

Request for Proposal (RFP)

On

‘Fundamental and innovative research in Cachexia Tuberculosis to address the needs and gaps in India’

प्रस्ताव के लिए अनुरोध (आरएफपी)

भारत में कैक्सिया ट्यूबरकुलोसिस की आवश्यकताओं और अभावों को दूर करने के लिए मूलभूत और नवीन अनुसंधान

Under Grand Challenges India (GCI),

Biotechnology Industry Research Assistance Council (BIRAC)
(A Government of India Enterprise)

ग्रैंड चैलेंजेज इंडिया के अंतर्गत (जीसीआई),

जैव-प्रौद्योगिकी उद्योग अनुसंधान सहायता परिषद (बीआईआरएसी)
(भारत सरकार का उद्यम)

Jointly funded by

Department of Biotechnology (DBT),
Ministry of Science and Technology, Government of India

&

Bill & Melinda Gates Foundation (BMGF)

संयुक्त रूप से वित्त पोषित

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&

बिल एंड मेलिंडा गेट्स फाउंडेशन (बीएमजीएफ)

I. Grand Challenges India

The Department of Biotechnology (DBT), Government of India, and the Bill & Melinda Gates Foundation (BMGF) signed a Memorandum of Understanding (MoU) in 2012, where both parties agreed to collaborate on scientific and technological research to alleviate some of the world's most critical global health and development issues, for the benefit of the people of India and other developing countries. Grand Challenges India (GCI), a Program Management Unit of this joint-partnership housed at Biotechnology Industry Research Assistance Council (BIRAC), New Delhi, seeks to identify opportunities to support studies focused on early-stage research and product development to tackle health and developmental issues with special emphasis on innovative, impactful research in existing strategies or creating completely new opportunities and pathways to the outcomes, sought on the broader global health and developmental challenges.

GCI specifically, focuses on encouraging research and exploring translational avenues across a range of health and developmental priorities ranging from Infectious Diseases, Non-Communicable Diseases, Drug discovery, Vaccines, Devices & Diagnostics, Therapeutics, Maternal & Child Health (MCH), Nutrition Research to Agriculture, WaSH among others.

Grand Challenges initiatives follow these core principles:

- i) Strategic and well-articulated grand challenges serve both to focus research efforts and capture the imagination and engage the world's best researchers.
- ii) Projects are selected based on national and societal need and transparent calls for proposals seeking the best ideas.
- iii) Funders, investigators and other stakeholders actively collaborate to accelerate progress and integrate advances to ensure these advanced technologies reach to developing countries masses
- iv) Projects are selected not only for scientific excellence, but also to achieve the desired impact, and these are milestone-driven and actively managed to that end.
- v) Projects and investigators will have to follow global access commitments to ensure the fruits of their research are available to those most in need.

GCI announces a call for proposals on 'Fundamental and innovative research in Cachexia Tuberculosis to address the needs and gaps in India' a program directed to encourage basic research studies aiming to improve knowledge in the field and addressing knowledge gaps in this important but neglected debilitating condition in tuberculosis pathophysiology and care.

This Request for Proposals (RFP) is specific to Indian researchers and collaborations are encouraged across the country where opportunity exists within the scope of study to build on established collaborations.

II. Program Overview

Tuberculosis (TB), a highly infectious disease continues to be a consistent global health concern in defiance of ongoing efforts to limit its incidence and associated mortality. India bears the largest share of global burden of TB cases as per WHO estimates, incurring significant

health and economic repercussions. Government of India has already announced the ‘National Strategic plan 2017-2025’ to eliminate TB from the country implying less than one case of TB per ten lakhs of population by 2025. Achieving this ambitious milestone demands accelerated involvement of all responsible stakeholders to implement commensurate actions. One of the aspects of TB free India program is to strive for comprehensive patient-centric efforts to improve treatment care and support cascade.

Recognising this challenge, GCI under the ambit of DBT-BIRAC and BMGF is launching a program on ‘Cachexia in TB’, one of the critical areas in TB treatment and patient-care where research efforts have been largely insufficient, thereby necessitate the boosting research and evidence generation across a spectrum of gap areas to explore the unresolved questions and potentially closing the gaps in TB care.

Background

Cachexia also known as wasting syndrome, is a debilitating physical emaciation that often leads to other complications, and profoundly impacts the disease severity and outcome in people with tuberculosis (TB). It has long been labelled as hallmark of TB and its presentations include anorexia, unintentional excessive weight loss, inconsistent muscle-mass wasting and depletion of functioning, inflammation and loss of quality of life. In spite of its immense individual and public health consequences, cachexia in TB often goes unnoticed and overshadowed by the clinical manifestations of the disease itself or confused with malnutrition.

Cachexia has multiple contributory factors and earlier investigations have recognized a complex relation between tuberculosis, nutritional status, inflammation and other host immune responses but the exact underlying pathophysiological mechanism by which cachexia manifests is poorly understood in tuberculosis. The prevalence of cachexia depends on the underlying disease and in the case of TB, its actual estimates are not available in the affected Indian population. There is no consensus on classification or treatment algorithm for cachexia management and thus, it remains an important health concern with limited therapeutic options. As India strive towards the ambitious goal of eliminating tuberculosis, it becomes imperative to identify and understand the research gaps and address the intricate interplay between TB and cachexia to uncover better patient-centric solutions for early identification, reducing mortality rates and improving response to treatments and care in TB.

The Challenge

Tuberculosis (TB) compounded by cachexia is distressing for patients that make treatments more challenging and result in poor prognosis and worse health outcomes. The clinical characteristics of cachexia are often confused with malnutrition and despite a major push in global and local strategies to eliminate TB, little attention has been extended to research in TB cachexia. There is a gravity of the knowledge gaps that needs investigations to provide better understanding of molecular mechanisms and solutions for cachexia management in TB. Addressing the research questions and unknown in TB cachexia will help in closing the gaps in care-cascade but this will require systematic and innovative research approach drawing upon the existing strengths in its science. **The objective of the program is to support consortia-**

based proposals consisting of motivated individuals or partners with strong scientific and technical background who will be able to utilise multidisciplinary approach to undertake quality research and innovative solutions in cachexia TB.

III. Scope of call

Grand Challenges India is soliciting research proposals in TB cachexia on following areas:

- i) *Address the basic gaps in knowledge:*
 - Proposals providing novel information and evidence on cachexia in people with tuberculosis, its susceptibility, probable mediators, factors and pathways responsible for initiating the cachexia in TB patients. Studies investigating the underlying metabolomic and genomic mechanisms, genetic, environmental and other risk factors enabling cachexia and its susceptibility, role of metabolome, anabolic hormones and nutritional enhancement and other exploratory mechanisms.
 - Studies assessing the available data from various ongoing nutritional supplementation programs for TB patients to evaluate links, if any, in cachexia susceptibility and its progression in affected populations. Investigations on the role of antibiotic treatments are encouraged.
 - Animal models to identify molecular mechanisms, role of microbiome and inter-organ cross-talk, cross-talk between host factors, infection and disease pathogenesis, clinical studies, possible role of metal ions homeostasis and diabetes (comorbidity) in TB.
 - Studies answering key research gaps on deregulation of host immune responses, that occur in cachexia TB and how does deregulation impact TB progression in patients and what could be the role of deregulation pathways in preventing or reversing cachexia.
- ii) *Identifying the innovative solutions:* Studies aiming to identify novel and specific biomarkers, early predictors, new or improved diagnostic tools and cachexia specific diagnostic panels will be supported under the call.
- iii) *Assessing the burden:* Proposals are sought on assessing the burden of cachexia in TB in the Indian population to generate evidence that can contribute to better strategies for treatment and patient care. Proposals evaluating the impact of addressing cachexia on disease progressions and treatment outcomes are encouraged.

While key research questions can vary for each research gap, we invite the collaborative research interests that combine complementary and synergistic research strengths as per above scope but not mandatory or limiting to these only. Proposals on relevant research question that are not listed in scope are also welcomed. Research proposals must provide a strong rationale for the work proposed, demonstrating a clear understanding of the problem in national context and needs, present a defined hypothesis and plan for undertaking the proposed work. Proposals must incorporate progress indicators clearly against each objective and timelines within the timespan of the grant. The roles and responsibilities all consortia-partners should be mentioned clearly.

IV. Program Structure

i. Eligibility Criteria

This RFA is India-led and consortia-based proposals are solicited from Indian nationals having good scientific record and working within the country in established academics, research institutions, medical research institutions, Indian companies, not-for-profit organizations, trusts, foundations. If selected for financial support, duration of the study will be 36 months subject to expert evaluation and milestone achievements.

- The proposal should have a clearly defined plan with details of proposed activities, specific milestones and timelines, a robust collaboration of partners and plan detailing the role and responsibilities of each partner, and the budget estimates.
- Research proposal must be budgeted clearly indicating the budget components to carry out each proposed activity on a milestone basis. Funding will be awarded for 3 years, subject to the applicant complying with agreed milestones. Funds will be released on achievement of each milestone.
- Research proposals will be supported financially at recognised academic institutions, universities, national laboratories, organisations and other recognized R&D institutions or organisation having all the necessary facilities to carry out the proposed research.
- Any existing IP needs to be mentioned with details in proposal.
- If selected, Investigators shall enter an agreement with BIRAC.
- Any change of Co-PI/partner or institution will have to be approved by GCI-BIRAC/DBT.
- The funding support shall be duly acknowledged when publishing/showcasing/presenting project particulars or outcomes in the manner as prescribed by BIRAC.

Note: Please read the following carefully to understand the category you will be applying under and the documentation that may be requested should your proposal be selected for further financial due diligence. This call is open to:

- i) In case of the applicant being an Indian academic scientist, researchers and Ph.D students (citizen of India) who must be willing to incubate at a recognized incubator submit a letter of intent for same.
- ii) Indian institution/ universities/ public research organization: Academic institutions established in India and having NAAC/ UGC/ AICTE or any equivalent recognition certificate or any other Public/Government supported organization; Non-profit organizations/ Government entities/ Institutes/ R&D Organizations will include Academic Research Institutes, Universities, Research Foundation, Medical Colleges and Institutes – both public and private who are valid legal entities such as Trust, Society or established under central or state statute.
- iii) An Indian Company is defined as one which is registered under the Indian Companies Act, 2013 and minimum 51% of the shares of the Company should be held by Indian Citizens holding Indian passport [Indian Citizens do not include Person of Indian Origin (PIO) and Overseas Citizenship of India (OCI) holders].

- iv) Limited Liability Partnership (LLP) incorporated under the Limited Liability Partnership Act, 2008 having a minimum half of the persons who subscribed their names to the LLP document as its Partners should be Indian citizens [Indian Citizens do not include Person of Indian Origin (PIO) and Overseas Citizenship of India (OCI) holders].
- v) Society/ Trust/ NGO/ Foundation/ Association established in India under the relevant Indian Law having at least half of the stakeholders (partners/ trustees/ members/ associates etc.) as Indians.

**Experts of the relevant discipline should be a part of the proposal such as healthcare professionals/clinicians, public health experts, scientists/researchers, statistician, data analytics experts, m-health specialists, management/logistics experts, M&E experts among others. Please note that the evaluation of eligibility shall be based on the status of documents as on the closing date of the call.*

ii. Project duration and grant

The projects will be supported for upto a period of three years (starting from signing of Agreement). This program aims to support consortia-based two projects and the funding level will be a grant of up to INR 4 crores (USD 500,000) per project that will be provided to the organization(s).

iii. Collaboration

GCI encourages collaborations based on the belief that synergies between experts across diverse disciplines are important for the challenges that we seek to address under this program. Should you wish to apply as a collaboration, please ensure that all investigators involved should be willing to collaborate and share experimental methods, data, and resources amongst each other and other members of the program consortium thus augmenting the abilities to compare and validate local research findings and/or develop interventions/solutions that can have impact

iv. Allowable Costs

The allowable cost will include following:

Non-Recurring Budget:

Equipment and accessories (upto 20% of proposed cost) list of equipment's, if required and justification in relevance to the project activities (Quotations supporting proposed equipment and accessories);

Recurring Budget (commensurate with project activities):

Manpower (upto 30% of proposed cost); Consumables (upto 20% of proposed cost); Travel; Research Contingency (On case-to-case basis); Outsourcing (In case any activity to be outsourced); Training cost if any; Overhead of each primary & other Cost recipients(s) (upto 10% of the recurring cost);

*Note: Justifications to be provided for roles of each manpower involved, consumables proposed, travel, training and research contingency. Budget heads without cap will be

considered on case-to-case basis and based on call specifics by Technical Advisory Group (TAG). The budget details should be provided separately for each involved collaborator/partner/Co-investigators.

v. Schedule

Call Opens	28 November 2023
Closure of Submission	3 rd January 2024; Online portal will close at 1600 hrs IST
Triage	January, 2024
Selection committee review and final selection	February-March, 2024
Award announcement	April-May, 2024
Process to initiate release of grants and study initiation	

V. Application Process and Instructions

i. Application Guidelines and Process

The proposals should be submitted online using online proposal submission portal on the BIRAC's website <https://www.birac.nic.in> under subject-line 'Cachexia Tuberculosis'. Prior to initiating the process of application submission, applicant should prepare the following:

- A research proposal clearly defining the scope of work, problem statement, rationale, summary of proposal, goals and objectives, methodology and implementation plan, deliverables and expected outcome;
- A description of how the proposed work will help in advancing knowledge in the field and possible translational value;
- Two-page Curriculum vitae of the PI, Co-PI(s)/partners highlighting academic and professional qualifications, total number of indexed publications, *h*-index (total and previous 5 years), fellow of academies, up to 20 important publication, patents, and achievements, link to web-research profile;
- Description of feasibility and available infrastructure and facilities to undertake proposed work;
- Details of Investigators/partners/collaborators and their clearly defined roles and duties, expertise and availability of host institutional expertise in relevant field;

The process of submitting the proposal online is detailed below:

- Go to BIRAC's website <https://www.birac.nic.in>
- Click on the 'Call for Proposal' and then 'Current Calls' tab in order to view the call detailed description.
- Click on the active call under subject-line 'Cachexia Tuberculosis' to submit your proposal on 'Fundamental and innovative research in Cachexia Tuberculosis to address the needs and gaps in India'.
- If you are already a registered user, then kindly enter your login credential at the below link in order to submit proposal: <https://birac.nic.in/login.php>

- If you are a new user then you need to register by clicking on tab ‘CLICK HERE TO REGISTER’
- Once you register, you will receive an auto-generated link on the registered email id entered at the time of registration.
- Once logged in, proceed to proposal submission.
- Write to Senior Program Manager at pmubmgf3.birac@nic.in regarding the queries about the application and submission of completed proposal.

Important Instructions

- Applicants are advised to fill-up and submit their applications early without waiting for the last date in order to avoid any last-minute contingencies. The online system will cease accepting applications automatically after 1600 hrs of the last date of submission.
- Applicants are advised to provide sufficient details in their applications to allow for an informed and fair evaluation/review.
- Applicants are advised to provide comprehensive information and other supporting materials can be provided as supplementary uploads.
- Requests for changes in the proposal once submitted will not be entertained.
- Applicants should read the guidelines for clear instruction and other details for comprehensive preparation of the proposal.
- Please read through the proposal in its entirety and ensure that your technical details, budget, and organization details are in compliance with the eligibility criteria provided.
- The proposed budget shall be made INCLUSIVE of all applicable taxes and shall be considered accordingly.
- Proposals that do not meet the eligibility criteria and/or do not fall under the scope of call will not be reviewed, regardless of other parameters.
- Applicants shall warranty that the statements and particulars contained in the full proposal and supporting documents are correct. They have to warrant that they are under no contractual restrictions or legal disqualifications or any other obligations which would prohibit them from undertaking the present Project, entering into any Agreement in this regard etc.
- We will not be able to provide individual feedback to applicants those who are not shortlisted under the call.

ii. Selection Process

Grand Challenges India (GCI) along with stakeholders’ team will screen the proposals for eligibility. If the application is found to be incomplete or not complying with the provisions described in the RFP, the application will be considered ineligible. After an initial triage, a subject expert review panel/ Technical Advisory Committee (TAC) established under the GCI partnership will evaluate the submitted eligible proposals.

Proposal will be evaluated based on evaluation criteria that will assess the novelty of proposed hypothesis, approach and methodology (realistic and clearly presented research plan, objective and methodology and proposed timelines), milestones, feasibility of proposal

components, organizational and investigator capabilities, collaborations and clearly defined collaborative arrangements, cost relevance to proposed work and value of research outcome.

- a. Post proposal review and legal eligibility check, the shortlisted applicants will be invited to present their proposals in detail to TAC.
- b. Pending financial and technical due diligence, the final awardees will be selected by the TAC.
- c. Once due diligence is successfully completed, award certificates will be awarded to the selected GCI applicants.
- d. PMU- BIRAC will then enter into separate funding agreements with successful GCI grant recipient(s) to govern the project terms and conditions and fund disbursement modalities.

iii. Evaluation and Decision-Making Criteria

Proposal Merit

- Does the proposal's approach align with the objective of RFP? Are the objectives, activities and milestones well defined?
- Does the proposal demonstrate usefulness of preliminary work for the proposed scope of work?
- Have the investigators provided an adequate description of the existing facility to understand their present capabilities?

Applicant

- Are the investigators or partners are competent to ensure the effective conduct of the proposed work?
- Do the investigators possess relevant capabilities and appropriate experience for the same?
- Do the investigators have any prior experience in the field?

Implementation

- Has the implementation methodology and work plan adequately detailed and realistic?
- Have the investigators provided clear metrics for monitoring project progress, including milestones and outputs expected timelines, budget?
- Has the applicant anticipated difficulties/risks that may be encountered? Have mitigation plans been considered in case of failure?

Budget Estimates

- Is the proposed budget reasonable in light of the defined scope of work? Have reliable references been provided for justification?
- Is the resource allocation across various stages, sufficient and appropriate?

Intellectual Property

- The applicant team should have the legal interests and the freedom to operate as related to IP, including consent from others where applicable.
- IP developed through this grant will be owned by and will be the responsibility of the applicant (unless stated otherwise) subject to pre-existing legal arrangements.

iv. Requisites for Funding

Successful proponents shall enter into necessary funding agreements. The fund disbursement will be subject to completion of required formalities by way of Grant-in-aid assistance and associated documentation. The fund recipient shall be accountable for fund utilization as per the sanction.

Fund Disbursement

The disbursement of funds for the research project will be carried out upon successful achievement of milestones. Disbursement will be done in four instalments as follows:

Signing of agreement	30%
1 st technical milestone	20%
2 nd technical milestone	20%
3 rd technical milestone	20%
Submission of final report	10%

Process of Sanction of Funding

- Site visits for Technical Due Diligence may be conducted (Physical/Virtual) however certified infrastructure pictures and details to be provided by the applicant to BIRAC as and when required.
- Financial Due Diligence (FDD) may be done on case-specific requirements as per BIRAC norms.
- After the final recommendation of the relevant applicable committee, application will be proceeded further for financial concurrence, legal concurrence and issuance of Agreement as per GCI/BIRAC/DBT norms.
- After successful execution of the above documents and fulfilment of other formalities, fund disbursement will be initiated by GCI/BIRAC/DBT.

Post Approval Review and Monitoring

The projects will be monitored and mentored regularly by a Project Review and Monitoring Committee (PRMC) constituted by GCI/BIRAC/DBT. On Successful completion of each Milestone, the investigator will be required to submit a detailed Milestone Completion Report (MCR) as per the prescribed format.

Contact Information

Further information can be obtained at BIRAC website. www.birac.nic.in

Write to us with the subject line 'GCI - Cachexia TB' at:

Dr. Shirshendu Mukherjee, Mission Director, Grand Challenges India,
Email: mdpmubmgf.birac@nic.in

Dr. Monica Sharma, Senior Program Manager, Grand Challenges India,
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Contact us

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संपर्क करें

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