Fast Track Funding Opportunities for Translational Immunology Approaches to COVID-19

Focus areas:

- **Cell based approaches for treatment or prevention of COVID-19 and associated disease sequelae**
- **Biologics or small molecule based modulation of immune system for therapy or prevention**
- **Immunogenetics and molecular epidemiology based population studies on COVID-19**
- **Novel diagnostic approaches for patient stratification and risk assessment for severity of sequelae.**

Background: The entire world today is facing the greatest pandemic in a century caused by a novel coronavirus, Sars-CoV2 which has caused the disease COVID-19. The disease originated in China and spread worldwide, including India. The disease is characterised, in its most severe form, by acute immune responses that appear to render the patient susceptible to cytokine release syndrome and acute respiratory distress. However, there appears to be vast differences between patients that succumb to the disease and those who remain asymptomatic, further suggesting the key role that the host immune defence systems play. As the disease counts rise in India, it is of utmost importance that we understand thedynamics of the disease process better, identify at-risk population, develop alternate immunomodulatory agents that could be helpful in treating severe forms.

Currently, there are over 78 vaccine and over 600 therapy related trials taking place around the world. To address these gap in treatment options for the Indian population, the **Indian Council of Medical Research (ICMR) invites full proposals (in ICMR Ad-hoc Project format) for fast track fundingfor Translational Immunology and Cellular Therapeutics approach targeting COVID-19.** This call aims to fill the gaps in research thrust in India by providing emphasis on the above focus areas which require more attention to address the needs for the increasing patient base.

Proposals: Research proposals are invited in the following areas focused on the theme of mission modetranslational immunology:

- **Cell based approaches for treatment or prevention of COVID-19 and associated disease sequelae:**

The immune system is composed of various kinds of cells which need to be harnessed correctly in order for treating COVID-19. Approaches that harness this potential in various ways to modulate the infection process, alter severity of the immune sequelae or prevent the viral infection process including studying differential responses of different groups of patients, clinical outcomes, etc can be proposed. Proposals may cover novel genetic and non-genetic modifications of immune cells for therapy, but must clearly indicate which aspect of the disease – viral infection or propagation, immune response or exaggerated immune outcomes does the therapy target.

- **Biologics or small molecule based modulation of immune system for therapy or prevention**

The immune system is regulated by a variety of secreted factors which in turn modulate the immune cells or local parenchymal cells to establish the disease process. Understanding this modulation and harnessing key aspects using antibodies, recombinant proteins or specific immune targeting modulators in order to treat COVID-19 can be proposed. Studies on virus-host immune system interactions, including biochemical and molecular biology aspects may also be proposed. Investigators are urged to identify the molecular process and indicate which stage or aspect of the disease will their approach address. It should be noted that vaccine approaches can also be included here with clear definition of the process of vaccine development and the rationale of the expected immune response.

- **Immunogenetics and molecular epidemiology based population studies on COVID-19 – consortium approach**

It remains unknown why certain proportions in the population are at risk of high morbidity and mortality. While many clinical co-morbidities are being associated with COVID-19 such as hypertension, diabetes, AIDS, cancer, lung diseases, etc, the exact molecular basis is not understood fully. Further, in the general population, why certain subgroup with same exposure and co-morbidities remain asymptomatic, mildly symptomatic or require ICU care is not understood. The answer may lie in inherent genetic differences in their

immune system genes or their epigenetic regulation. The proposals in this area should include large numbers to reflect the breadth of the affected population in the disease. Investigators in the area are strongly urged to form consortia with multiple hospitals and diagnostic centres to have a large affected population cohort targeted genetic study proposals. Broad generalised sequencing proposals are not encouraged.

- **Novel diagnostic approaches for patient stratification and risk assessment for severity of sequelae.**

Currently, a variety of COVID-19 tests are already available that determine the viral genome from mucosal membrane swabs. While a variety of antibody tests are also available in the market, there is a lot of confusion regarding efficacy of such tests given the high percentage of asymptomatic population and the fact that detectable antibodies typically develop later in the disease. Therefore, diagnostic approach proposals will have to describe their novelty in terms of process, sensitivity, specificity, strength of risk stratification and scalability.

- ✓ All proposals must clearly define how samples are to be obtained, safety and documentation of sample collection process, transport and usage in the lab must be defined as per current COVID-19 sample handling guidelines issued by RCGM/DBT.
- ✓ Proposals requiring isolation of live virus and or testing of live virus mediated viral functions against a therapeutic agent must demonstrate access to verified BSL-3 facilities. They must also include the detailed SOPs for the same and obtain local IBSC and EC approvals prior to fund release.
- ✓ The proposals are expected to clearly outline and test a path towards translation into human application as therapy, prevention, diagnosis or stratification.
- ✓ If pre-clinical animal models cannot be used prior to the trial, the same must be clearly justified in the proposal.
- ✓ Proposals must address both efficacy and toxicity aspects of the therapeutic approach.
- ✓ Proposals involving human clinical trials must describe cGMP production, toxicity testing and scalability of the therapeutic product as per drug manufacturing regulations and will require approval from CDSCO.

- ✓ Additionally, immunologic readouts should be part of the study design to evaluate the therapeutic approach.

Study duration: All studies should be for a period of not more than 24 months given the urgency of the global health situation.

Criteria for application: The proposals should adhere to the focus areas and disease areas described. Collaborations between institutes and between research and clinical teams are encouraged. Investigators are encouraged to work with hospitals that have access to patients. The scientific team should have demonstrable expertise in the areas of disease focus and immunology. Proposals must be written in the English language and clearly titled in the ICMR format. Project descriptions and style should conform to ICMR guidelines and have all requisite approvals and permissions required.

Timeline:

- Launch of call date: 21st April 2020
- Project Submission Ends: 1st May 2020
- Announcement of Successful Projects: 10th May 2020
- Project(s) are expected to start in June 2020 and should complete latest by the end of May 2022.

Eligibility: All scientific institutions, including Universities, DSIR certified institutes and laboratories are eligible.

Review process: The applications will be screened for technical correctness. Thereafter, each proposal will be reviewed for feasibility of the techniques proposed, scientific applicability of the approach for disease, novelty of experimental design or delivery, clarity in experimental design, demonstration of prior experience/preliminary data, achievable milestones and timelines and potential for clinical translation.

To submit a proposal to ICMR:

Interested applicants are required to email the detailed proposal to txim mun.icmr@gmail.com The guidelines and format for preparing the proposal,kindly refer to following link http://icmrextramural.in/ICMR/

For further information contact:

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Call for Letter of Intent for Participation in: Therapeutic Plasma Exchange in COVID-19: Protocol for a Multi-center, Phase II, Open Label, Randomized Controlled Study

Disclaimer

Therapeutic Plasma Exchange (TPE) is an experimental procedure for critically ill COVID-19 patients. Hospitals and Institutions planning to provide this modality of treatment should do so in a clinical trial with protocols which are cleared by the Institutional Ethics Committee. The protocols should be: -

1. Registered with the Clinical Trial Registry of India (CTRI: http://ctri.nic.in/Clinicaltrials/login.php).
2. They should be approved by Drugs Controller General of India, Central Drugs Standard Control Organization (https://cdsco.gov.in/opencms/opencms/en/Home).
3. Mechanisms to report adverse and serious adverse events to the CDSCO should be put in place.

At this moment ICMR does not recommend this as a treatment option outside of clinical trials.

ICMR is inviting a letter of intent from institutions with the equipment and infrastructure available to participate in a clinical trial to study the safety and efficacy of therapeutic plasma exchange in COVID-19 patients, subsequent to necessary approvals and clearances.

Institutions which are interested to collaborate with ICMR on undertaking this trial intervention, may express their interest by providing the details through the following link: https://forms.gle/7AaW528DMQbNZsUr9

For further details please contact:

Dr. Anup Agarwal

Email: mailanupagarwal@gmail.com

Therapeutic Plasma Exchange in COVID-19: Protocol for a Multi-center, Phase II, Open Label, Randomized Controlled Study

Primary Objectives

- To assess the efficacy of TPE in improving the clinical status of COVID-19 patients.
- To evaluate the safety of treatment with anti SARS-CoV-2 plasma in patients with COVID-19.

Study Design

- Multi centric, two arm, prospective, phase II, open label, randomized controlled trial.

Study Population

- Hospitalized COVID-19 patients who are critically ill, fulfill the inclusion and exclusion criteria, and are admitted for care at COVID-19 management facilities in India will be eligible for inclusion in the trial.

Intervention

- Therapeutic plasma exchange for critically ill COVID-19 patients

Primary Outcomes

- Composite primary outcome of improvement in clinical status and respiratory support needed.

For further technical details, please contact:

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