Funding Opportunity Title: MCI-BCM Sponsored Target Screening
Funding Announcement: 2021-400
Open Date: September 1st, 2021
Submission Type: Open, rolling submission

Section I: Opportunity Description

Purpose: This opportunity will facilitate the screening of validated male contraceptive targets for small-molecule inhibitors using the DNA-Encoded Chemistry Technology (DEC-Tec) core facilities available in the lab of Dr. Martin Matzuk and Center for Drug Discovery at Baylor College of Medicine (BCM)[1].

Background: Nearly half of all pregnancies worldwide are unintended. Furthermore, current contraceptive options do not adequately meet the needs of users who desire contraception. Male Contraceptive Initiative (MCI), a US-based 501(c)3 nonprofit, is a funding agency and advocate for male contraceptive solutions that are effective, safe, reversible, and non-hormonal.

Research Scope

The purpose of this opportunity is to allow investigators with validated male contraceptive targets to utilize state-of-the-art screening facilities to identify “hit” molecules that bind to the target of interest. MCI and BCM have entered into a collaboration that allows identified research projects to utilize the DEC-Tec platform available at BCM to screen for small molecule ligands that interact with validated male contraceptive targets.

The ideal research project will screen against a protein target that is easily expressed and purified, and investigators will have established *in vitro* assays to measure inhibitory activity of potential hits. Ideal projects will also have plans in place to either directly develop hits into lead compounds for pharmaceutical development or use identified hits to attract ongoing / followup funding that builds towards a contraceptive development program inside or outside of an academic institution.

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[1] Yu, Z., Ku, A. F., Anglin, J. L., Sharma, R., Ucisik, M. N., Faver, J. C., Li, F., Nyshadham, P., Simmons, N., Sharma, K. L., Nagarajan, S., Riehle, K., Kaur, G., Sankaran, B., Storl-Desmond, M., Palmer, S. S., Young, D. W., Kim, C., & Matzuk, M. M. (2021). Discovery and characterization of bromodomain 2–specific inhibitors of BRDT. *Proceedings of the National Academy of Sciences*, *118*(9), e2021102118. https://doi.org/10.1073/pnas.2021102118

Examples of a validated target for the purposes of this announcement include, but are not limited to:

- Targeted deletion of a gene that results in infertility in an animal model without other observed adverse phenotypes
- Inhibited expression of the gene encoding the target through RNAi or another gene silencing method that results in infertility as demonstrated by a secondary method such as mating studies or *in vitro* fertilization
- Peer-reviewed citations and clinical evidence that a target is at minimum strongly correlated with infertility in men

Targets eligible for screening must fulfill a number of technical criteria to be screened via the DEC-Tec platform. Please see the DEC-Tec Introductory Target Form in Section III: Application Information for more details.

Applicants are encouraged to submit projects aligned with MCI Research Priority Areas, which include the following:

- Approaches that target the post-meiotic phase of spermatogenesis
- Approaches that target sperm functions required for normal fertilization, such as sperm motility and the acrosome reaction
- Approaches that target post-testicular processes required for fertility, including epididymal maturation and sperm transport in the excurrent ducts
- Other approaches that could lead to fast-acting, reversible male contraceptives
- Approaches with the potential to result in Multipurpose Prevention Technology (MPT) products that act against sexually transmitted infections

Applications in the following areas are considered outside of MCI interests and will not be reviewed:

- Contraceptives with a proposed female delivery system
- Approaches that permanently inhibit fertility

Institutions should be aware of and amenable to the intellectual property consideration outlined in Section II.

Some projects may be eligible for further development by BCM after hits are identified, with the goal of building long-term collaborations. Applicants interested in this approach are encouraged to speak with the program administrator for more details.

Section II: Award Information

Overview

Support will be provided for the screening of one contraceptive target using the DEC-Tec platform, wherein a submitting investigator, approved by both MCI and BCM, delivers purified protein to BCM that is then screened for interacting molecules. If identified, hit molecules will be assessed for activity by the applicant using established assays.

Submitting investigators are responsible for delivering purified protein to BCM according to the guidelines provided in the DEC-Tec Introductory Target Form found in Section III. After delivery, DEC-Tec selection scientists will perform selection experiments, provide quality DNA sequencing data, and generate a selection output report for review.

Timeline

After the DEC-Tec selection team determines that the quality of target proteins meets the requirements for selection experiment (typically one week), it will spend two weeks performing selection experiments and preparing samples for DNA sequencing. The turnaround time for a typical Illumina HiSeq run and data analysis at the BCM genomic and RNA profiling core and in the Center for Drug Discovery is 3-4 weeks.

Investigators will collaborate with the DEC-Tec team to test the activity of molecules in established assays as time permits. Subsequent steps such as refinement of hit molecules, in vivo assays, and so forth may be undertaken by either BCM or the submitting investigator, depending on capabilities, but are not part of the scope of this announcement.

Eligibility

This application is open to academic institutions, for-profit organizations, and other entities, foreign and domestic. Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as a Principal Investigator (PI) is invited to work with their organization to develop an application for support.

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

Current MCI grantees are eligible to apply for support through this mechanism.

MCI will not accept applications that are duplicate or highly overlapping grant awards from other funding agencies.

Other information

Applications will be accepted on an ongoing basis until award resources are exhausted. Up to 5 awards are expected in relation to this announcement.

There are no direct funds associated with this award. Any costs to applicants, including direct, indirect, institutional overhead, and subcontracting, are not reimbursable.

A Collaboration Agreement has been developed between BCM and MCI that outlines specific details such as project deliverables, commercialization, and intellectual property considerations. Successful applicants will be required to develop a separate Collaboration Agreement between BCM and the awardee institution. Applicants may request a copy of this Agreement before submission.

The following table is an overview of the intellectual property agreement developed between MCI and BCM. After hit confirmation further development may be initiated by the applicant, and is subject to the intellectual property considerations outlined in Table 1 as well as other considerations outlined in the aforementioned Collaboration Agreement. Should applicants not have the time, resources, or other ability to further pursue hits, in appropriate scenarios with agreement from all parties, downstream development may be initiated by BCM. This scenario is outlined in Table 2.

Table 1: **H2L work performed by applicant**

Phase of Work	Percent share of IP ownership		
	BCM	Applicant	MCI
Hit confirmed - First tangible asset	48	48	4
<------ Follow-on Activities (beyond scope of original partnership agreement) ---------->			
Hit Optimization	43	53	4
Lead Optimization	38	58	4

Table 2: **H2L work performed by BCM (e.g. if applicant does not have in-house chemistry capabilities)**

Phase of Work	Percent share of IP ownership		
	BCM	Applicant	MCI
Hit confirmed - First tangible asset	48	48	4
<------ Follow-on Activities (beyond scope of original partnership agreement) ---------->			
Hit Optimization	58	38	4
Lead Optimization	62	34	4

Section III: Application and Submission Information

How to Apply

Research Application:

Applications are to be submitted to grants@malecontraceptive.org. The application must be in pdf format, 11 point Arial font, with at least 0.5 inch margins.

Subject line must be: “MCI DEC-Tec Screening Application.”

Applications must include:

Section I:
Title Page (one page):

1. Applicant’s name, title, institution, and contact information
2. Collaborator’s (if any) name(s), title, institution, and contact information
3. Project Title
4. Research Abstract

Section 2:
Research Proposal (maximum 5 pages, including figures)

1. Background and Project Narrative: Key published and unpublished data underlying the proposed target and its potential to be developed as a male contraceptive. Include plans for how hit molecules will be evaluated for their activity *in vitro*. Include preliminary data

that supports the feasibility of assays to be used. Include the relevance of the methods and approaches to be used in evaluating the activity of identified hits. Include plans on how completion of the proposed studies will build towards a contraceptive development program; provide plans for how current, proposed and future research might lead to pre-clinical and subsequent Phase I clinical trials.

2. Completed DEC-Tec Introductory Target Form

3. References

Section 3:
Project Management (up to 2 pages)

1. Applicant's role and responsibilities in performance of proposed research

2. Roles of key collaborators (if any)

3. Novel or essential facilities, equipment, and resources available for proposed studies or followup studies and how they will be accessed if not available

4. Project evaluation: Expected outcomes should be listed in detail, measured by specific milestones, and allow for evaluation at least once quarterly. Milestones should be specific and clear in how progress will be demonstrated. It is expected that proposed milestones will follow the SMART framework (specific, measurable, achievable, relevant, and time-oriented).

Section 4:
Curriculum Vitae (up to five pages each for applicant and key collaborators, the NIH biosketch format is preferred.

1. Education, current and prior positions and appointments

2. Current and prior research experience, source and amount of current and prior research support

3. Publications relevant to application

Section 5:
Appendix (optional, up to 2 pages)
Supporting data, figures, or unique methods and materials.

Review

Process and Confidentiality

Applications will be reviewed for scientific and technical merit by an appropriate review panel assembled by MCI. All applications reviewed by the panel will receive a written critique, which will be anonymized and provided to the applicant as constructive feedback.

Reviewers will be subject to confidentiality agreements and asked to destroy, delete or return to MCI all copies of information acquired or created during the course of performing a review.

Applications that do not directly address research areas designated in the RFA description will not be considered for review. The panel will be advisory to the MCI Board of Directors which has the final responsibility for funding decisions. Reviewers will certify adherence to the Conflict of Interest and Nondisclosure Rules adopted by the National Institutes of Health.

The following considerations will be taken into account with funding decisions:

- Scientific and technical merit as evaluated by the review panel
- Availability of funds
- Relevance of the proposal to the goals and priorities outlined in the RFA description
- Relevance of the proposal to MCI Priority Research Areas
- Relevance of the proposal to a balanced MCI funding portfolio
- Readiness of the proposal and project to move into later stages of contraceptive development
- Some targets may be excluded based on factors such as a lack of validation, appropriateness for downstream development, and ongoing work

For questions regarding the grant and application requirements please see “Section V: Contact”. For awarded awards, MCI is required by the IRS to publish a list of its grantees. MCI also provides general descriptions of its awards on its web sites, in press releases, and in other marketing materials. Awardees may be asked to participate in promotional efforts by MCI, which may include interviews, outreach, and other publicity. These efforts will be voluntary, and will not impact the terms of the award.

Section IV: Award Administration

A formal notification will be provided to the applicant organization for successful applications. The notification will be signed by the awards management officer and will be sent via email to the successful applicant.

Before initiating activities, a formal agreement will be developed. A copy of the proposed agreement is available on request.

MCI expects selected applicants to work with MCI staff in establishing a specific milestone plan for subsequent, post-award steps that facilitate development of the project.

Any costs incurred are at the risk of the awardee, and are not reimbursable.

Progress Reports & Monitoring

Post-project funding opportunities from MCI may be available, and will be contingent on satisfactory progress, project viability, future research plans, and availability of funds. All awards and projects are eligible to apply to other MCI funding mechanisms as a part of potential post-project funding.

MCI may arrange for confidential meetings with consultants with relevant expertise to facilitate the development of products resulting from funded projects.

Awardees are responsible for submitting a Progress Report at the conclusion of the project period to grants@malecontraceptive.org. The Progress Report will be a confidential document and should be submitted in pdf format. It is to include:

Accomplishments (two pages maximum):

- What were the major goals and objectives of the project and what was accomplished for these goals?
- What were the benchmarks, were they met, and what is the evidence of successful research progress?
- Were there problems or delays or changes to original goals and objectives that require modification of research plans?

Open Access

MCI is committed to dissemination of published research resulting from project funds to enable unrestricted access and reuse of all peer-reviewed publications (“Open Access”). Grantees shall publish all publications in a manner that will permit all users of the publication to have Open Access so that any reader may have access to an article without further permission or fees being required. Applicants may request reimbursement of Open Access fees from MCI under select conditions.

Global Access

Any commercial exploitation of the Project shall be in keeping with MCI's mission and charitable purpose to ensure availability and access to male contraceptives for the relief of the poor, distressed, and underprivileged, the advancement of science, and the promotion of health by seeking to secure global access to new, low-cost drugs or devices (both therapeutics and prophylactics) ("Global Access").

Global Access requires that (a) the knowledge gained during the Project be promptly and broadly disseminated, subject to the need to file for patent protection on information arising from the Project, or other obligations of confidentiality as raised by any of the parties herein; and (b) best efforts are made to ensure that the intended product(s) be made available and accessible at low cost to people most in need within developing countries and public sector markets in developed countries.

Section V: Contact

Questions regarding any aspect of the award or award process are encouraged. Please contact:

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