1077 INVESTIGATION OF THE RADIOADAPTIVE RESPONSE IN BRAIN AND LIVER OF PUR288 *LacZ* TRANSGENIC MICE.

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The radioadaptive response (RA), where a small priming dose of ionizing radiation can lessen the effects of subsequent exposure to a higher radiation challenge dose, was investigated in multiple tissues within a transgenic organism. Well characterized in *in-vitro* models, current RA research has focused on particular cell types (i.e., lymphocytes), and does not provide comparative data for responses of multiple tissues within an organism. Transgenic animals are useful for such comparisons, because the transgene is integrated into all cells in the body. The pUR288 *LacZ* plasmid based transgenic mouse model utilizes a plasmid vector allowing highly efficient recovery of mutation targets, and is robust to large size change mutations that result from radiation exposure. Female C57Bl/6 pUR288 *LacZ* mice were exposed to priming doses ranging from 7.5 to 37.5 R x-rays over a three day period. After three weeks they received an acute challenge dose of 250 R x-rays. Animals were euthanized three weeks post-challenge, and brain and liver were flash frozen in liquid nitrogen, and stored at -80°C until analysis. Spontaneous mutant frequencies (MF) were significantly higher in liver than in brain (6.62×10^{-5} vs. 3.51×10^{-5}). In the absence of a priming dose, the 250 R challenge doubled the MF of both liver and brain (13.38×10^{-5} and 7.63×10^{-5} respectively). There were no apparent radio-protective effects from any priming dose in liver, while priming doses of 15, 22.5, and 37.5 R significantly reduced (by 40%) the mutagenic effects of the 250 R challenge in brain. Restriction analysis of mutants revealed a significant decrease in large size-change mutations at the three priming doses in brain. This study demonstrates the utility of this model for the investigation of radiological processes of large size-change mutations, as well as demonstrating a radioadaptive response in brains, but not livers of mice *in vivo*. (Supported by U.S. DOE DE-AC09-756R000 and the American Foundation for Pharmaceutical Education.)

1078 MUTATION FREQUENCIES OF MINISATELLITE REPEAT NUMBERS IN HUMAN SPERM BEFORE AND AFTER CANCER CHEMOTHERAPY WITH ALKYLATING AGENTS.

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The spontaneous frequency of minisatellite repeat number changes in the human germline is relatively high. We chose minisatellites as mutation targets to determine whether they can be used as sensitive indicators of heritable genetic damage caused by chemical mutagens. We compared the mutation frequencies in sperm of the same Hodgkin's disease patients pre- and post-treatment with alkylating agents. Small pool polymerase chain reaction (SP-PCR) (PCR on DNA equivalent to approximately 100 sperm) and Southern blotting techniques were used to detect mutations and quantify the frequency of repeat number changes at the minisatellite MS205 locus. At least 7900 sperm in each sample were screened. The mutation frequencies of pre- and post-treatment for the two patients treated with 3 to 4 cycles of Cytoxan, Vinblastine, Procarbazine, and Prednisone (CVPP) / Adriamycin, Bleomycin, Dacarbazine, CCNU, and Prednisone (ABDIC) were 0.22 and 0.23%; and 0.94 and 0.98%. The mutation frequencies for one patient treated with 6 cycles of Mechlorethamine, Oncovin, Procarbazine, and Prednisone (MOPP) were 0.79 and 1.14%. The mutation frequency of the patient after MOPP treatment was 1.44 times as high as that before treatment, which was statistically significant. Since the samples were collected 9 to 15 years after receiving alkylating agent chemotherapy, we conclude that there is no effect of CVPP/ABDIC regimens on the mutation frequency in spermatogonia. However, the higher doses of the alkylating agent procarbazine in the MOPP treatment may increase the mutation frequency at the MS205 locus in spermatogonia.

1079 ASSESSMENT OF DNA DAMAGE IN WORKERS EXPOSED TO ROOFING ASPHALT.

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To determine the potential for increased genetic damage due to asphalt-fume exposure, the single cell gel electrophoresis (comet) assay was used to measure DNA strand breaks in peripheral blood leukocytes at the start and end of a work week that involved exposure to asphalt fume, and in some cases coal-tar pitch. The study population consisted of 25 roofers exposed to hot asphalt and 12 construction workers not exposed to asphalt during the past 5 years. Air monitoring and urinary 1-OH-pyrene levels were used to assess PAH exposure. DNA damage is expressed as %Tail DNA (±S.E.M.). The average %Tail DNA at the start of the week was 15.1±0.6 among all roofers and 14.3±1.1 among controls. The average %Tail DNA at the end of the week was 16.7±0.6 among roofers and 14.5±1.0 among controls. In some cases roofers (n=18) were exposed to coal tar pitch during removal of existing roofing materials prior to applying hot asphalt. These roofers had higher air levels of total particulates and benzene solubles as well as urinary 1-OH-pyrene than a subset of roofers (n=7) not exposed to coal-tar pitch for at least 3 months. Start of the week levels of DNA damage were lower in the non-pitch exposed group of roofers (13.7±0.7) than in the pitch exposed group (16.1±0.6). End of the week levels of DNA damage were somewhat higher in the pitch-exposed roofers (16.9±0.8) compared to the group of roofers who were not exposed to pitch (16.1±0.6). Coal-tar pitch may contribute to higher basal levels of DNA damage than exposure to asphalt fume alone.

1080 ANALYSIS OF THE COMPONENTS OF EDIBLE OIL FUMES IN THE KITCHEN AND THEIR GENOTOXCITY IN *DROSOPHILA*.

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The objective of this study was to test the components of the condensation of edible oil kitchen fumes and their genotoxicity in Drosophila. Analytic method of the components was carried out by gas chromatography and mass spectra (GC/MS) and the genotoxicity of the condensate was detected using the sex-linked recessive lethal (SLRL) test in Drosophila. Results of GC/MS analysis showed that 74 kinds of organic compounds were detected out in the organic extracts of condensed oil from kitchen fumes. The compounds included hydroxylic acids, hydrocarbons, alcohols, esters, aldehydes, ketones, aromatic compounds, and steroids, etc. The total frequency rates of SLRL induced at the concentrations of 110, 320 and 960μg/ml were 1.732%, 4.306% and 1.707%, respectively. Meanwhile, their sterility rates of the first broods were 2.6%, 2.1% and 2.8%, respectively ($p<0.05$ as compared with the control). The frequency of SLRL in the second brood was 0.5% at 320μg/ml and 0.5% at 110μg/ml ($p<0.001$). We conclude that condensates of edible oil fume have many kinds of organic components which include hydroxylic acids, hydrocarbons, alcohols, esters, aldehydes, ketones, aromatic compounds, and steroids, and that the condensate of edible oil fume has genotoxic activity in Drosophila.

1081 SINGLE-STRAND DNA BREAKS FOLLOWING EXPOSURE TO COMBINED THERAPEUTIC HIV/AIDS AGENTS.

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The Single Cell Gel Assay (Comet Assay) was used to measure DNA single-strand breaks occurring in human lymphoblast cells (GM03798, NIGMS Human Genetic Mutant Cell Repository, Coriell Institute for Medical Research, Camden, NJ) exposed to therapeutic HIV/AIDS agents either individually or in combination. Azidothymidine (AZT) had been noted to cause such DNA damage by other detection methods. We wished to determine if the Comet Assay would also detect the damage by AZT and if more damage would occur with combined therapeutic agents. Therefore, we also examined zalcitabine (ddC) and didanosine (ddI) individually, in binary combinations with AZT, and as mixtures of all three chemicals. All three compounds are nucleoside analogs used to treat HIV/AIDS. Viability of the cell cultures was determined with trypan blue. For the Comet Assay, the cells were treated with each of the compounds for various times and concentrations to determine the optimal concentrations and times for testing. AZT caused increasing amounts of cell death and DNA single-strand breaks as the concentration was increased from 100 to 800 μM. The maximum loss of viability occurred at 48 hrs. When individually tested at 200 to 800 μM, neither ddC nor ddI caused the loss of cell viability or the DN single-strand breaks noted with AZT. Combinations of ddC at the highest concentration tested (800 μM) with AZT at 200 μM (a concentration producing minimal comets) increased the size of the comets noted with AZT alone indicating additional DNA damage. Similar combinations of ddI and AZT showed the same effect. Mixtures of ddC (800 μM), ddI (800 μM) and AZT (200 μM) produced the greatest amount of damage.

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