



**Department of Biotechnology  
Ministry of Science and Technology  
Government of India**

**Request for Applications (RFA) on “Host directed therapies against TB”**

***Background:***

The Government of India has placed high priority for ‘TB Mukht Bharat’ by 2025, considering the high disease burden of Tuberculosis and associated societal and economic impact. Efforts are being undertaken by the Department of Biotechnology (DBT) to aid the country's vision of a TB free India. DBT has been supporting basic and applied research on TB over the past three decades with major focus on disease biology, drug discovery and vaccine development. The Department has launched Data Driven Research to Eradicate TB –“**Dare2eraD TB**”, an umbrella TB program of DBT on World TB Day.

To address the increasing need for new and potent therapeutic options against TB and in order to reduce the duration of TB treatment, alternative approaches are being explored. Host-directed therapy (HDT) is one such approach which aims at reducing inflammation/ modulating autophagy/ potentiating the immune response or creating an unfavourable intracellular milieu for the pathogen. This may be achieved in a variety of ways which include use of repurposed drugs; vitamins; monoclonal antibodies; cytokines; recombinant proteins or cellular therapy for disease amelioration or clinical cure. Recent work on host-pathogen interactions suggests that adjunctive therapy with host-directed agents could lead to shorter treatment and improved outcomes for drug-sensitive and multidrug-resistant TB. HDT agents may decrease local inflammatory tissue pathology and the resulting bacterial sequestration from antibiotics and immune effector cells. They may allow dormant bacilli to re-activate or cause changes in their metabolic state, which in turn, increases their susceptibility to TB drugs. Host directed adjunct therapy offers the advantage of being agnostic of the anti-TB drug regimen being used for a patient; considerable shortening of the existing TB drug regime and associated side effects and issues of quality of life post treatment; and very low probability of emergence of drug resistance. Host directed therapies against Tuberculosis thus offer an exciting opportunity for developing newer & better treatment regimens against this age-old disease.

### ***Scope of this Call:***

The Department of Biotechnology invites applications under the Data Driven Research to Eradicate TB –“**Dare2eraD TB**” program, for developing and advancing host directed therapies against Tuberculosis. The purpose of this RFA is to support research proposals for lead optimization, preclinical studies, development of clinical trial protocols and conduct of proof-of-concept clinical trials for TB treatment using host- directed agents. Of particular interest will be proposals aimed at shortening of TB therapy using adjunct host-directed therapies.

Types of agents (alone or in combinations) that could be studied include small-molecule agents that:

- Enhance bactericidal mechanisms, macrophage Mtb killing
- Reduce bacillary growth by creating unfavorable intracellular milieu
- Modulate destructive pro- inflammatory responses, reduce immune-pathology and improve lung function/ protection from tissue damage
- Strengthen immune clearance of TB
- Improve effectiveness of antimicrobial therapy
- Disrupt structures and penetrate granuloma to expose Mtb to anti-TB treatment

The proposal must include brief description of the proposed host directed therapy agent; rationale for the choice and a clear hypothesis stating the proposed mechanism by which, the identified HDT agent could lead to shorter treatment and improved outcomes for drug-sensitive and multiple drug-resistant TB. The proposals must be backed by strong preliminary data. Exploratory proposals and proposals aimed only at elucidating mechanistic details of host-pathogen interaction in TB or using surrogate systems such as *M. smegmatis* for evaluating HDT are beyond the scope of the current grant call.

### ***Eligibility criteria:***

#### **i. Eligible Organizations**

- a. Central/State Govt. Institutions of higher education and research.
- b. Private Institutions of higher education and research.

#### **ii. Required Registrations**

- a. The institution must be recognized by DSIR as a Scientific and Industrial Research Organization (SIRO).
- b. Private institutions/ NGOs should also be registered with Darpan Portal, Niti Aayog.

### ***Proposal contents:***

Proposal should be written with clearly defined objectives, work plan, expected outcomes in terms of quantifiable targets, tentative budget estimates and biodata of the investigator/s giving details regarding the expertise along-with the list of relevant research papers in the proposed research area. Applications lacking clearly defined milestones and timelines will be deemed incomplete.

### **Evaluation Criteria**

Applications would be evaluated for scientific and technical merit following the DBT Competitive Research Grant System guidelines. Reviewers will consider each of the review criteria listed below for decision making:

1. **Significance:** Does the project qualify in terms of scientific, technical, or medical significance and originality of the proposed research; appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research.
2. **Investigator(s):** Are the PI(s), collaborators, and other researchers well suited to the project? Early Stage Investigators or those in the early stages of independent careers should have proven record of appropriate experience and training. Established investigators are expected to have demonstrated credentials for accomplishing project objectives. Collaborative or multi-PD/PI are expected to have complementary and integrated expertise.
3. **Approach:** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?
4. **Environment:** Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed?

### **Mode of Selection:**

Proposals received will be screened and short-listed for funding support by the Technical Expert Committee- Infectious Disease Biology/ DBT Apex Board as per the Competitive Research Grant System Guidelines of DBT.

### **Mode of Submission:**

Proposals should be submitted online **only** in the DBT R&D format through DBT eProMIS (<http://dbtepromis.nic.in/Login.aspx>) under Area-‘Infectious Disease Biology-1: Bacterial & Fungal’ clearly stating ‘Against Call for Proposals’.

**For any queries please contact:**

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**Timeline:**

Call for Proposal opens: 1.08.2022

Call for Proposal closes: 15.09.2022