antioxidant enzymes and changes in anti and pro-inflammatory cytokines. We are concluding that C20 might be a useful agent against small intestine dysfunction caused by acrolein-induced inflammatory and oxidative response.

https://doi.org/10.1016/j.toxlet.2022.07.768

LP-28
Lead-exposure associated miRNAs in humans and Alzheimer's disease: Potential biomarkers of the disease and disease processes

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Background: Alzheimer's disease (AD) is a neurodegenerative disease that eventually affects memory and behavior. The identification of biomarkers based on risk factors for AD helps understand the disease since the exact cause of AD remains unknown. Several studies have proposed microRNAs (miRNAs) in blood as potential biomarkers for AD. Exposure to heavy metals is a potential risk factor for onset and development of AD. Blood cells of subjects that are exposed to lead detected in the circulatory system, potentially reflect molecular responses to this exposure that are similar to the response of neurons.

Methods: First, we identified lead exposure related miRNAs based on 186 blood samples of general population from the EU's Envirogenomarkers project (website), with known levels of heavy metals (lead, cadmium) in erythrocytes, using feature selection and linear mixed model. Second, we verified these miRNAs' presence in human brain with a publicly available dataset (GSE157239), and identified their positively or negatively related gene targets and validated the expression of these targets in human brain with brain tissue samples (3 brain regions of 5 AD cases and 2 controls) from the EU Interreg Memories project (www.herinneringen.eu). Third, through pathway analysis, we analyzed relevant pathways that the targets of these miRNAs enriched in. Lastly, since some targets were transcription factors (TFs), to exhibit the complex regulation among miRNAs, gene targets and TFs, we developed the interacting regulation and visualized it via Cytoscape.

Results: A total of 4 miRNAs were identified as lead exposure-associated, with hsa-miR-3651, hsa-miR-150-5p and hsa-miR-664b-3p being negatively and hsa-miR-627 positively associated. All 4 miRNAs were detected in the human brain, of which 2 (miR-3651, miR-664b-3p) showed significant differential expression in AD brains versus controls, in accordance with the change direction of lead exposure. The miRNAs' gene targets were found enriched in AD-relevant pathways such as axon guidance. Moreover, we identified several AD relevant transcription factors such as CREB1 associated with the identified miRNAs. These findings suggest that the identified miRNAs are involved in the development of AD and might be useful in the development of new, less invasive biomarkers for monitoring the risk on, and development of AD, including identification of novel targets for therapies.

https://doi.org/10.1016/j.toxlet.2022.07.769

LP-30
Study Planning: Beneficial economic impact of using the RccHan®:WIST rat in toxicology studies

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Preclinical toxicology studies involving animal models require several factors allowing for study completion. Researchers rely on historical control databases for baseline information and may be hesitant to consider novel models. However, other factors should be considered in model selection, such as survivability, body weight and lesion incidence, which have animal welfare and financial implications. When planning a study, one must consider several factors when choosing the appropriate model to ensure a robust study and the ability to complete the study within budget. Additional considerations are cost of test article, vivarium space and technician time. An analysis of two rat models widely used in toxicology studies was performed. The RccHan®:WIST rat is widely used in Europe as the toxicology model of choice while the CRL:CD® (SD) rat is commonly used in the United States. To allow readers to gauge economic impact of model selection between these two rat models, a tool has been developed to allow researchers to calculate per study cost by utilizing various internal costs associated with these studies. This includes technician time, consumable, diet, bedding, and overhead. This tool will allow researchers to compare economic impact between the two models at various test article costs and study types by allowing the researcher to account for individual internal costs at a per study level. Briefly, with regards to body weight, at 104 weeks of age, the CD® male rat weighs 35% more than the Wistar Han® male rat (800 g compared to 594 g), and the CD® female rat weighs 30% more than the Wistar Han® female rat (500 g compared to 385 g). Additionally, body weight begins to diverge at approximately three months of age in the males. Further, survivability is 32 percentage points lower (35% compared to 67%) in the CD® compared to the Wistar Han® male and 33 percentage points lower (40% compared to 73%) in the CD® compared to the Wistar Han® female. Neo- and nonneoplastic lesion incidence are also improved at 104 weeks of age in the Wistar Han® compared to the CD® male and female rats. In conclusion, the lower body weight, robust nature, and improved survival rate of the Wistar Han® rat may translate into improved animal welfare and overall cost savings for the toxicology program. The use of this tool will aid investigators in model selection and could be considered for future studies.

Reference

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https://doi.org/10.1016/j.toxlet.2022.07.770

LP-31
Polystyrene and PMMA particle toxicity in chicken embryos and particle genotoxicity using a novel high-content imaging workflow

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Plastic microparticles (MP) and nanoparticles (NP) have become a matter of environmental as well as human health concern. Recently, evidence of MP and NP was found in human blood. The potential