Opportunity Title: Non-canonical Protein Translation and Expression Processes, Synthetic Biology, and Biosecurity
Opportunity Reference Code: ICPD-2023-24

Organization	Office of the Director of National Intelligence (ODNI)
Reference Code	ICPD-2023-24
How to Apply	**Create and release your Profile on Zintellect** – Postdoctoral applicants must create an account and complete a profile in the on-line application system. **Please note: your resume/CV may not exceed 2 pages.**

Complete your application – Enter the rest of the information required for the IC Postdoc Program Research Opportunity. The application itself contains detailed instructions for each one of these components: availability, citizenship, transcripts, dissertation abstract, publication and presentation plan, and information about your Research Advisor co-applicant.

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	2/28/2023 6:00:00 PM Eastern Time Zone
Description	**Research Topic Description, including Problem Statement:**

Viruses have provided the template for numerous natural non-canonical protein expression modalities to include alternative splicing, frameshift slippage, and overlapping genes. Current estimates indicate that more than 50% of viral genomes contain one or more overlapping genes. Recent discoveries have shown similar overlapping genes do exist in humans and eukaryotes but at a much lower occurrence, roughly between 1% to 26%. While viral genomes are smaller by multiple orders of magnitude compared to most living organisms, limiting the total length of potential nucleotides for encoding proteins, other facets related to protein structure, function, and expression are at play ranging from evolutionary driven replication efficiencies and community survival, all of which likely play a role in which organisms have adapted non-canonical protein translation.

Recent research has led to the development of computational tools and laboratory techniques for the rational engineering and expression of 'entangled proteins' in bacterial systems. This research has successfully demonstrated expression of overlapped genes and provided multiple examples of the biosecurity implications, especially from an evolutionary escape perspective, of such engineering practices. While successful, the current published approaches focused predominately on sequence alignment and gene overlap. The algorithms have focused on substitution and alignment approaches with minimal optimization to capture secondary interactions and disruptions to protein expression. While novel, additional research is necessary to continue informing towards improving our understanding and control over non-canonical expression modalities.

The Intelligence Community Postdoc program seeks post-doctoral level research proposals focused on improving our understanding of non-canonical expression systems and methods for rational design of entangled or otherwise engineered proteins. This can include research to enhance the

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understanding of the design of entangled or otherwise non-canonically expressed proteins, that improve the ability to predict the function of entangled proteins, and/or pushing the boundaries of what is possible in regard to expression and encoding non-canonically expressed proteins that align with improving biosecurity capabilities.

Example Approaches:

The intelligence community is interested in fundamental capabilities aligning towards characterizing protein expression, function, and associated biosecurity concerns. The recently completed IARPA Fun GCAT program, focused on threat detection of short DNA fragments. The papers referenced below include concerns from the screening community regarding the impact of non-canonical protein expression.

Recommended references for related research:

https://www.science.org/doi/10.1126/science.aav5477

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8924478/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8665328/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8528312/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8490965/

https://www.nature.com/articles/s41586-021-03511-5

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8294169

Relevance to the Intelligence Community (IC):

The S&T priority on biotechnology directly aligns with this research topic as the better the field is able to understand the wide variety of protein expression mechanisms, the better we can design our biosecurity capabilities to detect future biothreats.

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
- 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

Key Words: #Frameshift Slippage, #Leaky Translation, #Alternative Splicing,

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#Entangled Proteins, #Biosecurity, #Structure-to-function, #Protein Expression

Eligibility Requirements	
Citizenship: U.S. Citizen Only	
Degree: Doctoral Degree.	
Discipline(s):	

- **Citizenship:** U.S. Citizen Only
- **Degree:** Doctoral Degree.
- **Discipline(s):**
  - **Chemistry and Materials Sciences** (12 👁)
  - **Communications and Graphics Design** (5 👁)
  - **Computer, Information, and Data Sciences** (17 👁)
  - **Earth and Geosciences** (21 👁)
  - **Engineering** (27 👁)
  - **Environmental and Marine Sciences** (14 👁)
  - **Life Health and Medical Sciences** (48 👁)
  - **Mathematics and Statistics** (11 👁)
  - **Other Non-Science & Engineering** (2 👁)
  - **Physics** (16 👁)
  - **Science & Engineering-related** (1 👁)
  - **Social and Behavioral Sciences** (29 👁)