyzed using oligonucleotide microarrays. Mice received a single topical exposure of 10% TMA on the dorsum of each ear and auricular lymph node tissue was isolated 24 h to 120 h later. Of the 34,000 probe sets represented on the array, 21,000 were detected in lymph node tissue, but only 46 genes with statistically significant allergen-specific alterations were identified. The most strongly up-regulated gene was the T cell cytolytic molecule granzyme B. In the current experiments, changes in granzyme B expression in tissue isolated from mice treated with TMA, or with the contact allergen 2,4-dinitrochlorobenzene (DNCB), have been measured using real time PCR. Mice were exposed to 10% TMA, to 1% DNCB or to vehicle alone on the dorsum of both ears. Draining lymph nodes were excised 24 to 120h later, total RNA prepared and changes in gene expression quantified by real time PCR. Levels of granzyme B were normalized against the housekeeping gene HRPT and expressed as fold changes relative to naïve (untreated) controls. Treatment with TMA resulted in a marked increase in granzyme B expression (fold changes of 5.7+/-2.4, 20.7+/-1.9 and 9.0+/-0.9 induced 48, 72 and 96h after exposure, respectively, n=3). Less marked changes were observed for DNCB-activated cells (fold changes of 3.51+/-0.1, 5.6+/-0.7 and 3.11+/-1.0 induced 48, 72 and 96h after exposure, respectively). Less than 2fold changes were observed throughout the time course for tissue derived from vehicle-treated animals. Selective up-regulation of granzyme B gene expression has been observed following exposure to the respiratory chemical allergen TMA, consistent with recent observations that granzyme B may be the preferential mechanism for Th2 cell death.

1363 ASSESSMENT OF PROTEIN ALLERGENIC POTENTIAL IN MICE : RESPONSES TO ARA H 1, ARA H 2 AND POTATO LECTIN.

I. Kimber and R. J. Dearman. *Syngenta CTL, Macclesfield, CHESHIRE, United Kingdom.*

Assessment of the potential allergenicity of novel proteins is an important issue, particularly for those derived from genetically modified plants. We have shown previously that the measurement of specific IgE antibody production induced by systemic (intraperitoneal) exposure of BALB/c strain mice to a range of proteins correlates with allergenic potential. In the current investigations, immune responses to the purified peanut allergens ara h 1 and ara h 2 and to potato agglutinin, a material considered to lack allergenicity, have been compared. Specific IgE antibody was measured by homologous passive cutaneous anaphylaxis assay and specific IgG antibody measured by enzyme-linked immunosorbant assay. Intraperitoneal administration of peanut agglutinin (1%w/v) induced relatively vigorous IgG antibody production but failed to cause detectable IgE antibody production. Treatment with 1% w/v ara h 1 stimulated a comparatively weak IgG antibody response but nonetheless IgE antibody production was detected. In contrast, exposure to ara h 2 under the same conditions failed to induce either detectable IgG or IgE antibody. The relatively poor immunogenicity of both peanut proteins in the BALB/c strain mouse may be a reflection of prior dietary exposure to cross reactive soy proteins. Further experience with a wider range of proteins is required, but results to date are encouraging that this approach may constitute a method for the prospective identification of protein allergens, provided that lack of allergenicity (IgE) is only considered a secure negative when robust immunogenicity (IgG) is demonstrated.

1364 THE SENSITIZER NISO4 TRIGGERS THE PRODUCTION OF THE BIO-ACTIVE FORM OF INTERLEUKIN-12 BY HUMAN DENDRITIC CELLS.

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Dendritic cells (DCs) are professional antigen presenting cells which capture and process antigens such as invading bacteria, viruses and haptens. After antigen uptake, DC undergo a maturation process leading to the upregulation of surface markers and production of cytokines. We and others have already shown that NiSO4, a metallic hapten, induces the maturation of human DCs, in vitro.

In this work, we address the question whether NiSO4 by itself or in synergy with other signals can induce the secretion of Interleukin-12 (IL-12) by human DCs derived from CD34+ progenitor cells (CD34-DC) or from human monocytes (Mo-DC).

In CD34-DC, NiSO4 alone induces the secretion of IL-12p40 but not the production of IL-12p70, the bio-active form of IL-12. The production of IL-12p70 induced by NiSO4 in CD34-DC needs a complementary signal provided by IFN-gamma. IL-1 beta, a proinflammatory cytokine, synergizes with both signals to augment the production of IL-12p70. We then analysed the expression of IL-12p35 mRNA using RT-PCR and found that IL-12p35 mRNA was expressed only in the presence of NiSO4 and IFN-gamma and further enhanced with the addition of IL-1 beta.

Mo-DC activated with NiSO4 alone produce a high level of IL-12p40. The presence of IFN-gamma is sufficent for a strong induction of IL-12p70 showing differences with CD34-DC. We also show that the bacterial lipopolysaccharide (LPS) can act in synergy with NiSO4 to induce the production of IL-12p70.

These results suggest first that NiSO4 alone is able to induce the production of high levels of IL-12p40 in human DCs but no detectable amounts of IL-12p70 are measured. Second, IL-12p70 production induced by NiSO4 in both models needs the presence of IFN-gamma. Finally, a bacterial product such as LPS in combination with NiSO4 produce high levels of IL-12p70 in Mo-DC. Signalling pathways induced by these different combinations are still to identify.

1365 PHARMACOLOGICAL DIFFERENTIATION OF EARLY AND LATE PHASE ASTHMA-LIKE RESPONSE IN TRIMELLITIC ANHYDRIDE (TMA) SENSITIZED AND CHALLENGED BROWN NORWAY RATS.

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Trimellitic anhydride (TMA) is a low molecular weight chemical that may induce specific-IgE and occupational asthma. We have previously demonstrated that dermal exposure to dry TMA powder with subsequent TMA challenge produces asthma-like early (EAR) and late airway responses (LAR) in Brown Norway rats (BNR), as indicated by Penh (an index of airway resistance). Potential mediators involved in LAR or EAR were examined, using selective pharmacological inhibitors, in the present study. Eight BNR were sensitized by 4, weekly, 4 hr dermal exposures to 40 mg dry TMA powder. Two weeks following the final dermal exposure, BNR were given a 10 min, 40 mg/m^3 TMA nose-only aerosol challenge. Pharmacological agents were administered either prior to and/or 1 hr after EAR, and Penh was recorded every 0.5 min for 16-20 hrs. Results: Dexamethasone (2 mg/kg, i.p.) inhibited TMA induced EAR or LAR in TMA sensitized and challenged BNR. Intranasal steroid, fluticasone, (10µl/nostril, daily for 3 days before airway challenge) did not inhibit EAR and LAR, suggesting that the Penh changes were not due primarily to upper airway responses. An aerosol of 1% Salbutamol, a β2 agonist neither prevented or reversed the EAR or LAR. Both Ketanserin, (10 mg/kg, i.p.) a 5-HT2-receptor antagonist, and Cetirizin, a H1-blocker, (30 mg/kg, i.p.) administered 1 hr after TMA challenge inhibited the subsequent LAR. Montelukast (10 mg/kg, i.p.), a leukotriene receptor antagonist, inhibited EAR, but not LAR, when administered either before or 1 hr after challenge. The adenosine antagonist, aminophylline (30 mg/kg, i.p.) also inhibited LAR in some, but not all treated/challenged rats. Selective pharmacological inhibition of mediators demonstrates different pathophysiological mechanisms of EAR and LAR for the asthma-like responses in the BNR TMA model.

The findings and conclusions in this abstract have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent agency determination or policy.

1366 OPTIMIZATION OF THE HUMAN CD34+-DENDRITIC CELLS MODEL FOR DETECTION OF CHEMICAL SENSITIZERS.

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Allergic contact dermatitis is a delayed-type hypersensitivity reaction caused by exposure to contact allergens. Animal assays are currently used to identify the sensitizing potential of new chemicals. However, such studies must be replaced by alternative methods in a near future due to public concern for using animal testing. Our laboratory is part of a national project launched by AFSSAPS (French Medicinal Products Agency) to develop in vitro models for allergy prediction. Due to the variability of different dendritic cell (DC) and langerhans cell (LC) models described in the literature, our initial goal is to characterise and optimize the CD34+-DC model to obtain a robust test system. Another laboratory will optimize the monocytes-DC system in view of comparing both models. CD34+-DCs were cultured in RPMI medium supplemented with 10% of foetal bovine serum (FBS) in the presence of GM CSF (200 U/ml) and TNF-alpha (50 U/ml), as well as Flt3-L (50 ng/ml)

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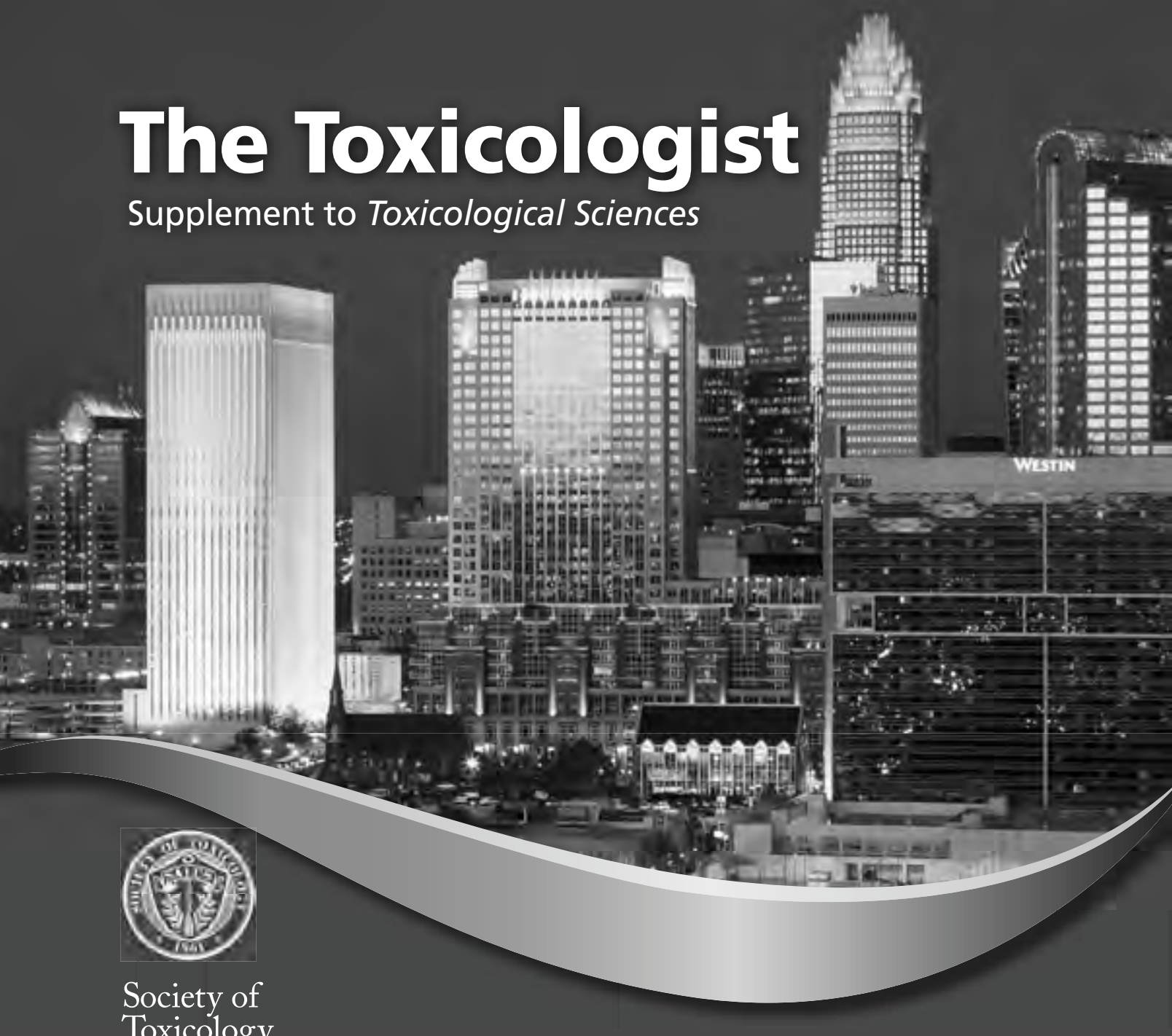

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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