THE CYPRUS INSTITUTE OF
NEUROLOGY & GENETICS

# PhD Topics

## Academic Year 2026–2027

PhD Applications Deadline: 15 July 2026

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# Message from the Dean

Dear Applicants,

It is my great pleasure to introduce the PhD research opportunities offered by the Cyprus Institute of Neurology and Genetics (CING) for the Academic Year 2026-27. Through this booklet, I warmly invite you to explore the available PhD positions and research topics, and to consider joining our vibrant and ambitious scientific community. At CING, we are deeply committed to advancing science that not only pushes the boundaries of knowledge but also benefits patients and the society. As a PhD student at CING, you will be immersed in a stimulating, interdisciplinary, and highly competitive research environment. You will work alongside dedicated scientists and clinicians who are experts in their respective fields and deeply committed to mentoring the next generation of scientists. Our PhD programmes are designed to promote a rigorous research culture, intellectual curiosity, scientific integrity and equip you with the skills and confidence needed to thrive in an increasingly demanding global job market.

Beyond academic training, your doctoral journey at CING will be a formative personal experience. You will become part of a scientific community, develop lifelong professional skills, and build friendships and collaborations that extend beyond your studies. Our graduates have pursued successful careers in academia, research institutes, healthcare, and industry, both in Cyprus and internationally. You can learn more about our students' experiences here.

This booklet is intended to provide prospective doctoral candidates with a comprehensive overview of the available PhD topics, the hosting departments, and the research supervisors. The listed PhD topics reflect the multidisciplinary character, breadth and rigor of our research environment. I encourage interested candidates to review these opportunities carefully and identify topics that align with their research interests and priorities. We look forward to welcoming motivated and talented researchers at CING.

Dr Petros Petrou
Dean

# T5: Cholinergic Modulation of Memory Circuits in Alzheimer's Disease Models Using Chronic Neural Recordings

**The topic is eligible for the following Programmes:**

PhD in Neuroscience
PhD in Molecular Medicine
PhD in Medical Genetics

**Hosting Department / Group:**
Cognitive Neuromodulation Group

**Contact Persons:**
Dr. Georgios Keliris

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**Mode of Study:**
Full Time

**Project Plan for years 2, 3 & 4:**

**Year 2 — Foundations**
- Training in stereotactic surgery, DREADD targeting, chronic Neuropixels implantation.
- Set up and optimize automated cue-based memory task environment.
- Train wild-type mice and establish baseline neural and behavioral metrics.

**Year 3 — Cholinergic Modulation Experiments**
- Activate or inhibit basal forebrain cholinergic neurons using hM3D(Gq)/hM4D(Gi) DREADDs
- Perform longitudinal recordings during memory acquisition, retrieval, and consolidation.
- Quantify changes in oscillatory signatures (theta/gamma, coupling), ensemble dynamics, and task performance.
- Apply the protocol to AD model mice.

**Year 4 — Alzheimer's Disease Model & Biomarkers**
- Test the extent to which cholinergic enhancement rescues memory deficits or circuit disruption.
- Extract neural biomarkers predictive of improved memory performance.
- Prepare manuscripts and complete thesis.

**Abstract**:
Cholinergic neuromodulation is a central regulator of memory and cognitive flexibility, and its disruption is strongly implicated in Alzheimer's disease (AD). This PhD project will investigate how manipulating cholinergic output influences memory performance and neural circuit dynamics in freely moving mice. Using well-established memory paradigms delivered in a controlled behavioral environment, the student will quantify short-term and working-memory performance while recording neural activity longitudinally with chronically implanted Neuropixels probes.

Basal forebrain cholinergic neurons will be selectively activated or silenced using Cre-dependent DREADDs, allowing precise modulation of cholinergic tone during learning, retrieval, and consolidation. Comparisons between healthy mice and AD models will reveal whether increasing cholinergic drive can mitigate memory impairments or restore disrupted network dynamics, including theta-gamma coupling and ensemble-level coordination—features known to be altered in AD (e.g., van den Berg et al., 2025).

The student will also have the opportunity to interact with collaborating labs at Harvard Medical School (Smirnakis Lab) that study circuit-level plasticity using advanced approaches such as two-photon imaging and spatial transcriptomics, providing exposure to cutting-edge methodologies and potential avenues for integrative analyses. Overall, this project will establish a platform at CING for understanding cholinergic control of memory circuits and for developing neural biomarkers relevant to future theranostic strategies for cognitive disorders.

**References**

van den Berg, M., Heymans, L., Toen, D., Adhikari, M. A., Audekerke, J. V., Verschuuren, M., Pintelon, I., Vos, W. H. D., Linden, A. V. der, Verhoye, M. & Keliris, G. A. Partial normalization of hippocampal oscillatory activity during sleep in TgF344-AD rats coincides with increased cholinergic synapses at early-plaque stage of Alzheimer's disease. Acta Neuropathol. Commun. 13, 96 (2025). doi: 10.1186/s40478-025-02016

Meshulam, L., et al., A brain-wide map of neural activity during complex behaviour. Nature 645, 177-191 (2025). doi: 10.1038/s41586-025-09235

Findling, C., et al., Brain-wide representations of prior information in mouse decision-making. Nature 645, 192-200 (2025). doi: 10.1038/s41586-025-09226

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## T10: Fine-mapping breast cancer susceptibility loci through integrative multi-omic analysis

**The topic is eligible for the following Programmes:**

PhD in Molecular Medicine
PhD in Medical Genetics

**Hosting Department:**
Biostatistics Department

**Contact Persons:**
Dr. Kyriaki Michailidou
Dr. Maria Zanti

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**Mode of Study:**
Full Time

**Abstract**:
Genome-wide association studies (GWAS) have identified numerous loci associated with breast cancer susceptibility; however, for most loci the underlying causal variants and molecular mechanisms remain unresolved. This is largely due to linkage disequilibrium and the predominance of non-coding variation, as well as limited integration with downstream molecular phenotypes. The UK Biobank provides an unprecedented opportunity to address these challenges by combining large-scale genotype data with rich phenotypic and multi-omics measurements in a population-based cohort.

This PhD project aims to fine-map breast cancer susceptibility loci and characterise their molecular consequences using integrative multi-omics data from the UK Biobank. The project will apply state-of-the-art statistical fine-mapping methods to breast cancer GWAS signals to identify credible sets of candidate causal variants. These variants will then be integrated with multiple molecular layers available in the UK Biobank, including plasma proteomics, metabolomics, clinical biochemistry measures, and quantitative trait loci derived from these data.

Colocalisation and causal inference approaches will be used to link genetic variants to intermediate molecular traits and breast cancer risk, enabling prioritisation of putative effector genes, proteins, and pathways. By leveraging population-scale multi-omics data, this project will provide refined maps of breast cancer susceptibility loci, identify molecular mediators of inherited risk, and improve biological interpretation of GWAS findings with potential relevance for risk stratification and biomarker discovery.

**Project Plan for years 2, 3 & 4:**

***Year 2 – Breast cancer GWAS and fine-mapping***

**Identify target regions for fine-mapping analysis**
- Select breast cancer susceptibility loci from large-scale GWAS, including UK Biobank and international consortia.

**Statistical fine-mapping**
- Apply Bayesian and likelihood-based fine-mapping methods (e.g. SuSiE, FINEMAP) using UK Biobank-derived LD matrices.
- Generate credible sets and posterior probabilities for candidate causal variants.

**Variant annotation and prioritisation**
- Annotate fine-mapped variants using regulatory, epigenomic, and conservation features relevant to breast and immune-related tissues.
- Develop supervised machine-learning models that integrate fine-mapping probabilities with functional annotations to prioritise likely causal variants.
- Compare AI-derived prioritisation with traditional statistical fine-mapping approaches to assess performance and robustness.

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***Year 3 – Multi-omics integration with proteomics and metabolic traits***

**Proteomic analysis**
- Analyse UK Biobank plasma proteomics data (e.g. Olink Explore panels) to identify protein quantitative trait loci (pQTLs).
- Assess overlap between pQTLs and fine-mapped breast cancer loci.

**Integration with additional omics**
- Integrate metabolomic and clinical biomarker data to identify metabolite QTLs (mQTLs) and biochemical QTLs.
- Incorporate relevant eQTL data from public resources (e.g. GTEx) where appropriate.

**Colocalisation analyses**
- Perform statistical colocalisation to test whether breast cancer GWAS and molecular QTL signals share causal variants.
- Prioritise proteins and metabolites likely to mediate genetic risk.

**Causal inference**
- Apply Mendelian randomisation and mediation analyses to evaluate causal relationships between molecular traits and breast cancer risk.

***Year 4 – Integration, interpretation, and thesis completion***

**Synthesis of findings**
- Integrate fine-mapping and multi-omics results across loci to identify convergent biological pathways and networks.
- Compare findings with known breast cancer biology and drug-target databases.

**Risk prediction and translational relevance**
- Evaluate whether prioritised variants or molecular traits improve breast cancer polygenic risk scores.
- Discuss implications for biomarker development and population risk stratification.

**Thesis writing and dissemination**
- Complete thesis writing, submission, and defence.
- Finalise and submit manuscripts; present findings at international conferences.

## T11: Computational Modelling of the Exposome: Integrating Environmental, Lifestyle and Biological Triggers of Disease

**Abstract**:
Human health is determined not just by genetics, but by the "Exposome"—the cumulative measure of environmental influences and associated biological responses. This project operates under the "One Health" framework, integrating data on environmental factors (air pollution, viral infections, nutrition, lifestyle stress, and extreme environments like microgravity) to understand their impact on the host. The goal is to build a unified computational framework to model how these external triggers cause dysregulation in the biological mechanisms and host immune modulation, leading to disease. The project is in the direction of Advanced Systems Bioinformatics & Network Medicine. It is purely computational, leveraging the power of Big Data, Network Science, and Artificial Intelligence to solve complex medical problems. While the project is purely computational relying on publicly available data, opportunities for small-scale experimental validation within CING labs or with external partners exist for interested candidates, though this is not a prerequisite.

Candidates will employ state-of-the-art methodologies, such as:

- Omics Analytics (bulk and single cell, spatial omics), multi-omics data integration (genomics, transcriptomics, proteomics, metabolomics).
- Network Science: Construction of protein-protein interaction (PPI) networks, regulatory networks, and diseasome (disease-to-disease networks) analysis.
- Advanced Modelling and AI: Networks-of-Networks, Probabilistic Graphical Models (PGMs), and Graph Neural Networks (GNNs).
- Translational Goals: Pathway analysis, complex biomarker discovery, and computational drug repurposing.

**The topic is eligible for the following Programmes:**

PhD in Neuroscience
PhD in Molecular Medicine
PhD in Medical Genetics

**Hosting Department:**
Bioinformatics Department

**Contact Persons:**
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**Mode of Study:**
Full Time

**Project Plan for years 2, 3 & 4:**

**Year 1: The Exposome Knowledge Graph**

- Aggregation of heterogeneous data: Environmental / lifestyle / biological data (pollutants, viruses/pathogens, various stressors, radiation, microgravity), and Host Omics from public cohorts.
- Data harmonization
- Development of a Knowledge Graph linking external stressors to biological pathways

**Year 2: Multilayer Modelling & Networks-of-Networks**

- Development of a "Network-of-Networks" architecture connecting:
  - The Exposome (External factors).
  - The Host Interactome (Signaling/PPIs, etc).
  - Disease Triggering Networks
- Implementation of computational models (e.g. Probabilistic Graphical Models and GNNs) to infer causality between environmental triggers and disease onset.
- Analysis of specific case studies, including the impact of stress, air pollution, viral/pathogen infection and spaceflight (radiation/microgravity) as distinct stressors.

**Year 3: Predictive Analytics & Therapeutics**

- Identification of complex composite biomarkers (integrating exposome with host-ome).
- Network-based Drug Repurposing: Identifying compounds that can disrupt the pathogenic flow from external stressors to host.
- Thesis writing and preparation of manuscripts for impactful peer-reviewed journals.

**References**

[1] Ibáñez, A., Duran-Aniotz, C., Migeot, J. et al. Computational whole-body-exposome models for global precision brain health. Nat Commun 16, 11078 (2025). https://doi.org/10.1038/s41467-025-67448-3

[2] Wan, M., Simonin, E.M., Johnson, M.M. et al. Exposomics: a review of methodologies, applications, and future directions in molecular medicine. EMBO Mol Med 17, 599–608 (2025). https://doi.org/10.1038/s44321-025-00191-w

[3] Sarigiannis D, Karakitsios S, Anesti O, Stem A, Valvi D, Sumner SCJ, Chatzi L, Snyder MP, Thompson DC, Vasiliou V. Advancing translational exposomics: bridging genome, exposome and personalized medicine. Hum Genomics. 2025 Apr 30;19(1):48. https://doi.org/10.1186/s40246-025-00761-6. PMID: 40307849; PMCID: PMC12044731.

[4] Oulas A, Minadakis G, Zachariou M, Sokratous K, Bourdakou MM, Spyrou GM. Systems Bioinformatics: increasing precision of computational diagnostics and therapeutics through network-based approaches. Brief Bioinform. 2019 May 21;20(3):806-824. doi: 10.1093/bib/bbx151. PMID: 29186305; PMCID: PMC6585387.

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## T14: ERK-dependent regulation of cilia in laminopathies

**The topic is eligible for the following Programmes:**

PhD in Molecular Medicine
PhD in Medical Genetics

**Hosting Department / Group:**
Nuclear Envelopathies Group

**Contact Persons:**
Dr. Maria Chatzifrangkeskou

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**Mode of Study:**
Full Time

**Abstract**:
Laminopathies are a group of rare but severe genetic disorders caused by mutations in the LMNA gene, leading to cardiomyopathy, skeletal muscle disease, and neurological involvement. Despite clear clinical manifestations, the cellular mechanisms linking nuclear envelope defects to tissue dysfunction remain incompletely understood. Accumulating evidence indicates that aberrant activation of the MAPK/ERK signaling pathway is a central pathogenic feature in several laminopathy mouse models and human patients, and that pharmacological inhibition of ERK signaling can partially improve disease outcomes.
Cilia are microtubule-based organelles that coordinate developmental, metabolic, and mechanosensory signaling in multiple tissues, including heart, muscle, and brain. Defects in ciliogenesis or ciliary signaling can cause phenotypes that overlap with laminopathies, yet the contribution of ciliary dysfunction to laminopathy pathogenesis has not been systematically investigated. Preliminary observations suggest that active ERK localizes to the basal body region of cilia in both primary and motile cilia, raising the possibility that excessive ERK signaling disrupts ciliary structure and function.
This PhD project aims to define how ERK hyperactivation affects ciliary dynamics and cytoskeletal organization in cultured cells and clinically relevant mouse models of laminopathies. By integrating molecular, cellular, and in vivo approaches, the project will identify ciliary defects as potential contributors to tissue pathology and assess the therapeutic potential of targeting ERK signaling.

**Project Plan for years 2, 3 & 4:**

**Year 2 – Ciliary phenotypes in laminopathies**
- Characterize ciliogenesis and ciliary architecture in cultured cells and tissues derived from established LMNA mouse models.
- Perform immunofluorescence and histological analyses to assess cilium number, length, and basal body organization.
- Analyze global cytoskeletal alterations, focusing on microtubule acetylation and actin organization.
- Determine ERK activation status and sub-cilliary localization.

**Year 3 – Mechanistic link between ERK signaling and ciliary dysfunction**
- Investigate how ERK hyperactivation regulates microtubule acetylation and ciliary stability.
- Dissect the role of basal-body-localized ERK in ciliary assembly and disassembly using genetic and pharmacological modulation.
- Assess the impact of ERK modulation on cilia-dependent signaling pathways relevant to skeletal and cardiac muscle function.

**Year 4 – Therapeutic modulation and functional outcomes**
- Test whether pharmacological inhibition of ERK signaling (e.g. MEK inhibitors) can rescue ciliary and cytoskeletal defects in mouse models.
- Evaluate functional outcomes at the tissue level, including cardiac performance and muscle physiology.
- Correlate improvements in ciliary structure and signaling with disease phenotypes to assess clinical relevance.
- Integrate findings into a disease mechanism framework and prepare manuscripts and thesis.

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