

Opportunity Title: Evaluation of Environmental Chemicals that Decrease Testosterone Production in the Testis

Opportunity Reference Code: EPA-ORD-NHEERL-TAD-2018-11

Organization U.S. Environmental Protection Agency (EPA)

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How to Apply A complete application consists of:

- An application
- Transcripts – [Click here for detailed information about acceptable transcripts](#)
- A current resume/CV, including academic history, employment history, relevant experiences, and publication list
- Two educational or professional references

All documents must be in English or include an official English translation.

If you have questions, send an email to EPArpp@oraui.org. Please include the reference code for this opportunity in your email.

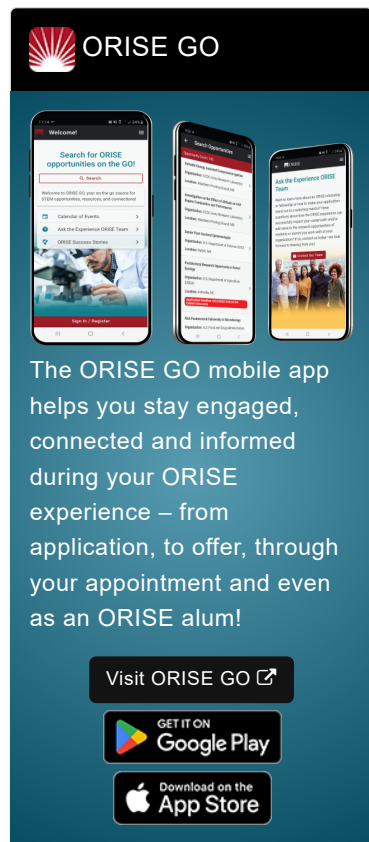
Description Epidemiological data suggest that semen quality is declining. Compromised testosterone production in the fetal or adult testis can lead to abnormal male reproductive development such as quantitative and qualitative alterations in sperm production, and possibly reduced fertility. There is a need for a sensitive, biologically-relevant testis-based assay to directly measure chemical induced alterations in testosterone production. We recently developed such an assay using highly purified rat Leydig cells to complement the adrenal cell high throughput H295R assay and serve as an additional screen when H295R test chemicals were found to be negative for decreased testosterone; notably 85% of the negative chemicals tested in the H295R cell line significantly reduced testosterone in our assay. We are now following up with format modifications to the H295R assay in hopes of finding better predictivity of alterations in decreased testosterone production by Leydig cells. Ongoing and future work will provide information on data poor chemicals relevant to Toxic Substance Control Act (TSCA) and be of interest to program offices such as Office of Chemical Safety and Pollution Prevention and Office of Water as well as NCCT.

This project will involve both the isolation and culture of highly purified Leydig cells using methodology established by the Mentor and the culture of H295R cells, an adrenocorticocarcinoma cell line. A number of previously studied chemicals will be tested for their ability to decrease testosterone in both cell systems. We will attempt to optimize the H295R assay such that these cells are more predictive of the observed decreases in testosterone by Leydig cells. With this we will have established a high throughout cell line model that will minimize the need to use Leydig cells isolated from rat testes. However, given the significantly greater dynamic range and LH responsiveness of the Leydig cell, these cultures will still be warranted to identify the lowest effective concentration for high priority chemicals. This will become important with in vitro-in vivo extrapolation studies designed to test downstream adverse outcomes such as infertility.

Under the guidance of a mentor, the research participant will have the opportunity to learn how to serve as a project lead on this important and exciting project. They will receive guidance from the Mentor on several laboratory procedures as well as data presentation and manuscript preparation.

Learning objectives:

- Learning about the utilization of the H295R cell line for detecting toxicant-induced decreases in steroidogenesis
- Understanding how test compounds elicit changes in testosterone production by H295R cells
- Understanding how test compounds elicit changes in testosterone production by purified Leydig cells



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- Understanding the correlation between the results (i.e. lowest effective concentration) obtained with the H295R cells vs purified Leydig cells
- Learning data processing, statistical analysis and graphical presentation
- Improving oral presentation skills
- Writing and editing scientific manuscripts for submission to peer-reviewed journals

Under the guidance of a mentor, the research participant may be involved in the following training activities:

- Handling small laboratory animals (rats) and limited survival surgeries
- Cell isolation and culture
- Necropsy and preparation of tissues for histological, hormonal and biochemical analyses
- Testosterone radio-immunoassay
- In vivo dosing via oral, ip, sc routes
- Histological analyses, sectioning, immunotraining, imaging
- Tissue extraction for proteomic analysis

This program, administered by ORAU through its contract with the U.S. Department of Energy (DOE) to manage the Oak Ridge Institute for Science and Education (ORISE), was established through an interagency agreement between DOE and EPA. The initial appointment is for one year, but may be renewed upon recommendation of EPA and is contingent on the availability of funds. The participant will receive a monthly stipend commensurate with educational level and experience. Proof of health insurance is required for participation in this program. The appointment is full-time in the Research Triangle Park, North Carolina area. Participants do not become employees of EPA, DOE or the program administrator, and there are no employment-related benefits.

Anticipated Appointment Start Date: January 31, 2019

Qualifications The qualified candidate must have received a bachelor's degree in biology, environmental sciences, animal science, biochemistry or a closely related field. Degree must have been received within five years of the appointment start date.

Preferred skills:

- Knowledge of male reproductive biology
- Experience in handling animals
- Experience with aseptic procedures
- Experience with PowerPoint and Excel files

Eligibility Requirements

- **Degree:** Bachelor's Degree received within the last 60 month(s).
- **Discipline(s):**
 - **Environmental and Marine Sciences** ([1](#) )
 - **Life Health and Medical Sciences** ([10](#) )
 - **Social and Behavioral Sciences** ([1](#) )