

BPA, carries reproductive toxicity. However, some of their mechanisms of toxicity are distinct, especially with regards to the meiotic recombination, and need to be further studied.

PS 1174 Morphologic Changes in 3D Human Breast Microtissues following Exposure to Endocrine Disruptors

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As a method to develop human cell-based *in vitro* assays, 3-dimensional (3D) cell culture models are intriguing due to their ability to bridge the gap between animal models and traditional 2-dimensional (2D) cell culture, allowing for the growth of human cells in an environment that is closer to the *in vivo* environment. While many 3D models rely on scaffolded matrices for the growth of cells at low densities, scaffold-free models allow cells to aggregate and maximize cell-cell contact, free of the influence of surrounding matrix. The use of scaffold-free agarose hydrogels provides a system in which cells form spheroids, initiating contact with other cells and the matrix they produce for themselves. We have demonstrated the use of this system to culture MCF-7 human breast carcinoma cells, which self-aggregate and develop into differentiated spheroids, possessing a defined luminal space in this model. As shown by transmission electron microscopy, cells in MCF-7 spheroids display tight junctions, desmosomes, secretions into the luminal space and apical/basal polarity. MCF-7 cells grown in the scaffold-free 3D system display increased expression of breast-specific markers including cytokeratin 18 and milk fat globule. To evaluate the effects of estrogenic endocrine disruptors, samples were exposed to the estrogen receptor alpha agonist propylpyrazolotriol (PPT). PPT exposure for 7 days result in a reduction in luminal ratio (luminal area/total cellular area) in a concentration dependent and statistically significant manner, suggesting the utility and sensitivity of this system in assessing morphological and molecular changes following exposure to estrogenic endocrine disruptors. We have used this system to assess morphologic changes associated with exposure to endocrine disruptors including diethylstilbestrol and bisphenol A and have observed qualitative and quantitative phenotypic changes. The use of a differentiated scaffold-free 3D culture system offers a unique opportunity to study the phenotypic and molecular changes associated with exposure to EDCs.

PS 1175 In Vitro Spermatogenesis Model for Assessing Male Reproductive Toxicity

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Reproductive toxicity testing in animals represents one of the largest uses of animals. It has been an extraordinarily challenging area to implement *in vitro* alternatives due to the complexity of reproductive systems. We previously developed a three-dimensional testicular cells co-culture from rat testis and validated this *in vitro* model can discriminate developmentally toxic phthalate esters (PEs) from non-toxic PEs. However, this model still employs a large number of animals for isolation of primary testicular cells. The goal of this study is to establish a testicular cells co-culture system (3D-TCCS) from the testicular cell lines including spermatogonial stem cells C18-4, Sertoli cell TM4 and Leydig cell TM3. We examined both the morphology and cellular biomarkers of this novel *in vitro* 3D-TCCS model. In an effort to establish a toxicity-based high throughput model, we compared the dose-dependent effects on cell viability of known male reproductive toxic PEs (DPP, DBP, BBP and DEHP) and non-toxic PEs (DEP, DMP and DOTP). Cell viability was measured by Neutral Red assays at 24 and 48 h. DBP, DEHP, BBP and DPP treatments were found to result in dose-dependent decreases in cell viability. Those observations are consistent with the fact that these four PEs are classified as developmentally toxic. The advantage of this 3D-TCCS allows further to clarify the target cells by examining the cellular responses in an individual cell culture model. We found that DBP and BBP targeted on both spermatogonia C18-4 cells and TM3 cells, while DPP targeted all three types of cells. DEHP was found to target both the TM3 and TM4 cells while DEP, DMP and DOTP only induced decrease of cell viability at the highest concentration of 400 μ M in the TM4 cells. All these data demonstrated that this animal free *in vitro* model has the potential to offer predictive modeling for assessing male reproductive toxicity without sacrifice of animals. We are currently further developing an integrated pathway HCA and HTP screening assay in the 3D-TCCS model for male reproductive toxicity evaluation (Supported by ARDF and [R21 OH010473](#)).

PS 1176 Diet, Thermal Environment, and Early-Life Exposure to Methylmercury: *Daphnia pulex* As a Model Organism for Evaluating Multistressor Interactions across the Lifespan

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Interactive effects between chemical toxicity, nutritional status and the physical environment are an important area of ongoing research. Promising high-throughput cell-based toxicity screening assays are being developed and validated, yet these assays cannot address integrative effects at the organismal level, such as the relevance of early life exposures on the development of adult-onset diseases. The short lifespan (median 40 days) and gestation time (approx. 36 hrs), transparency throughout life, and clonality of *Daphnia pulex* are advantages for efficiently detecting latent effects over a lifespan. We have examined consequences of early life exposure to methylmercury (MeHg) under standard and reduced food ration, as well as under a standard or low iron (Fe) diet. We have also examined the consequences of differing food ration across standard and daily fluctuating temperature regimes. An additive effect of MeHg and reduced food ration was found on decreasing lifespan when *D. pulex* were exposed to varying concentrations of MeHg within the first 72 hrs. of life (0, 200, 400, 800 and 1600ng/l MeHgCl) and thereafter kept on either a standard or reduced food ration. MeHg concentration did not affect survival linearly. Low food ration and MeHg concentration were also predictive of reduced reproduction, with some evidence of an interaction (p=0.048). Compared to *D. pulex* on a standard Fe diet, *D. pulex* on a low Fe diet show increased mortality after exposure to an acute heat stress. Analysis of lipids stained with Oil Red O suggests significantly lower lipids in *D. pulex* fed a low Fe diet, while early life MeHg exposure increased lipid levels at 5 days post-exposure.

PS 1177 Germline Defects in Mitochondrial Cholesterol Transporter *C. elegans* Mutants following Bisphenol A or Low Cholesterol Exposures

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Bisphenol A (BPA) treatment results in abnormal oocyte development in mammalian species as well as in the nematode *C. elegans*. In *C. elegans*, these defects are prevented by exposing the worms to cholesterol. We have therefore begun to investigate whether there is an interaction between BPA and normal cholesterol homeostasis in the germline. Previously, we have shown that mammalian homologs to cholesterol transporters (Steroid Acute Regulator Protein; StAR, 18kDa translocator protein; TSPO, and STAR related lipid transfer protein 3; StarD3) mimic germline phenotypes found in BPA-treated worms. Here we show that developing germ cells of these mutants have increases in germ cell nuclei apoptosis, an elongated germline transition zone and reduced fertility when exposed to low cholesterol. Protruding vulva, as well as missing or underdeveloped gonads, are also frequently seen in *strl-1* (homologous to StAR) worms. To investigate a possible interaction between BPA and mitochondrial cholesterol transport, wild type and *strl-1* worms were treated with BPA. Diakinetic analysis of the -1, -2 and -3 oocytes from control-treated worms reveals an increased incidence of abnormal chromatin arrangement in *strl-1* mutant worms compared to wild type (29, 49 and 78 versus 0, 5 and 25 percent). Interestingly, the occurrence among wild type and *strl-1* worms is similar following BPA treatment (6, 34 and 71 percent in wild type versus 7, 30 and 73 in *strl-1*). Together, the data suggest that BPA can at least partially rescue the sensitive germline phenotype in *strl-1* mutants, possibly by acting downstream of mitochondrial cholesterol import.

PS 1178 *C. elegans*, a Valuable Model for Predicting Chemicals' Acute Toxicity in Rodent

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Toxicity assays in the nematode *Caenorhabditis elegans* (*C. elegans*) can be fast and inexpensive; however few studies have been performed comparing toxic responses in the nematode with data on acute rodent toxicity. We assayed the acute toxicity of 21 chemicals using *C. elegans*. The nematodes were exposed to different concentrations of chemicals in 96-well plate for 24 h. The lethality rate was observed, median lethal concentration (LC50) and median lethal times (LT50) were calculated. The results indicated that the chemical pH tolerant range for *C. elegans* was more

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55th Society of Toxicology Annual Meeting and ToxExpo™

New Orleans, Louisiana

March 13–17, 2016

Ernest N. Morial Convention Center

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2. To provide attendees with an opportunity to learn about state-of-the-art technology and how it applies to toxicological research
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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 54th Annual Meeting of the Society of Toxicology, held at the San Diego Convention Center, March 22–26, 2015.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 529.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 553.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

Scientific Session Types:

EC Education-Career Development Sessions	PL Platform Sessions	R Roundtable Sessions
FS Featured Sessions	PS Poster Sessions	S Symposium Sessions
IS Informational Sessions	RI Regional Interest Session	W Workshop Sessions

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