Endocrine Disruptor Screening and Primary Human Thyrocytes

Endocrine Disruptors (ED) are "exogenous substances or mixtures that alter the function of the endocrine system and consequently cause adverse health effects in an intact organism, its progeny or (sub)populations".[1] ED vary by chemical class and are used in a variety of applications.

Observations of adverse effects due to ED were noted in the 1960s. Then, in 1996, there was a concerted focus to screen for these compounds with the passage of two US laws: the Food Quality Protection Act and the Safe Drinking Water Act Amendments. By 1998, the Endocrine Disruptor Screening Program (EDSP) was established which set up a two-tiered testing regimen focused on detecting and understanding the influence of compounds on estrogen, androgen, and thyroid levels. However, most of these screening assays involve non-human biological components and systems.

The current guidelines are included in "OECD Series on Testing and Assessment: Revised Guidance Document 150 on Standardized Test Guidelines for Evaluating Chemicals for Endocrine Disruption".[2] This guidance sets the stage for testing future manufactured compounds as well as legacy manufactured compounds which have not been thoroughly tested. The suggested safety testing can apply to newly manufactured entities including chemicals, food additives, drugs, cosmetic ingredients, and pesticides and can fall under various regulatory organizations, such as the US Environmental Protection Agency (EPA) and the Food and Drug Administration.

Based on Guidance Document 150, the EPA published a revised 5-Tier Screening Battery of *in vitro* and *in vivo* tests. Only three of these assays are human based. The majority of the tests are mammalian and aquatic and are, traditionally, designed to assess development and reproductive toxicity (DART). The DART assays try to determine generational effects in the parents as well as the progeny.

Recently, the EPA issued a directive to eliminate all mammal study requests and funding by 2035. It was suggested to accelerate the development of New Approach Methods (NAMs), which is focused on incorporating human cells and tissues into screening assays. In part to address this directive, the EPA designed a three-dimensional thyroid microtissue assay.[3]

LifeNet Health LifeSciences has been the supplier of the primary human thyroid epithelial cells, or thyrocytes, for this model. Further work by the team at LifeSciences has replicated this assay and optimized the cryopreservation of the human thyrocytes.[4]

This NAM is fully human and maintains the major thyroid hormones in culture for at least 14 days. It allows for a 3D representation of the thyroid *in vitro* by creating follicular-like structures (microtissues) in culture. Being able to cryopreserve thyrocytes allows investigators to perform experiments on their own timelines and not be dependent on the availability of freshly isolated cells. These products are currently under development, but please contact LifeSciences to inquire about pre-market testing opportunities.

References:

1. Damstra, T, Barlow, S, Bergman, A, Kavlock, R and Van Der Kraak, G, eds. International programme on chemical safety: Global assessment of the state-of-the-science of endocrine disruptors. WHO/PCS/EDC/0.2.2 (2002).
2. OECD Series on Testing and Assessment: Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption (2018).
3. Deisenroth, C. et. al. Development of an in vitro human thyroid microtissue model for chemical screening. Toxicol. Sci. 174(1): 63-78 (2020).
4. Cryopreserved Primary Human Thyrocytes for Screening Thyroid Disruptive Chemicals

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