National Research Foundation (NHRF) Vasileos Konstantinou 4811635, Athens Tel. +30 210.72.73.516 email: grammateia@eie.gr

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NHRF/ICB ERA CHAIR PROF. KASTRITIS ESTABLISHES THE FIRST CRYO-EM PIONEER. LABORATORY IN SOUTHEAST EUROPE



We offer ERA CHAIR-funded positions: COORDINATORS | PH.D. STUDENTS | POST-DOCS

Cutting-edge research on the structural analysis of biomacromolecules. The first-of-its-kind research direction in the whole region.

A laboratory with 4 cryo-EMs, top biochemistry and extensive computing.

Open call for expression of initial interest: The ERA Chair lab in NHRF/ICB offers attractive management positions in grant coordination & EU-funded research positions in cryo-EM and/or computational structural biology. TAKE ACTION

INFORMATION/APPLICATION "send your motivation letter and CV panagiotis.kastritis@bct.uni-halle.de **OPEN CALL** https://blogs.urz.uni-halle.de/kastritislab/

Funded by the European Union hot4cryo, GA: 101086665 "ERA Chair Holder to establish the electron cryo-microscopy analysis of cellular and artificial nanomachines



Open call for initial expression of interest for the staffing of the Cryo-electron Microscopy Laboratory *ERA Chair*

National Research Foundation, Institute of Chemical Biology Scientific Leader: Jun-Prof.-Dr. Panagiotis Kastritis [ERA Chair].

Goal:

Hot4cryo aims to attract and maintain a prominent researcher (ERA Chair) together with a highguality supporting team to advance multidisciplinary research in the National Hellenic Research Foundation (NHRF) by founding the high-resolution electron cryo-microscopy Unit for Excellence, i.e. CryoUNITe, unique in Greece, the Balkans, and Southeast Europe. While cryo-EM technology is transforming international research in exciting, multiple directions, substantial disparity exists in its possession across European countries and is absent in the complete Southeast Europe. This hampers innovations in biomolecular and materials structure research and development and limits progress of EU Missions Cancer, Soil, and Green Deal, which align to the research directions of NHRF and the prospective ERA Chair Holder. Hot4cryo plans to address this issue, aims to eliminate this disparity, and envisions to urgently transmit the "resolution revolution" to Greece and the wider region, emerging as a cultural hub for seeding Horizon Europe's strategic plan across players and the society. CryoUNITe will be embedded in NHRF, enhancing institutional structural transformations. Hot4cryo will bring high-end cryo-EM knowledge for a wide range of systems in alignment with ERA priorities. The modern technology and innovation potential involved will undoubtedly progress digital transformation within NHRF, improve research cohesion across all involved partners, and foster fundamental and applied research opportunities of outstanding quality. As a result of this action, hot4cryo will produce a Unit of Excellence, improve direct access to excellence for partners and collaborators and strengthen the interactions between science and society. Ultimately, hot4cryo will contribute to reverting the current brain drain to "brain gain" while promoting brain circulation within the EU, positively affecting local and regional economies. [https://cordis.europa.eu/project/id/101086665]

Research Focus:

Enzymopathies are metabolic disorders, often genetic, resulting from missing or defective enzymes. In order to prevent, combat or repair defective enzymes that lead to disease, it is vital that we understand the structure, function and interactions of enzymes and their complexes, ideally within their native cellular context. In their native cellular environment, enzymes are neither isolated nor randomly distributed. Instead, they co-compartmentalize, and often transiently interact to form supercomplexes of metabolic pathways (commonly referred to as metabolons). The formation of metabolons allows the intermediate product from one enzyme to be passed directly into the active site of the next consecutive enzyme of the metabolic pathway. Their role and existence were biochemically known for years but due to their sheer size and transient nature, understanding their molecular organization remains a challenge. As a consequence, traditional structural biology methods have helped us in understanding the structure and function of their constituent enzymes but not their higher-order assembly and how their interfaces are formed. My research vision is to understand the molecular architecture of metabolons by integrating structural, biophysical, biochemical and biocomputational methodologies. This multidisciplinary approach aims at elucidating the molecular mechanisms that underpin cellular respiration in atomic details. In the long term, these methodologies will allow discerning cellular metabolons by visualizing their components and examining the interactions between the molecules that form the assemblies. This research will ultimately provide new crucial insights not only to cellular respiration but also an entirely new view of cell mechanisms in general. The unsolved mystery of temporal and spatial synchronization of a myriad of protein subunits to perform a specific cellular function may be rationalized by the formation of supercomplexes. These unprecedented entities provide a whole new avenue for targeted drug design. Rather than targeting the active sites of individual subunits -which share many physical and chemical characteristics thus compromising specificity-I envisage a therapeutic strategy that targets the interface between proteins in the supercomplex that are likely to be unique. [https://blogs.urz.uni-halle.de/kastritislab/]



Positions:

At all levels at the Institute of Chemical Biology, NHRF, Athens, Greece: **Management**, **PhD** student level, post-doctoral researcher level, other types of scientists

References:

- *i.* Enabling cryo-EM density interpretation from yeast native cell extracts by proteomics data and AlphaFold structures. Tüting C, Schmidt L, Skalidis I, Sinz A, <u>Kastritis PL</u>. **Proteomics.** 2023 Apr 4:e2200096. doi: 10.1002/pmic.202200096.
- ii. Cryo-Electron Microscopy Snapshots of Eukaryotic Membrane Proteins in Native Lipid-Bilayer Nanodiscs. Janson K, Kyrilis FL, Tüting C, Alfes M, Das M, Träger TK, Schmidt C, Hamdi F, Vargas C, Keller S, Meister A, <u>Kastritis PL</u>. Biomacromolecules. 2022 Dec 12;23(12):5084-5094.
- *iii.* Cryo-EM structure of the SEA complex. Tafur L, Hinterndorfer K, Gabus C, Lamanna C, Bergmann A, Sadian Y, Hamdi F, Kyrilis FL, <u>Kastritis PL</u>, Loewith R. **Nature.** 2022 Nov;611(7935):399-404. doi: 10.1038/s41586-022-05370-0. Epub 2022 Oct 26.
- iv. Cryo-EM and artificial intelligence visualize endogenous protein community members. Skalidis I, Kyrilis FL, Tüting C, Hamdi F, Chojnowski G, <u>Kastritis PL</u>. Structure. 2022 Apr 7;30(4):575-589.e6. doi: 10.1016/j.str.2022.01.001. Epub 2022 Jan 31.
- Cryo-EM snapshots of a native lysate provide structural insights into a metabolonembedded transacetylase reaction. Tüting C, Kyrilis FL, Müller J, Sorokina M, Skalidis I, Hamdi F, Sadian Y, <u>Kastritis PL</u>. Nat Commun. 2021 Nov 26;12(1):6933. doi: 10.1038/s41467-021-27287-4.
- vi. Integrative structure of a 10-megadalton eukaryotic pyruvate dehydrogenase complex from native cell extracts. Kyrilis FL, Semchonok DA, Skalidis I, Tüting C, Hamdi F, O'Reilly FJ, Rappsilber J, <u>Kastritis PL</u>. Cell Rep. 2021 Feb 9;34(6):108727. doi: 10.1016/j.celrep.2021.108727.

Necessary qualifications:

Management: University degree, experience in management

Ph.D. students: Degree and Master's degree in Biology, Chemistry, Informatics, Materials science, Physics, Engineering, relevant thesis.

Post-docs: Research in proteins, biomacromolecules, structural biology or similar subject evident by publications, relevant knowledge of methods.

Other types of Scientists: Any level of education in natural sciences, relevant experience

Contact:

Please send Dr. Panagiotis Kastritis (**panagiotis.kastritis@bct.uni-halle.de**) an email with the following, ideally in English:

- [Last name] initial expression of interest for the staffing of hot4cryo lab [position]
- CV and cover letter and specific position targeted.

