



An Integrative method for Endocrine Disruptors Detection

Background

Endocrine disruptors & Male Fertility

The incidence of pathologies or abnormalities of the male reproductive function has considerably increased during the last fifty years. There has been an overall reduction in male fertility. Sperm count has decreased by 50% over the last 50 years. There has also been a significant increase in the number of testicular cancer and testicular dysgenesis syndrome.

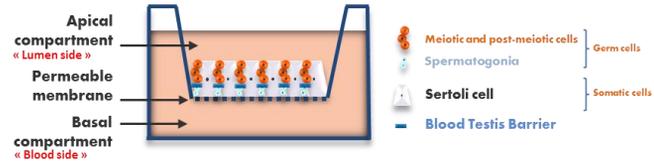
High exposure to chemicals or physical factors during critical growth periods of life are responsible for these disorders. These substances can interfere with the synthesis, release, transport, activity, signalling pathways or metabolism of natural hormones. They are called endocrine disruptors (EDs).

Spermatogenesis : a target process for Endocrine Disruptors

Spermatogenesis is finely regulated and requires an intricate network of signals and pathways. Sertoli cells are responsible for creating an adequate ionic and metabolic environment for germ cell development. Multiple signalling pathways regulate Sertoli cell function and several of these signalling pathways are hormone-dependent. Within the seminiferous tubules, both Sertoli and certain types of germ cells possess receptors for some hormones rendering them major targets for the hormonal signalling that regulates spermatogenesis. **Androgens, estrogens, FSH, thyroid hormones, insulin and other signalling pathways are involved in Sertoli cell function and spermatogenesis. Thus, any substance or molecule interfering with the mechanism of action of these hormones will disrupt the spermatogenesis process and will be detected by Bio-AlteR®.**

Protocol

1 Bio-AlteR® 3D Testicular Cell Culture (Seminiferous tubules primary cell culture)



2 Add substances - compounds (concentration range- time course)



3 Investigation of Endocrine Disruptor effects

- Androgen receptors (AR) expression analysis
- Estrogen receptors (ER α & ER β) expression analysis
- FSH receptors expression analysis
- Thyroid hormone receptors (TR α 1 & TR β 1) expression analysis
- Steroidogenesis enzymes
- ...

4 Investigation of testicular functions that can be altered by EDs

Blood testis barrier integrity, modification of cell number populations, analysis of specific cell gene expression ...

Key benefits

✓ Physiological relevance

Bio-AlteR® evaluates the effect of a compound on a physiological function: testicular function, which is sensitive to hormonal changes. Current recommended in vitro tests are often performed in a context far removed from mammalian physiology.

✓ One single test : Multiple answers

By using one single test, the impact of a molecule can be assessed simultaneously on several ED signalling pathways. Conventional in vitro tests for ED detection can only respond to a single question about a specific mechanism of action

✓ 'Physio' indicator

Many reports now suggest that sperm quality can be used as fundamental biomarker to indicate the overall health status of a man. By exploring testis function, Bio-AlteR® can thus be used as an informative and predictive tool to study health status and future possible abnormalities caused by ED.