Opportunity Title: Characterizing the Impact and Detection of Synthetic Monomers
Opportunity Reference Code: ICPD-2022-41

Organization Office of the Director of National Intelligence (ODNI)

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Additional information about the IC Postdoctoral Research Fellowship Program is available on the program website located at: https://orise.orau.gov/icpostdoc/index.html.

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

Application Deadline 2/28/2022 6:00:00 PM Eastern Time Zone

Description **Research Topic Description, including Problem Statement:**

Genetic material and proteins can be synthesized using synthetic biological monomers which are not found in the natural world. These can elicit significant structural and functional changes, with the potential for phenotypic consequences in organisms. Semi-synthetic organisms have already been generated incorporating synthetic nucleotides – E.coli using synthetic base pairs have been generated and have been shown to replicate, engineered using synthetic biology techniques. Synthetic or unnatural amino acids with novel characteristics have also been incorporated in protein engineering, with incorporation of unnatural amino acids demonstrated in both prokaryotic and eukaryotic cells, generating proteins with novel biochemical properties.

The ability to generate new forms of life using synthetic monomers could enable organisms to take on modified or new characteristics, including novel harmful effects or increased pathogenicity. Similarly, the incorporation of unnational amino acids into protein structures may allow the development of modified or novel toxins with enhanced or varied effects, such as increased toxicity. These applications for non-natural biological components could therefore present a biosecurity risk that is currently poorly understood.

Changes to fundamental biological building blocks and their incorporation into genetic or protein sequences may also have consequences for detection, whereby the success of current detection technologies are contingent on the recognition of naturally occurring microorganisms or sequences. Unnatural or synthetic components may bypass detection technologies, enabling their existence and impacts challenging to identify and attribute.

In order to address and mitigate these biosecurity risks, this proposal seeks

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to characterize the potential range of physiological impacts of biological materials and microorganisms comprised of synthetic monomers and better understand the impacts on the utility of current detection technologies, to support future detection and attribution capabilities

Example Approaches:

A possible approach may include:

- Reviewing and exploring existing and novel research on unnatural and synthetic biological monomers to characterize how their incorporation into biological components and systems to generate semi-synthetic products (from molecules to microorganisms) can lead to changes in properties and structure/function relationships. This might include:
  - Developing a method for determining structure/function relationships of semi-synthetic products;
  - Understanding how semi-synthetic products have different characteristics compared to naturally occurring products such as increased environmental persistence or resistance to medical countermeasures; enhancement of existing effects; introduction of new targets, mechanisms of action and subsequent effects;
- Characterizing how functional changes of semi-synthetic products can result in changes to physiological effects;
- Mapping and testing the ability of existing bio detection technologies to identify semi-synthetic products e.g. if existing/emerging sequencing technologies remain functional for semi-synthetic products;
- Developing novel detection frameworks and technologies to identify semi-synthetic products

Relevance to the Intelligence Community:

The incorporation of synthetic biological monomers e.g. nucleotides and amino acids into biological products and microorganisms may present a biosecurity risk, as the incorporation can impart structural and functional changes which in turn could lead to a different physiological effects. In addition, detection technologies developed for naturally occurring biological organisms and molecules may not recognize semi-synthetic versions, allowing their use to go undetected. In order to mitigate this risk, additional information is needed to characterize the changes that occur to the function of biological materials when synthetic components are incorporated, the types of physiological effects these can cause and the detection requirements to identify their use.

Key Words: Monomers; Nucleotides; Amino Acids; Semi-synthetic Organisms; DNA; Proteins; Synthetic Biology; Pathogens; Toxins; Detection.

Qualifications

Postdoc Eligibility

- U.S. citizens only
- Ph.D. in a relevant field must be completed before beginning the appointment and within five years of the application deadline

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- Proposal must be associated with an accredited U.S. university, college, or U.S. government laboratory
- Eligible candidates may only receive one award from the IC Postdoctoral Research Fellowship Program

Research Advisor Eligibility

- Must be an employee of an accredited U.S. university, college or U.S. government laboratory
- Are not required to be U.S. citizens

Eligibility Requirements

- **Citizenship:** U.S. Citizen Only
- **Degree:** Doctoral Degree.
- **Discipline(s):**
  - **Chemistry and Materials Sciences** (12 👁)
  - **Communications and Graphics Design** (2 👁)
  - **Computer, Information, and Data Sciences** (16 👁)
  - **Earth and Geosciences** (21 👁)
  - **Engineering** (27 👁)
  - **Environmental and Marine Sciences** (14 👁)
  - **Life Health and Medical Sciences** (45 👁)
  - **Mathematics and Statistics** (10 👁)
  - **Other Non-Science & Engineering** (2 👁)
  - **Physics** (16 👁)
  - **Science & Engineering-related** (1 👁)
  - **Social and Behavioral Sciences** (27 👁)