results in selective immunomodulation. (Supported by contract No. 271-91-9201 and Research Scientist Development Award DA-0130 from the National Institute on Drug Abuse).

1205 ALTERATIONS IN IMMUNE FUNCTION PRODUCED BY DELTA OPIOID RECEPTOR-SELECTIVE PEPTIDES

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The present study assessed the direct effect of a series of synthetic peptides selective for δ-opioid receptors on various in vitro immune functions. Murine B6C3F1 splenocytes and elicited macrophages were cultured in vitro with peptides at concentrations between 0.00001–10 μM. B-cell function was assessed by quantitating cell proliferation in response to an antigen analog, T-cell function was assessed by culturing splenocytes with peptides and anti-CD3 antibody, and subsequently quantitating cytokine production. Natural immunity was assessed by culturing lymphocytes with peptides for 24 h, then quantitating natural killer (NK) cell activity. Macrophage function was assessed by production of IL-6. Peptide exposure had limited effects on B-cell proliferation, whereas the production of IL-2 was significantly enhanced by exposure to DPDPE at concentrations between 0.00001 and 0.1 μM. Likewise, IL-4 production was significantly enhanced by DPDPE at these same concentrations. Conversely, the salt DPDPE-trifluoroacetate was inactive in both of these assays. NK cell function was significantly enhanced by in vitro exposure to a number of the peptides, with enhancement generally noted at concentrations between 0.00001 and 0.01 μM. Likewise, IL-6 production was generally augmented by δ-opioid receptor-selective peptides. These data suggest that δ-opioid agonists are broadly immunomodulatory at physiological concentrations. (Supported by contract No. 271-91-9201 and Research Scientist Development Award DA-0130 from the National Institute on Drug Abuse).

1206 EVALUATION OF TRANSPORTED LYMPHOID TISSUE FROM FISCHER 344 RATS AND B6C3F1 MICE FOR USE IN IMMUNOLOGICAL ASSESSMENT

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Studies were conducted to demonstrate the feasibility of integrating immunotoxicological and standard toxicological studies by transporting lymphoid tissue to a second laboratory site. Studies were carried out in female B6C3F1 mice and Fischer 344 rats. The T-dependent antibody forming cell (AFC) response to s-RBC and the natural killer cell response (NK) were the endpoints assessed. Spleens were removed from immunized animals and placed in Earle's Balanced Salt Solution (EBSS) on ice, for 0, 18 or 24 hours as whole spleens, sectioned spleens or spleen cell suspensions. No significant differences were seen with the spleen cell suspensions or the whole spleens at 24 hours as compared with the 0 time control. A rat NK response was evaluated at 0 and 24 hour time points. Both time points were within historical control values. The AFC assay was included in a rat inhalation study exposed at the Dow Corning Corp (DCC) facility. Whole rat spleens from DCC were transported to MCV Immunotoxicology Laboratory for assay 18 hours after sacrifice. Data is shown for the control groups: male (2056 ± 188) and female (1941 ± 290) mean AFC/10^6 spleen cells, evaluated on two separate days with no significant differences seen between the two days. These studies demonstrate that with proper shipping and temperature control, spleens can be successfully transported from one laboratory to another within a 24 hour period for evaluation.

1207 CONTACT HYPERSENSITIVITY RESPONSE TO ACRYLATE ESTERS

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Butyl Acrylate (BAC), Ethyl Acrylate (EAC) and 2-Ethyl-2-(Hydroxymethyl)-1,3-Propanediol Triacrylate (2-ETAC) were selected by the NTP for study as representatives of the acrylate class of agents. Chemicals of this class are widely used in manufacturing of numerous industrial and consumer products. The purpose of these studies was to assess the contact sensitizing potential of these acrylates using B6C3F1 mice. Irritancy studies were conducted to determine concentrations to be used for the hypersensitivity assays and to assure that the animals could tolerate 3 consecutive days of dosing. Each chemical was evaluated for its ability to elicit a contact hypersensitivity response using the Mouse Ear Swelling Test (MEST) and the Local Lymph Node Assay (LLNA). There were no treatment related effects on survival or body weights with any of the compounds tested. Testing concentrations up to 30%, there was no irritating concentrations detected with either EAC or BAC. The minimal irritating concentration for 2-ETAC was 1.0%. A positive contact hypersensitivity response to 2-ETAC was elicited with sensitizing concentrations as low as 0.03% when measured by the MEST and of 0.15% when measured by the LLNA. A positive contact hypersensitivity response to BAC was detected with sensitizing concentrations as low as 20% when measured by the LLNA, however this response was not detected using the MEST at concentrations as high as 30%. These studies did not indicate EAC as a sensitizer using either the MEST or the LLNA. These studies show that of the three acrylates tested 2-ETAC is the most potent contact sensitizer. Supported by NIEHS Contract ES 05288.

1208 IMMUNOSUPPRESSION IN RATS FOLLOWING ORAL EXPOSURE TO BIS(2-METHOXYETHYL)ETHER

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Bis(2-methoxyethyl)ether (BMEE) is one of a group of glycol ethers which is used as an industrial solvent and reaction medium for chemical synthesis. In this study, BMEE was administered daily by gavage to male F344 rats for one week at dosages ranging from 100 to 800 mg/kg/d and immune function determined. Rats exposed to BMEE at 400 and 800 mg/kg/d had reduced thymus weights in the absence of body weight changes compared to water controls. Antibody responses, measured by enumeration of plaque-forming cells (PFC), to the T cell-dependent antigen sheep red blood cells (SRBC) and the T cell-independent antigen trinitro-phenyl lipopolysaccharide (TNP-LPS) were suppressed in rats dosed at 800 mg/kg/d BMEE. Exposure of rats to 2-(2-methoxyethoxy)ethanol (MEE), the primary O-demethylation metabolite of BMEE in rats, failed to alter immune function. These data suggest that BMEE-induced immunosuppression resulted from the metabolism of BMEE via a previously described secondary metabolic pathway in the rat which involves hydrolysis of the central ether bond of BMEE to form 2-methoxyethanol (ME) followed by oxidation of ME to 2-methoxyacetic acid (MAA), which we have previously demonstrated to be immunosuppressive in the rat. (This abstract does not reflect EPA policy.)

1209 IMMUNOPHENOTYPING OF NORMAL HUMAN WORKER VOLUNTEERS: DISTRIBUTION AND RANGE STUDIES

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As part of a multi-year study of the effects of xenobiotics on the immune system of workers, blood (N = 100) was obtained from normal control volunteers from two worksites. The subjects (89 male and 11 female) were 31.9 ± 8.5 (±SD) years old and 37% were current smokers. Statistical analyses indicated asymmetric distributions for percentages (%) of CD56 (natural killer) and CD19 (B-cell), while CD3+/CD4+ (T-helper/inducer), CD3+/CD8+ (T-suppressor/cytotoxic) and CD3 (T-cell) had gaussian distributions. Percentages of total LY (median with 10th and 90th percentiles) were: CD3, 74.20 (61.66 to 84.36), CD3+/CD4+, 44.70 (34.56 to 57.98), CD3+/CD8+, 23.90 (14.16 to 31.59), CD56, 3.80 (1.11 to 6.79) and CD19, 14.00 (8.11 to 24.44). The distributions for the absolute number (#) of cells were asymmetric ($P > 0.05$) for all surface markers studied. Median numbers of LY (with 10th and 90th percentiles) were: CD3, 1642 (1170 to 2464), CD3+/CD4+, 987 (674 to 1548), CD3+/CD8+, 504 (338 to 832), CD56, 85 (20 to 180) and CD19, 320 (162 to 628). The median CD3+/CD4+:CD3+/CD8+ value was 1.87 (1.27 to 3.50) and also showed non-normal distribution characteristics. Significant age, sex and current smoking status associated differences were observed for %s and #s of some subsets. These data indicate that the distributions for #s and %s of some lymphocyte subsets are not symmetrically distributed, and that sex, smoking status, and age can have significant effects on some subsets. These results indicate the need to carefully control for these factors in the design of exposure studies of the human immune system.

1210 USEFULNESS OF ASSOCIATED INVESTIGATIONS IN THE IMMUNOTOXICITY ASSESSMENT OF DRUGS

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Functional tests are pivotal for assessing the toxicological significance of drug

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