



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_COM/i3S/1505/2025

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 "Neurotoxic Alpha-SYNuclein Oligomers: potential biomarkers and drug targets in Parkinson's Disease", with reference COMPETE2030-FEDER-00690800, funded by Fundação para a Ciência e tecnologia IP.

Scientific Area: Basic medicine - Neurosciences

1. Project summary and work plan

The protein alpha-synuclein (aSyn) is found mutated in familial cases of Parkinson's disease (PD) and is a major constituent of the Lewy body inclusions characteristic of PD. Although aSyn is intrinsically disordered, it can adopt different conformational states and self-assemble into different oligomers that, in some cases, predate the formation of amyloid fibrils. Unlike the aSyn aggregates on-pathway to form amyloids, off-pathway aSyn oligomers remain largely unexplored both as therapeutic targets and possible biomarkers of PD.

We serendipitously discovered a new type of neurotoxic aSyn oligomers (NASYNOS) that is formed in vitro without chemical additives and under physiological-like conditions. NASYNOS formation is catalyzed by the presence of glass beads due to a surface-induced change in aSyn conformation. Interestingly, NASYNOS are selectively proteolyzed by transthyretin (TTR), a transport protein with a neuroprotective role in Alzheimer's disease. Moreover, we found that even small amounts of NASYNOS are toxic when added to cell models of neuron function and differentiation, an effect that is rescued using inhibitors of aSyn aggregation previously discovered by us. Two imperative questions now arise: are NASYNOS also found in vivo? can NASYNOS' inhibitors be used as disease-modifying agents?

To answer these questions a workflow for quantification of different proteoforms of aSyn will be established using, e.g., conformation-specific antibodies available in our labs, and recombinant TTR to selectively proteolyze NASYNOS. A cross-sectional study will be performed to test for the presence of NASYNOS in biological samples from patients and healthy controls. Finally, rodent models showing aSyn-dependent toxicity will be used to test the efficacy of our inhibitors in vivo. By opening new avenues for the understanding, diagnosis and treatment of PD, we will contribute to lightening the heavy socioeconomic burden associated with this disease.

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

Chair: Isabel Cardoso; Other Members: Sandra Ribeiro, Pedro Martins; Substitute: Rosário Almeida, Pedro pereira.

4. Workplace

i3S - Rua de Alfredo Allen, 208 Porto, research group research group Biomolecular Structure & Function.

5. Professional category and monthly remuneration

Junior Researcher Level 3

€ 2.956,03, corresponding to index 44 of the TRU.

6. Obligatory requirements for admission

- a) Highly motivated candidates with Post-Doc experience in Biochemistry and Biophysics or a related discipline;
- b) Strong hands-on experience in protein production and purification;
- c) Previous relevant experience on (i) the biophysical characterization of aSyn and TTR and (ii) biomarker development based on protein aggregation;
- d) Holders of a FELASA accredited course, functions A, B and D, and previous relevant experience on the use of animal models of PD;
- e) Relevant publication track record in international peer-reviewed journals, preferably in Chemistry and Biophysics fields;
- f) Motivation Letter in English, in which it indicates immediate availability to start the contract;
- g) Fluent in spoken and written English;
- h) Good teamwork and interpersonal skills.

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 (85%):
 - a. Strong hands-on experience in protein production and purification; (25%)
 - b. Previous relevant experience on (i) the biophysical characterization of aSyn and TTR (ii) biomarker development based on protein aggregation and (iii) use of animal models of PD; (50%)
 - c. Participation in research projects (10%)
- b) Motivation Letter in English (5%)
- c) Interview – *optional* (10%)



If the jury decides to obtain further clarifications and additional information about the curricular elements presented, the 3 best candidates 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:

- a) PhD degree in / Copy of certificate or diploma;
- b) Detailed Curriculum Vitae;
- c) Motivation Letter in English.

The submission of applications is digital, in pdf format, from 15/05/2025 to 28/05/2025, in the following link:

<https://dozer.i3s.up.pt/applicationmanagement/#/addapplications/7c42aa6ff962d4f9a913785567919ad>

9. Start and duration of the contract

The anticipated start date of the contract is 01/07/2025 and is subject to budget availability. The duration of the contract will be 12 months, eventually extendable.

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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.