185 **CHEMICAL ANALYSIS OF REVERSE OSMOSIS MEMBRANE AND XAD RESIN ADSORPTION CONCENTRATES OF WATER DISINFECTED BY CHLORINATION OR OZONATION/CHLORINATION PROCESSES.** Simmons JE[1], Richardson SD[2], Schenck KM[3], Speth TF[3], Miltner RJ[3], Thruston AD[2]. [1]NHEERL/ORD/U.S. EPA, RTP, NC. [2]NERL/ORD/U.S. EPA, Athens, GA. [3]NRMRL/ORD/U.S. EPA, Cincinnati, OH.

Disinfection by-products (DBPs) are formed by reaction of chemical disinfectants with natural organic matter in source water. As DBPs are typically present at low levels, ug/L or less, in drinking water, they are frequently concentrated by XAD resin adsorption (XAD) for evaluation of mutagenicity. XAD results in an organic matrix (e.g. ethyl acetate) that must be removed and the remaining DBPs re-suspended in a medium suitable for biological assays. Although rarely used for this purpose, an advantage of reverse osmosis membrane (RO) concentration for preparation of water concentrate samples for in vivo and in vitro toxicological evaluation is that it results in a water matrix. As part of a project to evaluate RO preparation of water concentrates, a source water that had been spiked with bromide and iodide was disinfected either by chlorination (post-chlorination, CL) or by ozonation (pre-ozonation/post-chlorination, OZ/CL) processes and concentrated either by RO or XAD. The concentrates were analyzed by advanced GC/MS techniques (high and low resolution electron ionization and chemical ionization mass spectrometry). Many DBPs were identified in the RO samples, including brominated and iodinated compounds, such as bromo- and iodo-trihalomethanes and -acetaldehydes, halonitromethanes, halopropanones, halonitriles, and haloacetamides. Comparing RO to XAD, RO resulted in better recovery of halo-acetaldehydes, halo-propanoes and halo-nitromethanes. Although OZ/Cl did form a number of halogen-containing byproducts, they were fewer in number and lower in concentration than those formed by CL. These same RO and XAD concentrates were evaluated for mutagenicity in the *Salmonella* assay by Schenk et al. (poster, this meeting). This abstract may not reflect EPA policy.

186 **QUANTITATIVE CHARACTERIZATION OF ABERRANT SPLICING IN HUMANS.** Skandalis A[1], Uribe E[1], Ninniss P[1]. [1]Dept. of Biology, Brock University, St. Catharines, Ontario, Canada L2S 3A1.

Studies of mutagenesis have focused mainly on mutations at the DNA level. However, other processes, such as DNA methylation and RNA and protein processing and editing, can also malfunction and interfere with the accurate flow of genetic information. The focus of our research is to characterize and quantify errors occurring during the process of mRNA splicing in humans and to evaluate the mutagenic potential of transcripts with skipped exons or un-excised introns. Aberrantly spliced messages that get translated could produce non-functional protein mutants that may compete in a dominant negative function with the correctly spliced species. For example, mistakes in the splicing of mRNA for DNA replication or repair enzymes, may lead to a transient increase in mutation frequency that would contribute to cell senescence or neoplasia. In this communication we will present evidence of aberrant splicing of the hprt and polymerase β genes in primary human fibroblasts from individuals of various ages. We will discuss why only some exons appear to be prone to mis-splicing, the effect of aging on the frequency of aberrant splicing, and the translation efficiency of aberrant transcripts.

187 **SEMEN QUALITY AND CHROMOSOMAL INTEGRITY OF SPERM DECREASES WITH AGE AMONG HEALTHY MEN.** Sloter E[1,2], Eskenazi B[3], Nath J[2], Moore II D[4], Kidd S[3], Wyrobek AJ[1]. [1]Biology and Biotechnology Research Program, Lawrence Livermore National Laboratory, Livermore, CA 94550. [2]Genetics and Developmental Biology Program, West Virginia University, Morgantown, WV 26506. [3]School of Public Health, University of California, Berkeley, CA 94720. [4]California Pacific Medical Center, San Francisco, CA 94143.

The current trend towards fathering children at older ages has produced growing concern over the effects of age on male fertility and risk of transmitting genetic damage. Paternal age effects on semen quality and sperm chromosomal integrity were determined for healthy men aged 22-80y after controlling for identified covariates from questionnaires. Ninety-seven nonsmoking men with no known infertility or medical problems were evaluated for semen quality using conventional and computer-assisted semen analysis (CASA). The multicolor ACM FISH assay (Sloter et al. 2000) was used to detect sperm with breaks, duplications, deletions or aneuploidy involving chromosome 1. The results indicate that semen quality gradually decreases with age. The greatest effect was on sperm motility ($P<0.001$, after adjusting for a past history of urinary tract infections), with age-dependent declines in average path and straight-line sperm velocities ($P<0.05$) as well as linearity ($P<0.01$). ACM FISH analysis of the ten oldest (65-80y), nine youngest (22-29y) and four reference donors (43-50y) revealed an average increase of about 3% per year in the frequency of sperm carrying structural chromosomal abnormalities ($P<0.0001$). However, there was no age effect on the frequency of sperm with numerical abnormalities. Additionally, poor semen quality was not associated with increased frequencies of chromosomal abnormalities in sperm. Lifestyle habits, diet and environmental factors did not appear to confound the effect of age on chromosomal damage in sperm. These findings suggest that later fathering may be associated with increased risk for infertility and abnormal reproductive outcomes. [Work was performed under the auspices of US DOE by UC, LLNL contract W-7405-ENG-48, and funding from NIEHS Superfund P42ES04705 and WVU]

188 **ASSOCIATION BETWEEN DIFFERENT TYPES OF CHROMOSOMAL ABERRATIONS IN HUMAN PERIPHERAL LYMPHOCYTES AND CANCER IN DIFFERENT LOCATIONS.** Smerhovsky Z[1], Landa K[2], Rossner P[2], Juzova D[2]. [1]Laboratory of Genetic Ecotoxicology, Institute of Experimental Medicine AS CR, Videnska str. 1083, 142 20 Prague 4, Czech Republic. [2]National Institute of Public Health Prague, Srobarova str. 48, 100 42 Prague 10, Czech Republic.

The major goal of the present study is to evaluate the association between frequency of different types of chromosomal aberrations determined in human peripheral blood lymphocytes and incidence of cancer in subjects occupationally exposed to different chemical clastogens. We analyzed data on the historical cohort of 11,986 subjects who underwent 20,783 cytogenetic assays and experienced 415 cancer cases and 28 carcinoma in situ cases in the period from May 1975 to May 2001. The median age at first cytogenetic assay was 38 years, the total follow-up time was 115,162 person-years, median percentage of aberrant cells 2.0.Using Cox regression to model the association of interest, we have found the correlations between cancer of lymphoid and hematopoietic tissues and freq. of chromosome breaks (HR for individuals assigned into 3rd tercil of freq. of chromosome breaks 3.8, 95%CI 1.4-10.4, p=0.009), the association between lung cancer and freq. of chromatid exchanges (HR for subjects having > 1 chromatid exchange 2.9, 95%CI 1.2-6.7, p=0.015), the association between digestive organs cancer and freq. of aberrant cells (HR for individuals assigned into 3rd tercil of freq. of aberrant cells 1.6, 95%CI 1.06-2.4, p=0.026), and the association between melanoma and other skin cancers and freq. of chromosome breaks (HR for individuals assigned into 3rd tercil of freq. of chromosome breaks 2.0, 95%CI 1.06-3.7, p=0.31). We have also observed significant association between total cancer incidence and freq. of aberrant cells (HR for individuals assigned into 3rd tercil of freq. of aberrant cells 1.3, 95%CI 1.1-1.6, p=0.003). Acknowledgements: Supported by the EC, contract No. QLK4-2000-00628 and by the IGA of the Ministry of Health of the Czech Republic, grant No. 9NJ5177-3.