NOTICE OF OPENING OF AN INTERNATIONAL CALL FOR THE SELECTION OF A PhD HOLDER RESEARCHER UNDER DECREE-LAW NO. 57/2016

Internal code: Researcher/FCT_COMPETE_2025/i3S/0406/2025

A call is opened for the position of a PhD holder, for an unfixed term work contract to carry out research duties within the project "**Functional profiling of nucleotide alterations in pancreas regulatory sequences to predict Type 2 Diabetes risk**", with reference COMPETE2030-FEDER-00731800, Operation 16163, funded by COMPETE2030 and national funds (FCT), under the Call for Applications No. MPr-2023-12.

Scientific Area: Functional Genomics

1. Project summary and work plan

Type 2 Diabetes(T2D) is considered a pandemic of the 21th century and is caused in part by pancreas dysfunction. Like many other diseases, T2D has a genetic contribution and is related to nucleotide alterations (NucAlt) in enhancer sequences active in the endocrine pancreas. As a consequence of NucAlts, enhancer's target genes are dysregulated, propagating changes in downstream gene networks and impacting in cell function.

Indeed, Genome Wide Association Studies for T2D have shown that single nucleotide polymorphisms are more prevalently located in the non-coding genome, therefore affecting more frequently the regulatory genome, including enhancers, than coding sequences. Unfortunately, it is yet very poorly understood what are the consequences of NucAlts in enhancer sequences, how they impact target gene's expression and how ultimately impair cell function by disrupting gene networks. This is what we aim to achieve in the RegAlt-T2D project.

The RegAlt-T2D project addresses extremely important challenges at several levels. The outermost level is the problem of identifying the genetic background of Type 2 Diabetes (T2D) susceptibility. We will approach to this problem by: (a) focusing this study on regulatory sequences of the transcription (enhancers), since the large amount of putative regulatory sequences that overlap with T2D associated allels strongly suggest that these sequences are key players in T2D risk; (b) Using a novel approach, we will decipher the impact of enhancer's sequence alterations in function, which is currently vastly more challenging to predict than in other regions of the genome (e.g. coding sequences); (c) Using advanced computational methods to analyze a finite cases of enhancer's sequence alterations and its respective impact in genes' function, we will build models that will predict the impact of any sequence variation in the selected studied enhancers. The RegAlt-T2D project will be a proof-of-principle to a next generation type of study to create more accurate models that will greatly improve the prediction of T2D risk.

The RegAlt-T2D project also addresses a more internal level of challenges, applying novel concepts and going beyond the state-of-the-art. One of the main challenges is to

INSTITUTO DE INVESTIGAÇÃO E INOVAÇÃO EM SAÚDE
UNIVERSIDADE DO PORTO
Rua Alfredo Allen, 208
4200-135 Porto
Portugal
+351 226 074 900
info@i3s.up.pt
www.i3s.up.pt

obtain functional information from alteration of enhancer sequences without disturbing or separating them from their endogenous genomic landscape. This approach contrasts with most of the currently available state-of-the-art assays (e.g.MPRAs; 9, 10), that isolate enhancers and clone them in reporter constructs to infer the impact of nucleotide alterations in the enhancer's function. These assays do not take into consideration locus specific compensatory or synergistic mechanisms within enhancers landscapes and use reporter genes as a proxy for the impact in the target gene expression, which is an unreliable approximation. RegAlt-T2D project goes beyond these limitations.

2. Applicable Portuguese legislation
Decree No. 57/2016, of August 29 – Legal Framework for Scientific Employment (RJEC) – in its current version.
Portuguese Labor Code, in its current wording.

3. Jury
Chairman: Jose Bessa; Other Members: Alexandra Moreira and Margarida Santos Saraiva; Substitute: Elsa Logarinho.

4. Workplace
i3S - Rua de Alfredo Allen, 208 Porto, research group Vertebrate Development and Regeneration.

5. Professional category and monthly remuneration
Junior Researcher Level 2.
€ 2.622,58, corresponding to index 38 of the Tabela Remuneratória Única.

6. Obligatory requirements for admission
a) PhD degree in Regulation of Gene Expression or a related area;
b) Motivation Letter in English;
c) Relevant publication record, appropriate for the career stage;
d) Animal-research authorization: FELASA Category C (or equivalent) certificate;
e) Extensive hands-on expertise in molecular biology, cell culture and bioinformatic analysis of custom NGS datasets;
f) Fluency in written and spoken English;
g) Good teamwork and interpersonal skills;
h) Immediate availability to start the contract (to be referred in the motivation letter).

Additional preferential skills (not mandatory but valued):
a) Advanced knowledge in transcriptional cis-regulation with demonstrated experience in functional evaluation of enhancers;
b) Hands-on experience in Massive Paralel Reporter Assays using lentivirus systems;
c) Extensive experience in lentivirus production;
d) Hands-on experience in zebrafish genetic manipulation (transgenesis and mutagenesis);

INSTITUTO DE INVESTIGAÇÃO E INOVAÇÃO EM SAÚDE
UNIVERSIDADE DO PORTO
Rua Alfredo Allen, 208
4200-135 Porto
Portugal
+351 226 074 900
info@i3s.up.pt
www.i3s.up.pt

e) Hands-on experience in High-throughput genome editing.

7. Evaluation of the applications and publication of the results

The evaluation of the scientific and curricular background of the candidates should focus on the activity of the last five years that the candidate considers most relevant. The five-year period may be extended by the jury, at the candidate's request, when justified by suspension of scientific activity for socially protected reasons, namely for reasons of parental leave, prolonged serious illness, and other situations of unavailability for work that are legally protected.

Weight of the different curricular valuation criteria:

a) Detailed Curricula (80%);
b) Motivation Letter in English (10%);
c) Interview - *facultative* (10%).

If the jury decides to obtain further clarifications and additional information about the curricular elements presented, the 2 best candidates classified on the basis of the curriculum may be called for an interview.

Candidates who submit their application incorrectly or fail to meet the required qualifications for this competition will be excluded from admission.
The jury reserves the right to request any candidate, in case of doubt, to provide supporting documents for their statements.

False statements made by candidates will be sanctioned in accordance with the law.

The jury will draw up minutes of its meetings, which can be consulted at the candidate's request within 10 working days after the selection results are released.

The jury deliberates by means of a reasoned vote according to the evaluation criteria, with no abstentions allowed, and draws up a list of excluded and admitted candidates, ordered by respective classification.
All candidates are notified of the selection results by email. After notification, candidates have 10 working days to comment.

In the 90 days following the deadline for submission of applications, the jury's final decision is communicated to the candidates. Subsequently the institute Director, who is also responsible for the final decision of hiring, will ratify the decision of the jury.

This call is intended exclusively to fill the indicated position on offer and may be canceled before the final ranking list of candidates is ratified by the Director. Accordingly, the position will no longer be available.

8. Submission of applications

Applications must include all the documents proving that they fulfill the admission requirements, namely:

INSTITUTO DE INVESTIGAÇÃO E INOVAÇÃO EM SAÚDE
UNIVERSIDADE DO PORTO

Rua Alfredo Allen, 208
4200-135 Porto
Portugal
+351 226 074 900
info@i3s.up.pt
www.i3s.up.pt

a) Copy of PhD degree certificate or diploma;
b) Detailed Curriculum Vitae;
c) Motivation Letter in English, stating availability to start duties on 16/07/2025;
d) Animal-research authorization: FELASA Category C (or equivalent) certificate;
e) Other documentation relevant for the evaluation of qualifications in a related scientific area;
f) Contacts of two references. These will only be contacted during the interview stage.

The submission of applications is digital, in pdf format, from 04/06/2025 to 18/06/2025, in the following link:

https://dozer.i3s.up.pt/applicationmanagement/#/addapplications/21cc2cba42813eca1da9596dcbecbd4a

9. Start and duration of the contract

The anticipated start date of the contract is 16/07/2025 and is subject to budget availability. The expected duration of the contract will be 12 months, potentially extendable up to a maximum of 18 months.

10. Non-discrimination and equal access policy

i3S actively promotes a policy of non-discrimination and equal access. No applicant shall be privileged, benefited, prejudiced, or deprived of any right or exempted from any duty on the basis of ancestry, age, gender, sexual orientation, marital status, family situation, economic situation, education, origin or social condition, genetic heritage, reduced work capacity, disability, chronic illness, nationality, ethnic origin or race, territory of origin, language, religion, political or ideological beliefs, or trade union membership.

Within the framework of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers, i3S adopts the Open, Transparent and Merit-based (OTM-R) principles for the recruitment of researchers, with the aim of conducting fair and transparent recruitment processes, bringing equal opportunities to all candidates.

11. Applicants with disabilities

Under the terms of Decree-Law 29/2001, of February 3, the candidate with a disability is given preference in equal ranking, which takes precedence over any other legal preference. Candidates must declare under oath their degree of disability, the type of disability and the means of communication/expression to be used in the selection process, under the terms of the aforementioned decree.

INSTITUTO DE INVESTIGAÇÃO E INOVAÇÃO EM SAÚDE
UNIVERSIDADE DO PORTO

Rua Alfredo Allen, 208
4200-135 Porto
Portugal
+351 226 074 900
info@i3s.up.pt
www.i3s.up.pt