Frequently Asked Questions (FAQ) for the DARPA Generative Optogenetics (GO) Program

Proposer's Workshop

FAQ: Is attendance at the Proposer's Workshop required to submit an abstract in response to the GO Program Solicitation? If the PI cannot attend the workshop, will it hurt the chances of being selected by DARPA?

No. There is no requirement to attend the Proposer's Workshop. However, attendance and presentation of a poster and lightning round talk are strongly encouraged because DARPA is hosting this event to create a venue for organizations interested in responding to the solicitation to form a competitive team.

If a likely PI or CO-I cannot attend, they are most welcome to send a representative (e.g., researcher, scientist, engineer, BD person, etc.) from their organization to attend in their place. These representatives are still strongly encouraged to give a lightning talk and present a poster at the Workshop.

FAQ: Is Dr. Pava available to meet and offer feedback on an RFI submission and/or ideas we have about the program?

Due to scheduling limitations, and in the interest of fairness to all proposers, Dr. Pava will not be taking program related calls and meetings. The best way to receive feedback on an approach is through the submission of a proposal abstract prior to the deadline specified in the Program Solicitation (PS). The PS describes the program, including metrics, in detail. Specific questions may be submitted by email to this address. Proposers should be aware that submitted questions and answers may be published on an FAQ page, with revisions to remove proprietary information.

FAQ: What is expected in the content of posters and lightning talks? I am uncomfortable revealing key aspects of my proprietary technology or my specific approach to GO.

First of all, presentation of both lightning round slides and posters is strongly encouraged because this will afford participants an opportunity to showcase their technical competencies and ideas in a venue designed for team formation. It is expected that very few organizations will possess all of the technical abilities in-house that are necessary to be successful on GO. However, it is entirely up to the discretion of individuals and their affiliated organizations to determine the appropriate amount of detail presented in posters or lightning talks. Consequently, lightning talk and poster presenters should gauge what information they need to share to project their technical competencies and how

they might fit into/support a team in response to the GO funding opportunity. Similarly, they should determine what information they feel is appropriate to share with respect to teammates they are seeking. DARPA is not the primary audience for lightning round or poster content at the Proposer's Workshop, and DARPA will not consider any of this content when reviewing abstracts submitted in response to the Program Solicitation.

FAQ: Can individual attendees propose their technology and find potential teammates at the DARPA GO program workshop?

Yes, individuals can attend and are highly encouraged to present their technology/expertise at the GO Proposers Workshop. The workshop is designed as an opportunity for researchers in the community to connect with potential teammates. The aim of the workshop is to foster collaboration and facilitate discussions among participants. DARPA is encouraging all attendees to present their talents or ideas in-order to create new teaming opportunities to strengthen proposals and technical approaches. Attendees should actively engage in the workshop to build connections and identify complementary expertise for their projects.

FAQ: I am unable to attend the workshop in person. Can I still submit a Teaming Profile if we don't register/attend?

Yes. Please adhere to the format in Special Notice and email directly to <u>GO@darpa.mil</u>. We will circulate your teaming profile with all registrants for the Proposer's Workshop and anyone else who submits a Teaming Profile. Please be sure to include your contact information on the Teaming Profile you submit, so interested recipients of the profile can reach you.

Technical Questions

FAQ: What is a NAC?

A Nucleic Acid Compiler (NAC) is a term derived by DARPA to describe a protein complex designed to be expressed in living cells, capable of synthesizing DNA or RNA sequences directly in response to optical signals. The NAC operates template-free, integrating optogenetic control, substrate binding, and enzymatic activity to enable precise, programmable genetic information transfer within cells. This innovative system represents a foundational capability for massless genetic programming, allowing unprecedented control over cellular behavior and functionality.

FAQ: How many subcontractors can be included in a team, and what is DARPA's expectation for the lead organization?

DARPA does not impose restrictions on the number of subcontractors that can be included in a team. However, the lead organization is expected to have a substantial technical role in the program and must demonstrate the capability to execute a significant portion of the work for at least one of the program's key technical challenges. While subcontractors can provide complementary expertise, the lead organization must house the core expertise required to address

the program's objectives and cannot act solely as a program manager with minimal or ancillary technical contributions. DARPA seeks teams where the prime contractor plays a substantial technical role in addressing the program's objectives, ensuring that the core expertise required for success is housed within the prime organization.

FAQ: What are the expected applications of GO technology?

During the program, GO technology is not focused on any specific direct use case or a particular nucleic acid sequence. Instead, the metrics are designed to evaluate broad capabilities that could support a wide range of potential applications. DARPA is interested in demonstrating the ability to synthesize complex nucleic acid sequences, such as those with high GC content, which are typically challenging to produce using current methods. In Phase 2, DARPA may provide test sequences that are more difficult to synthesize to assess the full potential of performer NACs and their ability to meet program metrics. This approach ensures the development of a versatile platform capable of addressing diverse future applications.

FAQ: What factors should be considered when selecting a cell chassis for the NAC in the GO program?

DARPA does not have a cell chassis preference for the proposed NAC design; however, the choice of approach must be justified both scientifically and in terms of its potential for technology transition or clinical translation use cases. Proposals should provide a clear rationale for the selected cell chassis, considering factors such as, ability of the cell line to express the NAC to support template-free nucleic acid synthesis and its suitability for optical signal transduction. If multiple cell lines are proposed, the submission must explain their relevance and how they will contribute to de-risking the development of the NAC. Note, that embryonic stem cells (ESCs) are explicitly prohibited, and proposals involving ESCs will be deemed out of scope.

FAQ: To what extent is the biological demonstration of the NAC's capabilities weighted in the proposal evaluation? Specifically, would a team benefit from including a "power user" to validate the NAC's ability to drive complex cellular reprogramming or other advanced biological applications during Phase 1?

The program prioritizes the NAC's capability to write DNA/RNA accurately, rather than biological demonstrations or advanced applications such as tissue development or complex cellular reprogramming. Inclusion of a "power user" to validate advanced biological applications is not required. Biological demonstrations, including tissue development or cellular reprogramming, are not within the scope of Phase 1 or the overall program objectives. Instead, the focus of the program is on achieving technical milestones related to the NAC's synthesis capabilities.

FAQ: Does the program scope include the use of generative models to design the genetic payloads (e.g., gene circuits) written by the NAC to achieve specific cellular states? Additionally, how does the program address the connection between engineering the NAC and developing the biological "software" to program cells?

The program does not explicitly include the use of generative models to design genetic payloads (e.g., gene circuits), performers may choose to incorporate such tools to inform their approach, provided they align with the program's goals of demonstrating the NAC's synthesis capability.

The connection between engineering the NAC and developing the biological "software" to program cells is addressed by ensuring that the genetic sequences synthesized by the NAC integrate with the cell's natural machinery for transcription and translation. The design of specific cellular state programming is outside the direct scope of the program, which prioritizes the technical development and demonstration of the NAC's core capabilities.

FAQ: What are the target latency metrics for the NAC, and do the program's technical goals support applications requiring precise spatiotemporal control, such as rapid genetic "write" speeds to influence specific cellular processes like cell cycle phases?

The program does not define latency metrics for specific biological applications, such as interrupting cell cycle phases. The program's Phase 2 milestones include a synthesis rate of 1 second per base for sequences of 3 kb in length with a capability to sequentially program two different sequences with less than 1 Hr of downtime between finishing the first sequence and starting the second sequence (i.e., resetting the NAC between sequence A and sequence B). These metrics are designed to enable high temporal precision, which could potentially support applications requiring spatiotemporal control; however, specific biological demonstrations, such as influencing cell cycle phases, are outside the direct scope of the program.

FAQ: What is the best way for a researcher with a high-impact application or use case to connect with a Prime team participating in the GO program to contribute as a "Validator" or collaborator?

The GO program encourages collaboration and engagement between researchers. The best mechanism for connecting with a team is through the DARPA-sponsored <u>Proposer's Workshop</u>, which will be held January 7th, 2026 in Washington, DC and the GO Program Workshops held during Phase 1 and Phase 2 of the program. These workshops are designed to foster collaboration, identify talent, and address technical challenges. Researchers will be able to submit research abstracts for consideration to attend these workshops, where they can present their ideas and engage with program teams.

FAQ: Is Al-guided sequence design aligned with this program's interest?

Yes, the GO program encourages leveraging computational tools, including AI-driven approaches, to optimize the design and integration of molecular components. AI tools can complement empirical methods and rational design strategies, to help performers address technical challenges to meet program metrics.

FAQ: How is "in vivo" defined within the context of the GO program? Is demonstration organoid on a chip within scope of the program?

As per the GO Program Solicitation, in.vivo demonstrations of the NAC are defined as experiments that show functionality of the NAC (i.e., transducing information contained in an optical signal into a desired nucleic acid sequence) inside of a living cell. Demonstrations need not be in tissues such as an organoid, but this is not prohibited by the program. More complicated demonstrations such as these should be justified because they carry more risk, but they may also be highly relevant to particular applications of the technology that a team wishes to pursue. However, animal subjects research and human subjects research are explicitly out-of-scope for GO.

FAQ: Is DARPA interested in demonstrating NAC function at the level of whole cells or subcellular domains?

This will be up to individual proposing teams, but additional complexity of demonstrations at the sub-cellular level could bring additional technical risks in terms of experiments needed to prove sub-cellular restriction (i.e., higher resolution spatial addressability than whole cells) of NAC-based genetic programming. Thus, proposals taking this approach should justify why these risks are necessary versus demonstrating NAC-based programming at the resolution of whole, individual cells. Most of these risks would be incurred in Phase 2 of the program, and they will need to be discussed as part of the Concept Design Review when Phase 1 performers will present their finalized Phase 2 plan to DARPA. However, proposals in response to the GO Program Solicitation should discuss whether their NAC design will be appropriate for whole-cell programming if a team's ultimate goal is for sub-cellular specificity. Of note, development of novel, exotic optical systems is out of scope for GO, so any demonstrations at higher spatial resolutions than whole cells will need to be performed with commercial off-the-shelf optical components/systems.

Contracting-Related Questions

FAQ: Are there Seedlings or YFA associated with GO?

No, not at this time. However, DARPA is constantly releasing announcements for new funding opportunities, so please continue to check the DARPA website and SAM.gov for any future related announcements.

FAQ: It looks like we can request \$1.7M for RO1 and \$1.99M for RO1 AND RO2 in Phase 1. How much can we request for Phase 2?

After submitting abstracts, a subset of proposing teams will be invited to submit an Oral Presentation Package (OPP), which will include a Task Description Document (TDD) and cost spreadsheet (see attachment to the GO Program Solicitation) as part of the OPP. More details about the complete contents of the OPP, including a template TDD, will be provided upon abstract submission. However, the tasks included in the TDD and the costs provided in the cost spreadsheet should ONLY be for Phase 1. Awards made in response to the GO Program Solicitation will not include scope for Phase 2 initially. Scope.(tasks.and.costs.aligned.to.those.tasks).will.be.negotiated.

<u>separately.during.and.after.the.Concept.Design.Review.in.month.@of.Phase.7</u>; Please refer to the program timeline in the Program Solicitation.

Costs for Phase 1 are fixed, so if a team bids to RO1 and they are selected, the value of their OT-Prototype award will be \$1.7M. If a team bids to both RO1 and RO2 then the value of their OT-Prototype award will be \$1.99M. No awards will be made to RO2 alone.

FAQ: We want to include only RO1 in Phase 1, and both RO1 and RO2 in Phase 2. Is this possible?

It is <u>extremely</u> unlikely that a team will be allowed to perform on RO2 in Phase 2 without performing on RO2 in Phase 1. A team will have no data to justify their performance on RO2 in Phase 2 without performing on RO2 in Phase 1. The only conceivable path where this might be possible is if two Phase 1 teams determine to merge together, where one team as an RO1 only performer and the other was an RO1+RO2 performer. Responses to the Program Solicitation should not include this as a "plan" for Phase 2 work on RO2, when they have not performed on RO2 in Phase 1, because this will be impossible to predict as the composition of Phase 1 teams has not been determined.

Security-Related Questions

FAQ: What are the citizenship or clearance requirements for participation in the GO program, and can green card holders with pending naturalization applications be eligible?

The GO program does not explicitly require U.S. citizenship for participation; however, all participants must comply with applicable nondisclosure agreements, security regulations, export control laws, and other governing statutes. Green card holders may be eligible to participate, provided they meet these requirements. Please read over https://www.darpa.mil/work-with-us/communities/academia/fundamental-research and all of the links under Resources. The links will help identify what could be considered a likely risk or not. If there are no or only minor issues identified those can be mitigated for Phase 1 of the program. If there are larger concerns, then it may not be possible for an individual to perform or major mitigations could be needed. This process is the same for all individuals regardless of nationality. For Phase Two of the program DARPA will do an additional security review and weigh that against the unique abilities of personnel supporting the teams we fund. Depending on our review an individual may have no restriction for working on CUI, or they may need to be restricted from working on CUI. With other possible mitigation put in place, it is also possible that an individual may be limited to only the portions of CUI that their team is generating.

FAQ: How does the new developments in Generative Optogenetics change hybrid biosecurity and cybersecurity risks and their national security implications?

This is an excellent question and one that DARPA intends to explore via the Biosecurity Working Group (BSWG) that will act as a program-wide resource for GO. As per the Program Solicitation for GO, DARPA plans to release a separate solicitation in the near future for organizations to establish

and manage three working groups focused on commercialization of GO technologies, regulatory issues surrounding potential applications of GO technologies, and biosecurity.