Guidelines for implementation
Bilateral collaborative research Call for proposals 2024
Inserm – ICMR

Theme: "Vascular complications of Diabetes"

Deadline for the submission of expressions of interest (phase 1): Monday, 15th April 2024 5:00PM IST.

In accordance to Article. 2.5 of their joint Memorandum of Understanding (MoU) renewed in March 2022, the Institut National de la Santé et de la Recherche Médicale (Inserm) and the Indian Council of Medical Research (ICMR), collectively referred to as the Parties, have decided to launch a joint call for proposals on Vascular complications of diabetes.

1) Theme of the call:

Vascular complications of Diabetes. Please refer to the scientific background document and research areas for the details**- Annexure-I**.

2) Stages of the call for proposals:

The call will be scheduled in two phases:

- Expression of Interest (phase 1)
- Submission of a full application (phase 2)

3) Eligibility:

The call for proposals is open to:

- Researchers from Inserm teams (Principal Investigators must be statutory researchers);
- Scientists/faculty members working in regular capacity in Universities, National R&D laboratories/Institutes and Private R&D Institutes in India.

4) Number of selected Expressions of Interest, number of selected projects and duration of the projects:

The Parties will select up to 6 (six) Expressions of Interest, at the end of the first phase.

The Parties agree to fund up to 2 (two) joint research projects through this call for proposals.

The duration of the projects is set for 3 (three) years.

5) Funding:

Each party will cover the project funds of their respective PIs.

Inserm will:

- Allocate up to 20.000€ (twenty thousand euros) per year for 3 years to each selected applicant. Eligible expenses include travel, equipment and operating costs (excluding salaries).
- Support a 2-year post-doctoral contract within an Inserm laboratory.

ICMR will:

- Provide funding to each selected project to a maximum ceiling of Rs. 2.0 crore[1] for 3 years, depending upon the requirement and budget justification of the proposal.

6) Contents of the Expressions of Interest: A single PDF file of max. 4 pages should be submitted, which must include the following sections:

i. Background and Research Question
ii. Added value of the scientific collaboration
iii. Preliminary budget

In addition to the above, a CV (one page) of the Indian and French PI should also be submitted.

►Please complete the attached Expression of Interest form

Applicants must pre-identify a partner institution. If necessary, applicants are invited to reach out to Inserm/ICMR well before the deadline for phase 1 of the application in order to identify a partner institution.

7) Evaluation and selection:

The evaluation of the Expressions of Interest and full applications will be done separately and concurrently by ICMR and Inserm.

The Parties agree on the following common review criteria:

i. Strength of PI;
ii. Novelty/ Excellence and innovative nature of the project;
iii. Rationale of the project;

[1] Approximately 220 000€

iv. Possible impact on Health outcomes;
v. Feasibility of the project;
vi. Justification for foreign collaboration/ Team complementarities and added value of the collaboration.

The final selection of the projects will be operated by a joint selection committee meeting.

8) Reporting:

A joint midterm/annual/final scientific report (including a financial report) as applicable will be requested from the two Principal Investigators.

9) Intellectual property – Publication/communication:

9.1 Selected applicants are requested to duly address the intellectual property of the potential outcomes of their research cooperation according to their institutions' regulations and national laws.

9.2 Due acknowledgement of the Parties' support should be disclosed in any publication by the Parties derived from the cooperation initiated through the call for proposals.

10) Ethical issues:

The ethical issues will be deal in accordance with the extant laws, rules and regulations of respective country.

11) Open access:

In line with national and institutional open science policy, scientific publications from selected and financially supported scientific projects must be published in open access journals or, at least, the accepted author manuscript (AAM) of the publication must be deposited in the national open archive HAL.

12) Planned schedule of the call for proposals:

- 15th April 2024: Deadline for the submission of expressions of interest (phase 1)
- Mid of May: Announcement of the selected proposals (phase 1)
- Mid-July 2024: Deadline for submission of full applications (phase 2)
- Beginning of October / beginning of January: Announcement of the selected projects and start of the projects.

13) Submission of expressions of interest:

Identical expressions of interest must be submitted simultaneously to both the contacts below:

- For Inserm: Ms. Agnès Kergus, Department of National and Foreign Affairs (agnes.kergus@inserm.fr)

- For ICMR**:** Dr Tanvir Kaur, Scientist G, Non Communicable Diseases (NCD), Division, ICMR (eoi.ncdicmr@gmail.com)

14) Contact information: Any questions regarding the call for proposals should be submitted to the following addresses:

- For Inserm: Ms. Agnès Kergus, Department of National and Foreign Affairs (agnes.kergus@inserm.fr)
- For ICMR:
  Dr. Harpreet Sandhu, Head, International Health Division, ICMR
  (sandhuh.hq@icmr.gov.in)
  Dr Tanvir Kaur, Scientist G, Non Communicable Diseases (NCD Division, ICMR
  (eoi.ncdicmr@gmail.com)

Annexure-I

Introduction and background:

Diabetes mellitus, a chronic metabolic non-communicable disease, has attained epidemic proportions worldwide. Type 2 diabetes mellitus (T2DM) is one of the greatest health crises of the 21st century, as the number of people with T2DM is projected to increase by >50% by 2045.

There are currently close to 101million people with diabetes in India, and this number is expected to increase to 124 million by 2045. Rapid socioeconomic development and demographic changes, along with the increased susceptibility of Indian individuals, have led to a rapid increase in the prevalence of diabetes mellitus in India over the past four decades. There are considerable differences in diabetes prevalence between states in India. ICMR-INDIAB study showed evidence of an epidemiological transition, with a higher prevalence of diabetes in low SES groups in the urban areas of the more economically developed states. The spread of diabetes to economically disadvantaged sections of society is a matter of great concern, warranting urgent preventive measures. The overall prevalence of diabetes in all states of India is 7·3% (4.3%-10%). The overall prevalence of pre-diabetes is 10·3% (6.0-14.7%) and the prevalence of impaired fasting glucose was generally higher than the prevalence of impaired glucose tolerance. ICMR-INDIAB study demonstrated that rural-to-urban migration is associated with an increased risk of developing diabetes and other cardiometabolic abnormalities. Adoption of healthier lifestyle patterns among migrants could help prevent/delay the onset of these abnormalities in this population. Interestingly, T2DM in Asian-Indian people is characterized by a young age of onset and occurrence at low levels of BMI as compared to European populations.

In France, the prevalence of T2DM is currently 8%, which is close to the average of 10.5% of the adult population worldwide, but increasing at an alarming rate, mainly afflicting low-income and vulnerable segments of the population and exposing patients to reduced expectancy and quality of life. Whereas T2DM has long been classically a disease of the elderly, obesity in childhood and young adults is now causing T2DM at an earlier age representing a major threat for a rise of T2DM complications in the next decades. The prevalence of pre-diabetes (fasting glucose higher than 6.1mM) has also increased from 9.9% in 2014 to 14.2% in 2018. T2DM is the first cause of blindness, amputations and end-stage renal failure in France. Therefore, T2DM complications have disastrous consequences in terms of health costs, societal impact, increased unemployment in middle age and early mortality (36% of 30- to 69- year-old mortality). The cost of T2DM and complications is €68 billion annually in France and thus weighs heavily on health expenses.

T2DM also increases the risk of stroke, cognitive disorders, cancers, liver diseases, osteoarthritis, and musculoskeletal diseases (sarcopenia and osteopenia). Recently, T2DM has been uncovered as a critical vulnerability factor in infectious diseases, such as COVID-19, with a deleterious role of endothelial dysfunction and microvascular disease. Notably, 90% of T2DM patients suffer from at least two comorbidities during their lifetime, and half of them already suffers from one comorbidity at diagnosis. Over 65 years, T2DM patients have 6.5 associated complications. Large healthcare records show that 40% of cardiology patients are diabeticMicrovascular abnormalities lead to a metabolic shift in the liver and the adipose tissue, favouring nonalcoholic fatty liver disease (NAFLD). NAFLD affects up to 70-80% of T2DM patients and increases the risk of developing microvascular complications, such as cardiovascular and chronic kidney disease (CKD), independently of hyperglycemia. The adipose tissue in T2DM induces a chronic low-grade inflammation characterized by increased infiltration and activation of innate and adaptive immune cells. Likewise, platelet dysfunction during T2DM is the cornerstone of resistance to antiplatelet agents, activation of coagulation, hypofibrinolysis and endothelial dysfunction. In addition, T2DM is associated with other inflammatory diseases such as gout or rheumatoid arthritis.

Available data suggest that the susceptibility of Asian Indian people to the complications of diabetes mellitus differs from that of white populations. The prevalence of chronic diabetes complications ranges from 4.8–21.7% for retinopathy, 0.9-62.3%% for nephropathy, and 10.5-44.9% for neuropathy. Asian Indian people with T2DM tend to have a higher risk of coronary artery disease and, possibly, a lower risk of microvascular complications compared with white individuals.

All diabetic complications are typically preceded by an asymptomatic period, ranging from months to decades, in which silent transformations are happening in the metabolism and functioning of cells leading to abnormal interorgan cross-talk. Hence, it is important to study

this silent period of disease progression before the onset of clinical disease to gain an understanding of its etiology and discover predictive or prognostic biomarkers of diabetic complications such as diabetic kidney disease, cardiovascular disease or diabetic retinopathy.

2. Objective of the joint call

The joint call for expression of scientific interest will focus on vascular complications of T2DM to develop scientific collaborations between French and Indian research laboratories.

The call will capitalize on existing cohorts, phenotyping data and biobanks in India and France, enabling original intercontinental comparisons and scientific collaborative exchanges.

Preclinical models will help exploration of innovative mechanistic pathophysiological hypotheses.

The scientific proposal may include the following research areas:

a. Deciphering the relationship between changes in retinal vascular features (using deep learning algorithms-AI) and the occurrence of macular edema and retinal proliferation. Evaluating the genetic make-up for Hypoxia-inducible factor (HIF) or other major novel pathways and retinal vascular stability in patients with early onset diabetic retinopathy and those with late-onset retinopathy. Specific DNA methylation markers for non-proliferative and proliferative in diabetic retinopathy. Can regression of diabetic retinopathy be correlated with specific genetic or epigenetic markers?

b. Deciphering mechanisms of increased risk of metabolic disorders in children from mothers with gestational diabetes and of increased youth onset of T2DM

c. MicroRNA expression profile in patients with and without microvascular complications and role of serum metabolome profile in patients with/without microvascular complications. Genetic, epigenetic and other biomarkers of lipid dysmetabolism /inflammation in identification of novel clusters of T2DM with varying risk of complications along with biomarkers of vascular calcification and vascular ageing and cardiovascular risk in T2DM.

d. Urine proteomics or metabolomics to identify patients at high risk of development of diabetic kidney disease. Epigenetic modifications and genetic studies to understand difference between proteinuric and non-proteinuria Diabetic Kidney Disease.

e. Development and validation of the best animal and non-animal preclinical models of diabetic complications and groundbreaking experimental approaches to decipher causative pathophysiological mechanisms.

Bilateral Collaborative Research Call for proposals 2024

Inserm – ICMR

Theme : "Vascular complications of Diabetes"

Expression of Interest Form

*To be sent to the contacts below before Monday, **15th April 2024** 5:00PM IST*

DOCUMENTS REQUIRED

- **The Expression of interest form, duly completed, in PDF version (4 pages max.)**
- **Short CV (one page) of the French principal investigator (from Inserm)**
- **Short CV (one page) of the Indian principal investigator**

The documents must be attached one after the other in one (1) single PDF document. An identical copy of the documents in PDF version must be submitted by email to the following two coordinators:

Inserm - Department of National and Foreign Affairs (DPRE) **Agnès Kergus :** agnes.kergus@inserm.fr	**ICMR - Non Communicable Diseases (NCD), Division** **Dr Tanvir Kaur :** eoi.ncdicmr@gmail.com

TITLE OF THE PROJET

PRINCIPAL INVESTIGATOR - INSERM		
Last name and first name	**Inserm Unit**	**Email address**

PRINCIPAL INVESTIGATOR - INDIA		
Last name and first name	**Institution**	**Email address**

CO-INVESTIGATORS- INSERM			
Last name and first name	**Inserm Unit**	**Title**	**Email address**

CO-INVESTIGATORS FROM INDIA			
Last name and first name	**Institution**	**Title**	**Email address**

1. BACKGROUND AND RESEARCH QUESTION

2. ADDED VALUE OF THE SCIENTIFIC COLLABORATION

3. PRELIMINARY BUDGET

Signature of the principal investigator from France (Inserm)	**Date**

Signature of the principal investigator from India	**Date**