

**Job offer – Phd in Molecular and Cellular Biology**  
(For non-French scientists only)

**Research Project Short Title as Submitted to CEFIPRA:** “Rational design and functional validation of topologically associated domain (TAD) boundary sequences”

**Principal Investigator contact (Name and email id :** Dr. Thomas Sexton, I.G.B.M.C. - Institut de génétique et de biologie moléculaire et cellulaire, University of Strasbourg, [sexton@igbmc.fr](mailto:sexton@igbmc.fr)

**Reference Number of the Job Offer:** IFI\_CEF\_25\_12

**Project description**

- **Keywords :** TADs, chromatin architecture, machine learning, insulators, stem cells, transcription
- **Context :** 3D organisation of the eukaryotic genome is critical for compressing genetic material inside the small volume of a nucleus, while facilitating proper cellular functions including gene regulation. The genome is physically organised into topologically associated domains (TADs), where the region within a TAD is more likely to interact with itself than with other parts of the genome. TADs are evolutionarily conserved, implying their importance for genome function, although their link to transcriptional control remains unclear. Similarly, mechanisms underlying formation or disruption of TADs are also not fully understood, although their disruption has been associated with different diseases including cancer. While there is evidence of some transcription factors (TFs) binding preferentially at boundaries, particularly CTCF in mammalian species, motifs for these are neither sufficient nor necessary for TAD formation. Furthermore, tested genetic loci demonstrated highly variable sensitivities to deletions of such motifs; the sequence grammar of TAD boundaries thus remains unresolved.
- **Abstract of the Research Project :** We propose combining the strong expertise of the French PI in the area of 3D chromatin organisation with the expertise of the Indian PI and Co-PI in the area of regulatory sequence analysis and machine learning to determine the genetically encoded basis of TADs. Specifically, we will develop a de novo sequence-based model to distinguish between TAD boundaries and other genomic regions from existing high-resolution genome conformation data (Hi-C and Micro-C). Our preliminary results indicate that both probabilistic and deep neural models show predictive power in identifying TAD boundaries. We will expand further on these models and validate them experimentally with a functional knock-in screen established in mouse embryonic stem cells. This proposal thus has the potential for the rational design of synthetic, tissue-specific TAD boundaries.
- **Scientific Objectives of the Project :**
  1. How much of a TAD boundary is “hard-wired” in the DNA sequence? Is there
  2. a minimal sequence capable of making an invariant TAD border?
  3. Is there a specific sequence “grammar” for CTCF-independent TAD borders?
  4. How much can TAD boundaries be tuned by nearby functional outputs, such as transcription?
- **Methodology and Timeline of the Project :** 3 years PhD project: Clone candidate boundary sequences (direct from mouse, mutated variants, and synthetic designs) into constructs that can be knocked in with FLP-mediated recombinase-mediated cassette exchange into a reporter mouse embryonic stem cell line. Effects on transcription and chromatin topology are assessed by allele-specific qRT-PCR and 4C-seq, respectively, and the results are iteratively fed into the collaborators’ machine learning algorithms to predict newer generations of boundaries.

## Candidate profile

- Candidates can be all nationalities except French. In case of double nationality (French and another one), the candidate is not eligible. In the context of CEFIPRA, Indian candidates are preferred
- Applicants for post-doctorate must have a PhD degree (or be in the process of obtaining one);
- No competences in French language is required
- Candidate competences: training in molecular biology, experience with mammalian cell culture, understanding of bioinformatics principles and capabilities.
- Candidate know-how: strong organizational, interpersonal, and communication skills, advanced analytical reasoning, autonomy, rigor, responsiveness, versatility, and a collaborative team spirit.
- Expected starting date: 01-09-2025
- Expected duration: 36 months

## How to candidate ?

Documents to be provided :

- i. A cover letter (reasons for the candidature, professional project ...) max 2 pages
- ii. A copy of the master's degree or a proof of the program followed (and expected date of end) OR A copy of the PhD degree or a proof of the PhD program followed (and expected date of defense) max 1 page
- iii. A copy of results for previous scholarship (max 3 pages)
- iv. International curriculum vitae (max 2 pages)
- v. Two letters of recommendation: one from any Indian institution and one from the French institution planned to host the candidate –mandatory- (max 2 pages)
- vi. All should be submitted within 1 pdf file of no more than 10 pages.

Applications should be submitted to the following email address: [msi@ifindia.in](mailto:msi@ifindia.in) mentioning the reference number of the Job offer clearly.

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**Candidates are requested to contact the French scientific principal investigator of the project before submission. A recommendation letter from the scientific principal investigator is mandatory.**

**Benefits:**

- Monthly allowance of 1790 euros for PhD
- Travel allowance
- University fee
- Carte de séjour fee
- Campus France management fee
- Registration to the French social security scheme

**Selection process:**

Selection is made by a dedicated selection committee of at least 4 persons. Decisions will be transmitted by the Embassy of France to CEFIPRA. **No consideration will be given for candidates with no recommendation letter from the French institution.**

**Criteria for applicants' selection:**

Academic excellence

- Excellence of the Academic background, Academic records, Honors, Letters of support, Participation to international research projects, exchange programmes and conferences.

Motivation and qualities

- Academic maturity: appropriation of the thesis project (stakes and contexts) • Quality of the presentation (oral expression, skills for synthesis, English level) • Maturity of the professional project: capacity to project her/himself within five years in terms of career development.

**About CEFIPRA:**

Indo-French Center for the Promotion of Advanced Research (CEFIPRA/IFCPAR) is an Indian body which promotes scientific cooperation between France and India in advanced fields of Science and Technology. It is supported by the Department of Science and Technology, Government of India and the Ministry of Europe and Foreign Affairs of the French government