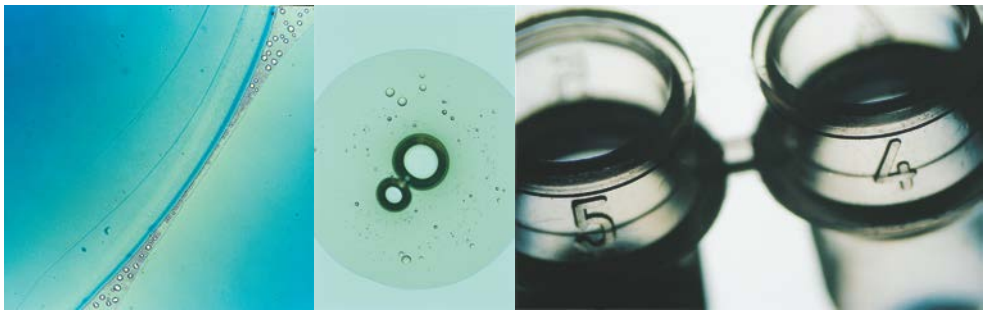
Centre for Defence Enterprise

Innate response targets for therapy

Competition networking event: Tuesday 25 March 2014, London
Competition close: Thursday 5 June 2014 at 17:00 hrs



The Centre for Defence Enterprise (CDE) proves the value of novel, high-risk, high-potential-benefit research sourced from the broadest possible range of science and technology providers, including academia and small companies, to enable development of cost-effective capability advantage for UK Armed Forces and national security.

Proposals for funding must be submitted by **17:00 hrs on Thursday 5 June 2014** using the Centre for Defence Enterprise Portal. Please mark all proposals for this themed competition with **"Innate response targets for therapy + challenge 1, 2 or 3"** as a prefix in the title (see 'Technology challenges' section below for a description of the challenges under this competition).

- **Technical queries** should be sent to cbrcde@dstl.gov.uk. Please see guidance on using this facility under the 'Queries and help' section below.
- **General queries** (including using the Portal) should be sent to CDE at cde@dstl.gov.uk.

CDE: www.science.mod.uk/enterprise
Dstl: www.dstl.gov.uk

SBRI Government challenges. Ideas from business. Innovative solutions.

[dstl] Defence Science and Technology Laboratory

Ministry of Defence

Innate response targets for therapy

Background

MOD has an interest in identifying host-pathogen interactions which can be manipulated in order to devise novel and generic therapies to meet the UK's current and future defence and security needs. Specifically, MOD is interested in ensuring the availability of therapies with broad activity against diverse microbial (bacterial and viral) challenges. Ideally, the solutions to such challenges will not be dependent on prior knowledge of the biothreat. To this end, we seek novel approaches to directing host responses for protection, therapy and survival.

The innate immune system provides a first line of defence against infection. Whereas pathogenic microbial challenges disrupt normal physiological function, the innate immune system aims to restore physiological equilibrium, in order to achieve repair and recovery. In some cases following microbial infection, the restoration of physiological equilibrium can take some time since it involves the clearing of apoptotic cells and the overcoming of a pro-inflammatory environment by the activation of anti-inflammatory host cells and pathways.

The host response to microbial challenge is complex and contains many checks and balances to prevent excessively prolonged disruption or the uncontrolled activation of pathways to generate a cytokine storm . As more is known about the subtle cellular interactions that underpin and control host responses, eg from transcriptomic and cell signalling and trafficking analyses, the potential for identifying new cellular targets or pathways for manipulation with new candidate therapies becomes apparent.

Novel approaches to the identification of new candidate therapies that beneficially direct or target host responses after a high-threat microbial challenge would strengthen UK defence and security. We are seeking novel approaches, in particular, to combat the pathogenicity resulting from inhalational exposure, followed by persistent intracellular infection which is resistant to antibiotic.

Technology challenges

The purpose of this CDE themed competition for short-term, proof-of-concept research proposals is to reach out to all sectors for highly innovative techniques, tools and approaches to facilitate the identification of therapies and the early stages of therapeutic development. It is envisaged that this will involve cutting-edge research that will advance the discovery of new therapies based on knowledge of the interaction of bacteria or viruses with host cells; the mechanisms used by highly pathogenic microbes to manipulate the host to their advantage; and the responses of host cells.

In this context, proposals are invited to address the following challenges. Proposals should address at least one of the challenges, could address more than one of the challenges, but do not have to address all the challenges.

Challenge 1 - Identification of new cellular or host pathway targets

In vitro and *in vivo* models of infection have identified some cellular targets and pathways involved in responding to and defending against infection. Here we are seeking proposals to address the challenge of identifying new host cell targets and pathways. This includes the conditioning of cells *ex vivo* or the targeting of cells *in situ* to redirect them, activate them or cause them to traffic or to traffic differently. This may involve, for example, the application of transfection factors, stimulants, modulators, chemokines, or cytokines, or the induction or blockade of chemokine/cytokine/growth factor receptors.

Alternatively, it may be possible to identify and exploit naturally occurring regulators to reduce inflammation and restore physiological equilibrium in appropriate models.

Proposals are invited for innovative approaches to identify new cellular targets or pathways and to demonstrate that they can be influenced for beneficial outcome, eg to prevent cytotoxicity, prevent or reduce microbial invasion, reduce microbial load and accelerate the restoration of normal cell functioning.

Challenge 2 - Identification of new candidate therapies

Here, we seek novel approaches to exploit knowledge about appropriate cellular targets and pathways, in order to identify new candidate therapies. This may revolve around (but is not limited to) examples such as enhancing cell-mediated immunity to clear intracellular infection, investigating novel combinations of therapeutic approaches, the identification of significant transcription factors, or the development of microRNA-directed therapies or antagonists. Ideally, the candidate therapies investigated should be druggable and generic (rather than personalised) and proposals should aim to show proof of concept. This challenge does not exclude the re-purposing or further augmentation of existing licensed therapies**.**

Challenge 3 – Identification of new generic platform technologies for assessing therapeutic benefit

Novel proposals are sought in this final challenge in support of challenges 1 and 2 above. Proposals would be welcome in (but not limited to) areas such as non-invasive methods of *in vivo/ex vivo* analysis (eg imaging or tracking) , transcriptomics including microRNA analyses and *in silico* modelling of host responses, or novel assays (*in vitro/in vivo*) to monitor the immune response.

What we want

In this CDE themed competition we are seeking:

- highly innovative approaches that are significantly different from existing technologies
- generic approaches (ie not pathogen-specific)
- approaches applicable to intracellular pathogens where appropriate
- approaches that will lead to a feasible clinical product.

What we don't want

We are not looking for:

- high technology readiness level (TRL) capability (TRL 6+) - proposals of TRL ≤ 3 are expected[1]
- serological (rather than cellular) targets only
- antibody-based therapies (this does not include antibodies as a targeting mechanism)
- existing solutions or technology that has already been tested and found to have limited utility
- proposals comprising a paper study, review or similar.

[1] For a description of Technology Readiness Levels (TRLs) see the Acquisition Operating Framework https://www.gov.uk/acquisition-operating-framework

- proposals for pre-exposure therapies or therapeutics
- topical therapies.

Exploitation

Each project will be assigned a Technical Partner in Dstl who will provide the interface between the project and the defence and security community and will, where appropriate, develop potential routes to exploitation, including exploitation outside defence if appropriate. Potential routes that could be available include additional research to develop or utilise the technology for MOD programmes.

Each project team will be invited to attend a stakeholder day, to be held at Dstl Porton Down, to present the outcomes from the project and review exploitation routes.

Dstl intends to take a number of the most successful projects forward for phase 2 funding. Up to £400k will be made available for this second phase and funding will be considered on a per-project basis.

Invitation for CDE proposals

This competition will be supported by presentations given at the Innovation Network event on Tuesday 25 March 2014. These will be available to download at: http://www.science.mod.uk/events/event_detail.aspx?eventid=297.

Proposals are invited from industry and academia in the UK and overseas for research that can demonstrate a proof of concept to meet one or more of the challenges for "**innate response targets for therapy**".

A total of £480k of funding is available for this competition.

There is no cap on the value of proposals but it is more likely that at this stage a larger number of lower-value proposals (eg £40k—£80k) will be funded than a small number of higher-value proposals.

Applicants to this CDE themed competition should detail in their proposal their consideration of the risk that their research could generate outcomes that could be misused for harmful purposes. Applicants should also detail in their proposal document what steps they will take to minimise the risks.

Proposals should focus on a short, sharp, proof-of-concept phase – typically, but not exclusively, 6-12 months in duration - with deliverables completed by September 2015 . Proposals can include a descriptive scoping for a longer programme of any duration but the proposal should be clearly partitioned with a costed proof-of-concept stage which is the focus of this CDE themed competition. Proposals for further work beyond the proof-of-concept stage will only be considered after the proof-of-concept stage has delivered, using the understanding gained to make an informed decision.

Proposals must include:

- a clear statement of what challenge the solution is aimed towards
- a clear description of what is novel and innovative in the solution
- a clear statement of the programme of work that would be carried out and the outputs (deliverables) from the work
- a clear statement of the expected outcome(s), how this will be proven or demonstrated and how it will provide evidence that the outputs can be exploited
- a clear description of the value of the solution to operational capability including the likely saving to through-life costs

- a statement on the anticipated practicality of adopting the proposed solution
- an outline of any data/equipment requirements of the proposal, and how these will be met. Any dependencies on the supply of data/equipment from MOD must be stated.

Proposals that do not include the required information are unlikely to be successful.

Proposals will be assessed by subject matter experts from MOD and Dstl using the MOD Performance Assessment Framework (PAF). Deliverables from contracts will be made available to Technical Partners and subject to review by UK MOD and wider government as appropriate.

Dstl will be available to provide advice and/or guidance via an appointed Technical Partner throughout the project and provide the interface with MOD and wider government stakeholder community.

Dstl does not commit to fund any follow-on work as a result of any contracts placed via this CDE themed competition, but more promising ideas will be considered for further funding where appropriate.

CDE proposal submission process

Key dates

- 25 March 2014 Competition networking event in London
- 1 April 2014 Post-launch webinar
- 5 June 2014 Competition closes at 17:00 hrs
- End of July 2014 Contract placement initiated and feedback provided
- By September 2015 Proof-of-concept research complete

Proposals for funding must be submitted by 17:00 hrs on Thursday 5 June 2014 using the CDE Portal. Proposals must be clearly marked with "Innate response targets for therapy + challenge 1, 2 or 3" as a prefix in the title.

Please plan the timeline for submitting your proposal carefully. If you have not used the CDE Portal before you will need to become familiar with the guidance, including how to open an account starting with the Quick Start Guide.

Other information and guides are available on the CDE website:

- General CDE advice: www.science.mod.uk/engagement/cde/working_with_cde.aspx.
- Contract & IPR guidance: www.science.mod.uk/engagement/cde/funding_contracts.aspx.
- Using the Portal: www.science.mod.uk/engagement/the_portal.aspx. The Portal is optimised for proposals based on physical sciences and engineering and we are aware that proposers sometimes struggle to adapt to using it with social science-based proposals. The key points (rather than the detailed questions) that are sought under the main headings still apply and further advice can be obtained from CDE.
- Presentation material giving advice on creating effective CDE proposals: http://www.slideshare.net/MOD_CDE/cde-creating-effective-proposals-part-1-of-2-final-na-u http://www.slideshare.net/MOD_CDE/cde-creating-effective-proposals-part-2-of-2-final-na-u.

Common errors in preparing and submitting a proposal include:

- **Character limit** – there is a limit of 1000 characters in each individual descriptive paragraph within the proposal; when completed they must be added to the document; additional paragraphs can be added if 1000 characters is insufficient.
- **It is a web-based tool** – please save your work regularly to avoid 'time-outs' that lose work.
- **Attachments fail** – They must be Word 97-2003 format, portrait format, should have generous margins with no material overhanging the margin and a max size of 1 MB. Please note that attachments should only be used for supplementary information, the main points of your proposal should be written into the online form. Care should also be taken to make sure that attachments are placed in the relevant section (eg technical information should not be attached to the commercial section).
- **Failing to properly submit** - **publish is not the same as submit**. You have **not** completed the submission process if your proposal is at the FINAL/PUBLISHED stage (in the status and published status columns respectively); CDE has no sight of the proposal at this stage. To complete submission you need to press 'submit' under the 'Tasks' column. This changes the status of your proposal to 'SUBMITTED'; it will then change (normally after a few days, often sooner) to 'RECEIVED' indicating that the proposal has been accepted by CDE for assessment.

For a proposal to be accepted for assessment:

- the standard terms and conditions of CDE must be unequivocally accepted
- there must be at least one deliverable against which payment can be made
- the commercial section of the proposal must be completed.

Do not leave submission of your proposal until just before the deadline. Past experience has shown that the Portal becomes heavily loaded near the competition close resulting in slow operation (up to one hour to publish rather than a few minutes) and that, with the pressure of the deadline, mistakes are made that mean proposals are not submitted or accepted.

All proposals and content placed on the Portal must be UNCLASSIFIED.

Queries and help

As part of the proposal preparation process, queries and clarifications are welcomed:

- **Technical queries** about this specific themed competition should be sent to cbrcde@dstl.gov.uk. ***Capacity to answer these queries is limited in terms of volume and scope. Queries should be limited to a few simple questions or if provided with a short (few paragraphs) description of your proposal, the technical team will provide, without commitment or prejudice, broad yes/no answers. This query facility is not to be used for extensive technical discussions, detailed review of proposals or supporting the iterative development of ideas. While all reasonable efforts will be made to answer queries, CDE and Dstl reserve the right to impose management controls when higher than average volumes of queries or resource demands restrict fair access to all potential proposal submitters.***

- **General queries** (including using the Portal) should be sent to CDE at cde@dstl.gov.uk.