Defence-related Research Action - DEFRA

ACRONYM: BE-PROTECT

Title: Belgian e-platform for Protein-based Refinement and Optimized Threat Evaluation using Computational AI-driven Technology

Duration of the project: 01/12/2026 - 01/03/2029

Budget: 1 414 000 €

of which RHID contribution: 956 000 €

Key words: proteins, molecular host-pathogen interactions, AI-based protein interpretation and design, biodefense, dual-use application

PROJECT DESCRIPTION

The last decades have seen an explosion of our molecular understanding of biology, with direct implications for health (e.g. novel cancer treatments) and agriculture (e.g. genetically modified organisms). Concurrently, natural biothreats are on the rise, driven by increasing human mobility, ecological niche disruption and climate change. With an ever-growing arsenal of advanced (bio-)molecular approaches at our disposal, the bioagents causing such threats can also be (re-)engineered with increasing ease, as can molecular therapies responding to threats. This foreshadows a biomolecular arms race, with bioagents employed by adversaries to affect our global health, agro-ecosystems, biodiversity and ultimately economical welfare.

Proteins are the key molecules of life that are targeted by bioagents or actively used by bioagents themselves. They are therefore essential to characterize biothreats at the molecular level and to formulate possible responses to them in any biodefense approach. They can also provide a functional, stable and precise differentiation between strains or species that may be highly similar genetically but behave differently in terms of pathogenicity. An improved characterization of proteins can therefore help to fill the gap left by current genetic analytical methods for pathogens identification. This is important for biodefence purposes, where the aim is to assess, prevent, prepare for, respond to, and recover from biological events whether after deliberate or accidental release (bioterrorism, biocrime) or of natural origin (outbreaks). Both can compromise force health, with NATO recognising a capability gap for the rapid and real-time accurate detection and identification of bioagents, specific at least at the species level and sensitive to low occurrence. Current experimental detection typically starts from genomic analysis (at the DNA level), which limits interpretation. Transforming the genome information to the protein (‘proteome’) level can greatly enhance the potential to characterize the bioagents, by looking for similarities with proteins from known organisms, identifying likely molecular modes of action, inferring host-pathogen protein interactions, and suggesting avenues for countermeasures, both short- and long-term.

BE-PROTECT creates enhanced 'made in Belgium' biodefense measures, aimed at optimizing assessment, prevention, and preparedness, as well as response and recovery in the event of biological incidents. To do so, BE-PROTECT formulates a computational pipeline for extensive *in silico* protein characterization that interprets experimental genome-level information on bioagents, naturally occurring or released with malicious intent. It will improve our knowledge of (un)known and (re)emerging threats and lay the foundations for more effective design of protein-based biosensing and (medical) countermeasures. The crucial novelty in our approach is that it also accounts for the non-folding flexible regions of proteins. Many pathogen mechanisms rely on such flexible regions to infect and interfere with host cells, but because of the difficulty in characterizing and interpreting these regions, they are mostly ignored. BE-PROTECT achieves this goal by employing a range of approaches, including unique ones developed at the VUB. By combining publicly available data, available methods and responsible use of AI, we computationally identify the function and likely targets of bioagent proteins through i) comparison with annotated pathogen proteins, as well as ii) comparison with host proteins, with pathogens often mimicking regions thereof. After identification of likely protein interactions between bioagent and host proteins, we will also identify possible bioagent disruptor drugs based on known public information ('drug repurposing') and create mini-binders, small proteins designed by novel AI methods. The computational pipeline for both these steps is intended to be fully dual-use with a public component for general public health measures, and a private component for biodefense relating to sensitive bioagents, where the input data for this pipeline and its results can be handled securely in a fully parallel fashion.

The BE-PROTECT platform so provides an integrative connection between the experimental detection, molecular characterization, and possible disruption of bioagents that is fully dual-use for public health and military biodefense. This will enhance Belgian Defense operational capabilities, readiness for unknown or emerging pathogens including Biological Warfare Agents (BWA) identification and characterization, tactical decision making for rapid response with strategic impact in prevention by anticipating pathogens spread between troops, and countermeasures as explained above. Besides drug repurposing to counter bioagents, the project intends to develop novel protein binders to bioagent proteins, further enabling innovation towards biosensors or novel drugs. The generic nature of the pipeline will also enable it to connect to other developments within the EU or NATO and enable direct interdisciplinary collaborations with other DEFRA and European defense or NATO STO initiatives. BE-PROTECT therefore as a whole contributes, in the short and long term, to DEFRA call priorities, by the development of key biodefence capabilities along with medical and CBRN countermeasures, in line with the Integrated Capability Development Plan (ICDP) and the Strategic Vision for Defence.

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LINK(S)

We will create a project website once the project has started, likely under the https://be-protect.be/ URL. In parallel, a LinkedIn page will be created.