were found in DC from k/o mice vs those detected in wt animals. Further, we estimated whether oxFFA in DC were esterified into the most abundant class of neutral lipids accumulating in DC of EL-4 tumor bearing animals, triglycerides (TG). We found that oxTG species containing HODE and corresponding to C16:1/C18:2-OH/C15:0 was present only in DC from tumor-bearing mice. Thus, we suggest that the presence of oxygenated species of lipids in plasma of EL-4 tumor-bearing animals may be responsible for their uptake by DC possibly resulting in the loss of their immuno-surveillance function. Supported by NIOSH OH008282; NIH U19 AI068021, HL70755, HL094488.

PS 1625 COMPARING THE IMMUNOSUPPRESSIVE EFFECTS OF CYCLOSPORIN A ON MOUSE SPLENOCYTES *IN VIVO* WITH MOUSE AND HUMAN T-CELLS *IN VITRO* BY TRANSCRIPTOME PROFILING.

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The immunosuppressive drug Cyclosporin A (CsA) is widely used to prevent graft-versus-host disease in humans. In a parallelogram approach we compared the effects of CsA on the transcriptomes of (i) mouse (CTLL-2) and human (Jurkat) T-cell lines (ATCC), in order to determine the degree of interspecies overlap, (ii) splenocytes of C57BL6 mice exposed *in vivo* with CTLL-2 cells exposed *in vitro*, to verify whether CTLL-2 cells are a suitable *in vitro* model for toxicogenomics. Methods: The mice were exposed for 11 days to CsA (3: low, 9: mid, and 27: high mg/kg bw) or to olive oil (Ctrl), respectively. The CTLL-2 and Jurkat cells were exposed for 6 hours to CsA, N=4 biological replicates. CTLL-2 cells were exposed to 7.5 μM (low) or 15 μM (high) CsA, and Jurkat cells to 8 μM CsA or 13 mM DMSO (carrier). Equal amounts of total RNA molecules (800ηg/sample) were hybridized on Affymetrix mouse GeneTitan HT430PM arrays, or on human U133A plus 2.0 arrays. These transcriptomes were analysed at the levels of individual genes and at functional pathway level. Results and Conclusions: We found that the CsA target genes overlapped by 5% between CTLL-2 and Jurkat cells, and by 2% between the mouse *in vitro* and *in vivo* data, respectively. At the pathway level CsA affected (i) metabolism, protein synthesis, and apoptosis in the Jurkat and CTLL-2 cells *in vitro*, and (ii) metabolism, cellular processes, and apoptosis/cell death in the mouse cells, both *in vivo* (splenocytes), and *in vitro* (CTLL-2), respectively (FDR<0.10). In conclusion, at pathway level the immunosuppressive effects of CsA overlap between mouse immune cells *in vivo*, and mouse (CTLL-2) and human T-cells *in vitro* (Jurkat). At the individual gene level these overlaps are more limited. Based on our results CTLL-2 cells are a suitable model for toxicogenomics.

PS 1626 INHIBITORY EFFECTS OF AZOLE-TYPE FUNGICIDES ON INTERLEUKIN-17 GENE EXPRESSION VIA RETINOIC ACID RECEPTOR-RELATED ORPHAN RECEPTORS ALPHA AND GAMMA.

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The retinoic acid receptor-related orphan receptors α and γ (RORα and RORγ), are key regulators of helper T (Th) 17 cell differentiation, which is involved in the innate immune system and autoimmune disorders. However, it remains unclear whether environmental chemicals, including pesticides, have agonistic and/or antagonistic activity against RORα/γ. In this study, we investigated the RORα/γ activity of several azole-type fungicides, and the effects of these fungicides on the gene expression of interleukin (IL)-17, which mediates the function of Th17 cells. In the ROR-reporter gene assays, five azole fungicides (imibenconazole, hexaconazole, triflumizole, tetraconazole and imazalil) suppressed RORα- and/or RORγ-mediated transcriptional activity as the benzenesulphonamide T0901317, a known ROR inverse agonist and a potent liver X receptor (LXR) agonist. In particular, imibenconazole showed RORγ inverse agonistic activity at concentrations of 10-6 M order. However, unlike T0901317, these fungicides failed to show any LXRα/β agonistic activity. Next, five azole fungicides, showing ROR inverse agonist activity, were tested on IL-17 mRNA expression in mouse T lymphoma EL4 cells treated with phorbor myristate acetate and ionomycin. The quantitative RT-PCR analysis revealed that these five fungicides suppressed the expression of IL-17 mRNA without affecting RORα and RORγ mRNA levels. In addition, the inhibitory effect of imibenconazole, as well as that of T0901317, was attenuated in RORα/γ-knocked down EL4 cells. Taken together, these results suggest that some azole-type fungicides inhibit IL-17 production via RORα/γ. This also provides the first evidence that environmental chemicals can act as modulators of *IL-17* expression in immune cells.

PS 1627 2, 3, 7, 8-TETRACHLORODIBENZO-P-DIOXIN INDUCES TRANSCRIPTIONAL ACTIVITY OF THE HUMAN POLYMORPHIC HS1, 2 ENHANCER OF THE 3'Igh REGULATORY REGION.

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2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is an environmental toxicant known to inhibit antibody secretion and Ig expression. Inhibition of Ig expression may be partially mediated through repression of the 3'Igh regulatory region (3'IghRR). TCDD inhibits mouse 3'IghRR activation and induces aryl hydrocarbon receptor (AhR) binding to dioxin response elements (DREs) within the 3'IghRR enhancers: hs1,2 and hs4. The human hs1,2 enhancer (hu-hs1,2) is polymorphic due to the presence of one to four invariant sequences (IS), which have been correlated with several autoimmune diseases. The IS also contains a DRE-like site. Therefore, the objective was to determine if hu-hs1,2 activity is sensitive to TCDD. Utilizing a mouse B-cell line (CH12.LX), we compared the effects of TCDD on mouse (mo-hs1,2) versus hu-hs1,2 enhancer activity. TCDD inhibited mo-hs1,2 similar to the inhibitory effect on mouse 3'IghRR activation. In contrast, hu-hs1,2 was activated by TCDD and antagonist studies supported an AhR-dependent activation. TCDD also induced hu-hs1,2 activity in a human B-cell line (IM-9). Absence of a Pax5 binding site is a major difference between the human and mouse hs1,2 sequence. Insertion of a Pax5 site in hu-hs1,2 markedly blunted basal reporter activity but did not alter TCDD's effect. Additionally, deletional analysis demonstrated a significant IS contribution to hu-hs1,2 basal activity but TCDD-induced activity was not strictly IS number-dependent. Taken together our results suggest that hu-hs1,2 is a significant target of TCDD and support species differences in hs1,2 regulation. Therefore, sensitivity of hu-hs1,2 to chemical-induced modulation may influence the occurrence and/or severity of human diseases associated with hu-hs1,2.

PS 1628 EFFECT OF LINDANE ON NITRIC OXIDE AND CYTOKINE RESPONSES IN RAW 264.7 MURINE MACROPHAGES.

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Lindane or gamma hexachlorocyclohexane is a persistent organochlorine pesticide that has been banned for agricultural use in the United States but remains an ectoparasiticide treatment for lice or scabies. Lindane may be present in potentially toxic levels in the environment and has been demonstrated to have immunotoxicity, developmental toxicity and genotoxicity. Our aim is to determine if exposure of RAW 264.7 murine macrophages to lindane has direct effects on their ability to respond to stimulation by bacterial Lipopolysaccharide (LPS) and interferon gamma (IFN). RAW 264.7 cells are maintained in continuous adherent culture with passage every 5-6 days. A concentration of $1x10^6$ cells per milliliter are prepared in a 24-well plate and grown overnight. Cells are pretreated with vehicle (DMSO), or a dose response of lindane (5, 50 or 200 μM) prepared in DMSO (final concentration less than 1%) for 24 hours. Following this exposure, cells are washed four times in culture medium and stimulated with a combination of 100 ng/ml LPS and 0.5 U IFN. After 24 hours of stimulation, supernantants are collected for analysis of nitric oxide (Greiss reaction) and cytokine (ELISA) production to determine macrophage functional responses. Cells are then lysed and proteins isolated for later Western blot analysis. Nitrite concentrations in supernatants were determined for no pretreatment controls (38.1 ± 2 μM) and DMSO vehicle controls (44.3 ± 3.4 μM) demonstrated no significant difference. Nitrite concentrations for lindane treatments of 5 μM (33.6 ± 1.7 μM), 50 μM (30 ± 4 μM) and 200 μM (26 ± 1 μM) treatments showed a significant decrease in nitric oxide response (ANOVA Dunnett's t-Test, $P<0.05$) in the 50 and 200 μM treatments compared to controls. Each value represents an average of four wells of treatment. Our initial findings suggest lindane has direct immunotoxic effects on macrophages in a model that could be used to understand previously demonstrated immunotoxic effects in the literature.