The Fertilized Avian Egg Fetal Liver Assays for Assessing DNA Damaging Potential of Chemicals: A Comparative Analysis with In Vitro and In Vivo Genotoxicity Assays and Rodent Carcinogenicity

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Abstract

The ability to produce direct DNA damage (genotoxicity) underlies the carcinogenic mode of action of various chemicals. As such, genotoxicity endpoints are typically evaluated in a regulatory-approved battery of in vitro tests with potential in vivo follow-up. Growing concern for animal welfare and implementation of new regulations which restrict the use of laboratory animals necessitated the introduction of New Approach Methodologies (NAMs). The avian egg-based (in ovo) models, the Chicken and related Turkey Egg Fetal Liver DNA Damage Assays, were developed as metabolically competent NAMs to potentially replace short-term in vivo genotoxicity assays for chemicals that are genotoxic in vitro. Both models utilize avian fetal livers for the evaluation of endpoints indicative of DNA damage produced by either direct or indirect mechanisms, specifically, the formation of nuclear DNA adducts and strand breaks. Moreover, avian embryos carry genetic and morphologic resemblance to mammals and can be used for an extensive evaluation of other endpoints including histopathology and tissue-specific genomic profiling. Avian fetal livers contain a full complement of metabolizing enzymes and are capable of bioactivation, detoxication, and elimination of xenobiotics. The comprehensive analysis of 87 and 59 chemicals assessed in the chicken and turkey models, respectively, revealed a stronger correlation with the results from in vivo assays demonstrating that in ovo models can detect the genotoxic potential of a broader range of compounds compared to in vitro assays with S9 supplementation. In conclusion, fertilized avian egg fetal liver assays offer a promising alternative to traditional in vivo genotoxicity assays.

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