

Pharmaceutical Application

Background

Male fertility toxicology studies are part of the Developmental And Reproductive Toxicology (DART) safety evaluation programs of pharmaceutical products.

Regulatory authorities recommend *in vivo* studies to investigate the impact of compounds on testicular function. While these studies yield precious results, they are performed at a later stage during the clinical development. They are also costly and time-consuming. Moreover, in addition to requiring the sacrifice of a high number of animals, the end points provided (e.g., histopathological examination of the testis, sperm analysis, hormone levels measurements) do not provide sufficient understanding of the test article's mechanisms of action. It is critical to identify those issues in a program at an early stage and modify the compounds accordingly.

Kallistem has developed an alternative *ex vivo* methods exploring at an early stage the impact of new pharmaceuticals on male fertility.

This integrated physiological approach uses a single technology to provide answers for several different aspects of male fertility.



FROM A SCREENING PLATFORM...

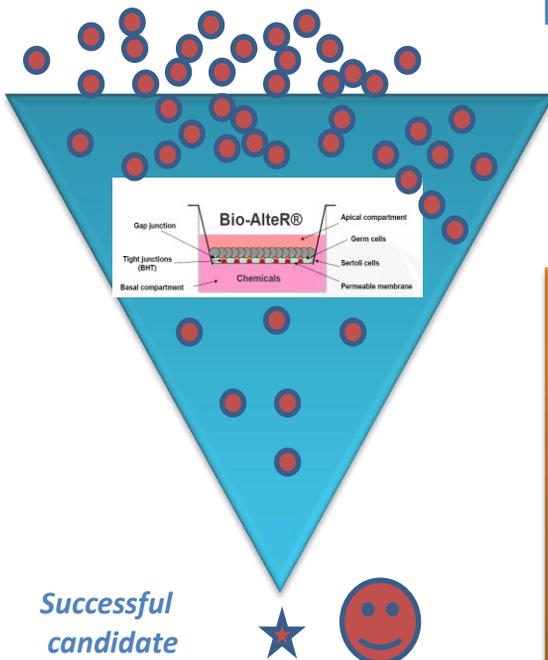
Bio-AlteR® adult or juvenile model

Blood testis barrier (BTB) integrity
Trans-epithelial resistance (TEER) measurement

✓ Modification of cell number populations
Cell viability and FACS analysis
Specific cell gene expression analysis
(6 different testicular cellular population and BTB components)

✓ Endocrine Disruptor effects
Specific cell gene expression analysis
(hormones & signalling pathway)

✓ Bio-AlteR® Sertoli Focus
✓ Sertoli cell culture / Leydig cell culture
(primary cells or cell line)



...TO A MODE OF ACTION DETERMINATION



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Why is Bio-AlteR® the solution to testicular toxicity issues ?

- Bio-AlteR® is a **3D cell based assay unique on the market.**
- Bio-AlteR® provides **reliable safety data on male fertility, relevant to effects on humans.**
- Bio-AlteR® allows substance **testing at «physio-toxicological» concentrations.**
- Bio-AlteR® can be used in **juvenile toxicology.**
- Bio-AlteR® is a **medium throughput assay** allowing the testicular toxicity screening of a large number of compounds, (8 weeks in average between the compound reception and the data report sending).
- Bio-AlteR® provides **a deep understanding of the mechanisms of toxicity** in male fertility .
- Bio-AlteR® supports **the identification of the target risk and has potential to reduce the amount of failure drugs that pass on the R&D pipeline.**
- Bio-AlteR® **dramatically reduces the use of animals** (from 20 to 30 times)
- Bio-AlteR® is a **cost effective solution** to rule out testicular toxicity

