by day 28. Serum levels of mortality-associated proteins such as FGF23 and IL-6 were reduced in those that recovered, which was corroborated by Olink analysis. Several kinases related to growth and survival increased in recovered patients, such as tyrosine-protein kinase Fyn, protein Wnt-7a, and Myc proto-oncogene protein, which either regulate glomerular integrity through the Wnt/beta-catenin signaling pathway or regulate angiogenesis, illustrating potential mechanisms of kidney recovery. Receiver operating characteristic (ROC) analysis resulted in AUC of 0.64-0.75 for these kinases and inflammation biomarkers. Thus, this study identifies potential novel predictive biomarkers of renal recovery from AKI-D patients.

1245 Decreased Trf1-Trf2 Negatively Regulates Telomere Length and DNA Damage Foci in Rat Liver Tissue after a High-Fat Diet and Welding Fume Exposure

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Telomeric DNA and shelterin proteins prevent loss of essential genetic information during cell division. Telomere attrition resulting in DNA damage contributes to liver pathology. The telomeric repeat-binding factor 1 (Trf1) and 2 (Trf2), and the protection of telomere 1 (Pot1) are involved in telomere maintenance by preventing telomere end-to-end fusion through proper folding of the telomere. The goal of this study was to describe the regulation of expression of these genes and proteins along with their relationship to telomere length in an animal model comparing different diets and a simulated occupational exposure. Male Sprague-Dawley rats were maintained on a regular (REG) or high fat (HF) diet for 24 wk. At wk 7 during diet maintenance, groups of rats from each strain were exposed by inhalation of stainless-steel welding fume (WF; 20 mg/m^3 x 3 hr/d x 4 d/wk x 5 wk) or filtered air until wk12, at which time some animals were euthanized. A separate set of rats were allowed to recover from WF exposure until the end of the 24 wk period. At 12 and 24 wk, the effect on shelterin proteins and telomere length was examined in peripheral blood mononuclear cells (PBMCs) and homogenized liver tissue. Double- and single-stranded telomere DNA-binding proteins Trf1/Trf2 and Pot1, as well as telomeric DNA damage foci λH2AX and 53BP1, were influenced at 12 wk and 24 wk by both diet and exposure. A significant reduction in telomere length in PBMCs was observed in the WF+REG and Air+HF groups, which was further shortened in WF+HF group. However, an opposite telomere length trend was observed in livers obtained from the same groups at both 12 and 24 wk. ATM kinase phosphorylation and DNA damage activation was observed in the liver at 12 wk of WF exposure. Single-stranded binding protein Pot1, initially up-regulated at 12 wk in the WF+REG group, was later down-regulated in liver tissue at 24 wk along with the WF+HF group. In conclusion, our data suggest that disruption/down-regulation of single-stranded Pot1 and double-stranded Trf1/Trf2 expression in liver might act as an anti-apoptotic mechanism in the DNA-damage response leading to multistep liver injury by involvement in the telomere response to diet changes and WF exposure.

1246 A Comparative Analysis of KIM-1 as a Kidney Injury Biomarker in Rat: Plasma and Urine Protein Levels and Kidney Gene Expression

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Kidney injury molecule-1 (Kim-1), also known as T-cell immunoglobulin mucin-1 (TIM-1) and hepatitis A virus cellular receptor 1 (havrc1) is now a well-established urinary biomarker for detection of kidney proximal tubule injury in rat and human. It has been shown that urinary Kim-1 outperforms traditional serum biomarkers blood urea nitrogen (BUN) and serum creatinine (SCr). However, unlike blood, urine is often not collected in animal studies conducted early in drug development and therefore a sensitive blood-based biomarker of kidney injury would be beneficial. We have evaluated Kim-1 as a potential blood-based (plasma) kidney toxicity biomarker and compared its performance to that in kidney tissue and urine, and also to the performance of BUN, SCr and histopathology outcomes in 10 rat *in vivo* studies with known kidney toxicants. To confirm specificity, Kim-1 was also measured in plasma of 11 rat studies with target organ toxicities other than kidney. The most sensitive Kim-1 endpoint (highest fold change observed) was gene expression in kidney. RNA increases were occasionally detected prior to the onset of injury as defined by histopathological changes as shown by ROC exclusion and inclusion models (AUC exclusion = 0.99, AUC inclusion = 0.81). While urinary Kim-1 generally matched kidney RNA expression, smaller fold changes observed with RNA were often not observed when urinary Kim-1 was evaluated. Plasma Kim-1 was the least sensitive method of kidney injury detection, increasing only when higher grade kidney injury was observed, and its performance was comparable to that of the BUN and SCr biomarkers (AUC BUN 0.84, KIM-1 0.85, SCr 0.78 in exclusion model). Plasma Kim-1 is mostly unchanged in non-kidney injury studies; however, in cases where T-cell numbers are decreased (cyclophosphamide) or increased (concanavalin A), plasma Kim-1 reflects those changes, indicating that the source of plasma Kim-1 could be both immune cells and kidney. In conclusion, even though plasma Kim-1 increases with kidney injury, it did not outperform traditional serum biomarkers BUN and SCr. Kim-1 gene expression analysis followed closely by urinary Kim-1 protein measurement are the most sensitive Kim-1-based endpoints to detect kidney injury.

1247 Detection of Anti-Polyethylene Glycol IgM Antibodies in Healthy Individuals

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Polyethylene glycol (PEG) is a biocompatible polymer that is widely used in biopharmaceuticals to increase bioavailability, reduce frequency of administration, and optimize pharmacokinetics. Anti-PEG antibodies have been detected in healthy individuals and may result in decreased efficacy and alter pharmacokinetics of pegylated biopharmaceuticals; however, the prevalence of anti-PEG antibodies is unclear. We have developed a flow cytometry assay to detect anti-PEG IgM antibodies and have assessed their presence in the plasma of 300 heathy individuals. Anti-PEG IgM antibodies were observed in 45% of the individuals, with values ranging from 15 ng/ml to 12 µg/ml. Their presence was confirmed by Western blotting assay. The prevalence of positive samples was 60% in individuals 15-24 years old, 43% in individuals 25-64 years old, and 20% in individuals ≥ 65 years old. The prevalence of anti-PEG IgM antibodies did not differ between sexes or among races (Black, Caucasian, or Hispanic). Our study indicates that the flow cytometry can be used to measure the presence of anti-PEG IgM antibodies in healthy individuals.

1248 Can Ethyl Glucuronide in Hair Be Associated with Alcohol Use in Heavy Drinkers?

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Ethyl Glucuronide (EtG) in hair is proposed as a biomarker for assessment of long-term alcohol consumption. The present study evaluated the association between EtG in hair with alcohol use. Using cross-sectional study design, ninety-one alcohol dependent patients (diagnosed as per International Classification of Diseases, Version-10) with last alcohol consumption within 24 hours were recruited after their consent. The subjective information included: socio-demographic details, alcohol use details and alcohol amount consumed in past three months (by beverage-specific quantity-frequency method). Three centimetre of hair from the posterior vertex region of the head was collected and analysed using gas chromatography-mass spectrometry. The obtained EtG values were compared and correlated with the amount of alcohol consumed. The mean age of the participants was 37.7 (SD: 7.7) years. All participants used alcohol daily, locally brewed liquor being the preferred beverage (51.6%). The mean age of onset of daily alcohol consumption was 27.7 (SD:6.3) years and the mean age of onset of early morning drinking was 32.8 (SD:7.3) years. Mean quantity of alcohol consumed in past three months was 261.7 grams per person per day. All hair samples showed EtG value higher than the cut-off (i.e. 30pg/mg). EtG values expressed a positive correlation ($r = 0.508$, $p = 0.01$) with quantity of alcohol consumed. A simple linear regression was calculated to predict EtG values based on amount of alcohol consumed in last three months, $b= 0.608$, $f (89) =4.213$, $p<0.001$. A significant regression equation was found; $F (1,89) = 52.084$ $p<0.001$, with an R^2 of 0.369. Wilcoxon signed rank test showed statistically significant differences between the hair EtG and quantity of alcohol consumed ($Z= -8.28$, $p<0.001$). The study showed that EtG hair can also be objectively used to assess the quantity of alcohol consumed.

1249 Comparison of Routine Clinical Pathology Parameters of Sprague Dawley Rats by Different Blood Collection Sites

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The Sprague Dawley rat (*Rattus norvegicus*) is commonly used in preclinical toxicity studies. Blood collection sites from either abdominal aorta or vena cave at termination are routinely used for a preclinical study. However, it is certainly necessary to evaluate the drug potential toxicity at interim period of a given study by collecting blood from the jugular vein for clinical pathology evaluations for some sub-chronic and/or long-term toxicology studies.

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and Scientific Sessions of the 59th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 15–19, 2020.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 542.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 580.

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