Opportunity Title: FDA Development of Exosomal Immune Complex Assays Fellowship
Opportunity Reference Code: FDA-CDER-2022-0827

Organization U.S. Food and Drug Administration (FDA)

Reference Code FDA-CDER-2022-0827

How to Apply ***Connect with ORISE...on the GO!*** Download the new ORISE GO mobile app in the Apple App Store or Google Play Store to help you stay engaged, connected, and informed during your ORISE experience and beyond!

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
- One educational or professional recommendation

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

If you have questions, send an email to ORISE.FDA.CDER@orau.org. Please include the reference code for this opportunity in your email.

Application Deadline 12/31/2022 3:00:00 PM Eastern Time Zone

Description ***Applications will be reviewed on a rolling-basis.**

A research opportunity is available in the Office of Pharmaceutical Quality/Office of Biotechnology Products (OBP), Center for Drug Evaluation and Research (CDER), Food and Drug Administration in Silver Spring, Maryland.

A significant portion of therapeutic monoclonal antibodies (mAbs) are intended to target proteins that are either over expressed on the cell surface or secreted as soluble proteins in the local milieu of various disease conditions such cancer, autoimmune diseases, and viral infections. These target molecules may also be expressed on extracellular vesicles or exosomes in all these indications. Exosomes are small double membrane particles ranging from 50 – 200 nm that are constitutively released by cells and communicate with other cells by carrying proteins, nucleic acids, and lipids. Exosomes have been shown to be involved in the pathogenesis of various autoimmune diseases, tumor progression and enhanced viral infection.

Currently, there is neither a formal understanding nor regulatory/industry expectations regarding mAb therapeutics binding to the proteins expressed on exosomal surfaces; however, a majority of mAb targets are expressed on extracellular vesicles or exosomes and their interaction with therapeutic products may impact safety by inducing immunogenicity and efficacy by interfering with binding to target cells and abrogating the mechanism of action (MOA) of a specific product. Aggregation can impact potency of mAb therapeutics, and the formation of an exosome-immune complex is much larger than a typical aggregated product. In addition to the expression of target antigens, EVs also express MHC molecules and integrins, which could enable the exosomal-immune complex to induce immunogenicity against the drug. The project will establish fit-for-purpose methods to fully characterize, including as part of a biosimilar comparative analytical assessment, the quality attributes of mAbs, such as the ability to bind the target on exosomes, valency, and size of the exosomal-immune complex and how this could impact the overall biological activity of the mAb.

Under the guidance of a mentor, the participant will train in classical immunology, molecular

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biology, and cell biology by characterizing exosomes isolated from various fluids such as cell culture supernatants, serum, plasma, and synovial fluid. The participant will gain knowledge on monoclonal antibody therapies and will be trained on antibody-dependent effector functional assays such as antibody dependent cell-mediated cytotoxicity (ADCC), antibody dependent cell-mediated phagocytosis (ADCP), antibody dependent cell-mediated cytokine secretion, complement dependent cytotoxicity (CDC) and complement dependent cell-mediated cytotoxicity (CDCC) via understanding the exosomal-immune complexes.

The Center for Drug Evaluation and Research (CDER) performs an essential public health task by making sure that safe and effective drugs are available to improve the health of people in the United States. As part of the U.S. Food and Drug Administration (FDA), CDER regulates over-the-counter and prescription drugs, including biological therapeutics and generic drugs. This research covers more than just medicines.

This program, administered by ORAU through its contract with the U.S. Department of Energy to manage the Oak Ridge Institute for Science and Education, was established through an interagency agreement between DOE and FDA. **The initial appointment is for one year, but may be renewed upon recommendation of FDA 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 at FDA in the Silver Spring, Maryland, area. Participants do not become employees of FDA, DOE or the program administrator, and there are no employment-related benefits

Completion of a successful background investigation by the Office of Personnel Management is required for an applicant to be on-boarded at FDA. OPM can complete a background investigation only for individuals, including non-US Citizens, who have resided in the US for a total of three of the past five years.

FDA requires ORISE participants to read and sign their FDA Education and Training Agreement within 30 days of his/her start date, setting forth the conditions and expectations for his/her educational appointment at the agency. This agreement covers such topics as the following:

- Non-employee nature of the ORISE appointment;
- Prohibition on ORISE Fellows performing inherently governmental functions;
- Obligation of ORISE Fellows to convey all necessary rights to the FDA regarding intellectual property conceived or first reduced to practice during their fellowship;
- The fact that research materials and laboratory notebooks are the property of the FDA;
- ORISE fellow's obligation to protect and not to further disclose or use non-public information

Qualifications

The qualified candidate should have received a bachelor's or master's degree in one of the relevant fields. Degree must have been received within five years of the appointment start date.

Knowledge in molecular biology, biochemistry, flow cytometry, immunological assays and bioinformatics are preferred.

Eligibility Requirements

- **Degree:** Bachelor's Degree or Master's Degree received within the last 60 month(s).
- **Discipline(s):**
  - **Life Health and Medical Sciences** (48 👁)

Affirmation

I have lived in the United States for at least 36 out of the past 60

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months. (36 months do not have to be consecutive.)