compared to larvae grown in normal E3 media. The EC50 values for 0 mM glucose was noted to be 850 ug/L while 120 mM glucose cultured larvae had an EC50 value of 3500 ug/L. We propose hyperglyemia provides a survival benefit against Cd toxicity due to bioenergetic compensation. Multiple developmental defects were noted in 0 mM glucose reared larvae which were not observed in hyperglycemic larvae. The current project highlights the role of Cd exposures as a key driver of whole-body metabolic dysfunction in a dose dependent manner.

PS 3041 Superficial Vascular Access in Uremic Animal Models to Test Medical Devices

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To explore the possibility of providing suitable superficial vascular access of varying durabilities, in various animal models and in some, inducing a uremic state in the animal by a technique using percutaneous embolization of both renal arteries using polyvinyl alcohol particles. Chronic kidney disease with end stage renal disease is a burgeoning issue worldwide reaching epidemic proportions with regular hemodialysis being the main modality of life saving treatment. Animal model testing remains an important component of preclinical safety evaluation of medical devices contributing to technology advancement. Long term hemodialysis access is commonly done using arteriovenous fistula (AVF) or arteriovenous grafts (AVG). During those interventions, native venous or synthetic grafts are arterialized, and then ready to use. There has been an explosion of new dialysis technologies, some, portable dialysis machines for home usage, others having unique features with significant advantages over existing machines. Concurrently, medical devices have been developed to increase the safety of the hemodialysis procedures, triggering alarms when safety parameters are breached. Though, there have been studies performing such preclinical procedures, none of them have attempted them in uremic animals, and also almost all of them have performed them in the lower limbs, which is not ideal, and does not test the ability to perform its ability to maintain the anephric patient in good health. Testing these devices preclinically needs a suitable superficial vascular access in a uremic/non-uremic animal model. Swine and sheep are common preclinical safety models because the sizes of their cardiac and central vascular anatomical structures being similar to those of humans. American Yorkshire pigs (60-80 Kgs) were the preferred animal, because they resemble humans in size and blood volume, have similar physiology, digestive tract and cardiovascular system and have a better community acceptance as a laboratory animal. AVG was selected as the primary vascular access. In addition, a tunnelled Permcath for shorter length of study and a double lumen Mahurkar dialysis catheter for single session of medical device testing. For AVG, a PTFE graft interposed 'side to side' between the carotid artery and the external jugular vein, with the vascular access superficialized subcutaneously to enable AV Fistula needle cannulation in the neck, was performed in 12 pigs. The AVGs were ready for usage after 3-4 weeks of maturation. In addition, those needing immediate vascular access, 5 pigs had a Permcath and 2 had a regular tunnelled temporary external jugular Mahurkar catheter into the external jugular vein. Procedure to make the animal anephric pigs was embolization of the both renal arteries with polyvinyl alcohol (PVA; Contour, Marlborough, MA, USA). Pre and post procedural angiographies were performed to ensure successful embolization. A total of 19 American Yorkshire pigs successfully underwent superficial vascular access to preclinically test various medical devices needing various specifications of the access design and longevity. 10 pigs underwent bilateral renal ablation using the PVA embolization technique. There is a growing need for superficial vascular accesses to keep pace with the technological advances that are happening in the dialysis field and our experience with the swine model and especially in the anephric state is an excellent and viable template to successfully test the various medical devices emerging and needing preclinical testing.

PS 3042 Impact of Airway Variability on Particle Deposition in the Lungs of Ferrets

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Ferrets have been used as an animal model in inhalation toxicology due to the ease of handing, utility in vaccine research and similarities to humans' tracheobronchial geometry. Currently, there is no widely available particle dosimetry model for the ferret that can be used to estimate inhaled doses or used for interspecies extrapolation. While transport mechanisms and thus deposition models are similar among most mammals and rodents, lung geometries and physiologies are species-specific. Based on existing measurements in the literature, a simplified computational lung geometry for ferrets, which included intraspecies airway geometry variability was developed. A double-path tree branching structure was used for the tracheobronchial tree where one pathway accounted for the conducting airways and the second for the alveolar airways if present (airway generation 5 and beyond). The major advantage of the new lung geometry was that it avoided artificial separation of conducting and alveolar regions based on airway generation number particularly for lung geometries with monopodial structures that are prevalent in rodents. Inclusion of intraspecies airway geometry variability typically seen in rodents increases the utility of the new lung geometry. The proposed geometrical structure can replace typical-path models, often used in the literature, to predict particle deposition more accurately in all species. Ferret-specific lung volumes and breathing parameters were used to predict particle deposition in the ferret using the Multiple-Path Particle Dosimetry model (MPPD, Applied Research Associates, Raleigh, NC). Model predictions showed that while regional deposition followed a similar pattern to that of typical-path models, deposition distribution as a function of airway generation number was significantly different. Deposition of micrometer-sized particles tended to deposit in proximal airway generations whereas nanoparticle deposition occurred in more distal airways. The developed ferret model provides a more realistic prediction of particle deposition distribution in the respiratory tract of ferrets and will be a useful tool for risk assessment applications. *The study was funded by the Cystic Fibrosis Foundation.*

PS 3043 Examination of the Exposome in an Animal Model: The Impact of High-Fat Diet and Rat Strain on Local and Systemic Immune Markers following Occupational Welding Fume Exposure

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An experimental model was designed to investigate the impact of multiple exposomal factors on susceptibility to acute lung toxicity and subsequent resolution of inflammation following an occupationally-relevant inhalation exposure. To assess the role of genetic influence, two rat strains—Sprague-Dawley (SD) and Brown Norway (BN)—were used. A high fat (HF) "Western diet" (14.8% protein, 40.6% carbohydrate, 44.6% fat) was also incorporated to evaluate the potential impact of behavioral/lifestyle factors. Accordingly, male SD and BN rats were maintained on a HF or regular (Reg) diet for 24 wks. Inhalation exposure to filtered air or stainless steel welding fume (WF; 53% Fe, 24% Mn, 17% Cr, 6% Ni, 0.4% Cu) occurred beginning wk 7 for 5 wks (target concentration of 20 mg/m^3 × 3 h/day × 4 days/week × 5 weeks). Rats were euthanized at 7, 12, and 24 wks to evaluate local and systemic immune markers corresponding to the baseline, exposure, and recovery phases of the study, respectively. At 7 wks, HF-fed animals exhibited several immune alterations (blood leukocyte/neutrophil number, lymph node B-cell proportionality) with effects more pronounced in SD than BN rats. Indices of acute lung inflammation were elevated in all WF-exposed animals at 12 wks; however, diet appeared to preferentially impact SD rats at this time point, as lymph node cellularity and bronchoalveolar lavage neutrophils were further elevated in HF over Reg animals. Overall, SD rats exhibited the greatest capacity for recovery of altered immune markers to baseline values by 24 wk. In BN rats, resolution of inflammation was further compromised by HF diet, as many exposure-induced alterations in local/systemic immune markers were still evident in HF/WF animals at 24 wks. Collectively, HF diet appeared to have a greater impact on global immune status and acute lung injury in SD rats, but a more pronounced effect on inflammation resolution in BN rats. These results illustrate the potential combined impact of genetic, behavioral, and environmental factors in modulating immunological responsivity and ultimately emphasize the importance of the exposome in shaping biological responses.

PS 3044 Toxicity and Human Health Risk Assessment of Topical *Aloe vera* Extract

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Various formulations of processed or unprocessed *Aloe vera* Gel (AVG) are indiscriminately used for skin beauty and enhancement, treatment of skin ailments, fading dark spots and anti-ageing, among many others. Recently, there have been concerns about skin lesions and even, possibly, potential for skin cancer due to AVG use. There have not been any meaningful toxicity and health risk assessment reports on its topical use. Four groups of rabbits (n = 8) had a 3 cm diameter circumference shaved at their back and treated by gently rubbing various preparations of AVG, once daily, for 30 days thus: Group 1 (control): 1 g of petroleum jelly (PJ) alone; Group 2: 1 g AVG + 1 g of PJ; Group 3: 2 g AVG + 1 g of PJ; Group 4: 4 g AVG + 1 g PJ. On day 31, skin sections were carefully scraped from five of the animals in each group for assessment of skin lesions, dermatitis and erythema. The remaining three rats in each group were left untreated for a further 15 days for reversibility tests. Results showed significant ($P<0.05$, ANOVA) lesion counts, vs control group. Following reversibility period, lesion parameters were restored to normal levels. Hazard identification and Dose-response relationships do not indicate skin carcinogenesis. Exposure assessment and risk characterisation indicate a hazard quotient of 1.4. In conclusion, prolonged topical exposure to AVG preparations has potential for reversible skin lesions, but not cancer, thereby warranting caution during long-term topical administration in humans.

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