PoLiMeR

Polymers in the Liver - Metabolism and Regulation

PhD positions in experimental and computational sciences for the Marie-Curie Innovative Training Network "PoLiMeR"

Project

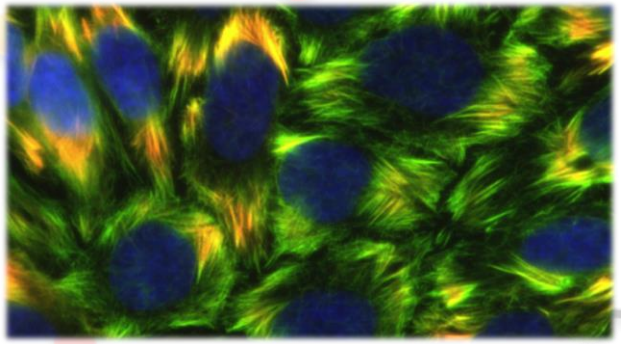
Metabolic diseases are a burden on the European population and health care system. It is increasingly recognised that individual differences with respect to history, lifestyle, and genetic make-up affect disease progression and treatment response. A Systems Medicine approach, based on computational models fed with individual patient data, has the potential to provide the basis for a personalised diagnosis and treatment strategy. The PoLiMeR consortium (Polymers in the Liver: Metabolism and Regulation) has identified the inherited, liver-related diseases of glycogen and lipid metabolism as the ideal starting point for innovative research training in personalised 'Systems Medicine'. These diseases are life-threatening for children. Since each specific disease is rare, research efforts are diluted. Our system-based perspective opens possibilities for the application of novel drugs and diagnostic tools to a range of different diseases.

Training

To advance diagnostics and treatment of metabolic diseases beyond the state-of-the-art, a new generation of scientists is needed. The complexity of the metabolic network and its aberrant behaviour in disease require truly interdisciplinary researchers, trained in the three 'pillars of Systems Medicine': experimental, computational and clinical research.

As a PhD student in this project you will be part of a highly international team of young researchers. You will have your individual research project at your host organisation, focusing on your discipline of interest. To complement your specialized training, you will do internships at a complementary PoLiMeR partner organization. In addition, you will follow advanced interdisciplinary courses by leaders in the field of Systems Medicine. Thus, you will be trained to become a Systems-Medicine expert with expertise in computational and wet-lab techniques, who can collaborate between clinical, academic, and industrial environments.

Are you interested? Please, check the different PhD positions available in the PoLiMeR project!



PhD positions

Challenge 1: Glycogen is a glucose-based polymer, comprising linear and branched components in a tree-like arrangement. Hence, an enzyme acting upon glycogen can cleave or rearrange the polymer backbone at multiple sites. The challenge will be to develop novel experimental and computational tools that can resolve spatiotemporal aspects of enzyme catalysis at the complex polymer surface and apply these to clinical samples and data to identify bottlenecks and therapeutic targets.

PhD student 1: Kinetic analysis of enzymes in glycogen metabolism
*Host organisation: John Innes Centre, Norwich UK**
contact: Rob.Field[at]jic.ac.uk

PhD student 2: Structural analysis of glycogen from *in vitro* models and patients with Glycogen Storage Diseases
*Host organisation: Iceni Diagnostics, Norwich UK**
contact: stephan.goetz[at]icenidiagnostics.com

PhD student 3: Mathematical modelling of glycogen metabolism and glycogen-related disorders
Host organisation: Heinrich Heine Universität Düsseldorf, DE
contact: oliver.ebenhoeh[at]hhu.de

Challenge 2: Enzymes are thought to have a specific affinity for one well-defined substrate. In contrast, enzymes acting on larger molecules catalyse the conversion of a functional group in the substrate with a lesser specificity for the remaining part of the molecule. This promiscuity results in a combinatorial explosion of different molecular species. The challenge is to develop innovative analytical methods and genome-scale modelling approaches to analyse and interpret complex lipid profiles in a meaningful way, and apply these to clinical samples and data to identify novel causes of patient-to-patient variability

PhD student 4: Quantitative and miniaturised assays for structure-resolved lipidomics
Host organisation: Leiden University, NL
contact: hankemeier[at]lacdr.leidenuniv.nl

PhD student 11: Development of *in vitro* liver models for inborn errors in glycogen and fatty-acid metabolism
*Host organisation: MIMETAS, Leiden NL**
contact: d.kurek[at]mimetas.com

PhD student 6: Stoichiometric modularisation of combinatorial lipid metabolism
Host organisation: University of Luxembourg, LU
contact: ines.thiele[at]uni.lu

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Challenge 3: If enzymes catalyse multiple reactions, alternative substrates compete with each other for binding to the enzyme, thereby inhibiting each other's conversion. At the level of metabolic pathways and networks this causes feedback and feedforward inhibition and may lead to complex dynamics. The challenge will be to develop novel experimental tools and computational models to analyse the impact of substrate competition on pathway dynamics, and apply these to patient samples and data to identify putative therapeutic targets

PhD student 9: Instability of glucose production in fatty-acid oxidation defects
Host organisation: University Medical Centre Groningen, NL
contact: b.m.bakker01[at]umcg.nl

PhD student 12: Interplay between coenzyme and energy metabolism in fatty-acid oxidation defects
Host organisation: University of Bergen, NO
contact: Mathias.Ziegler[at]uib.no

PhD student 8: Dynamic computational modelling of lipid synthesis and storage in the human liver
Host organisation: Heinrich Heine Universität Düsseldorf, DE
contact: oliver.ebenhoeh[at]hhu.de

PhD student 10: Dietary interventions and compensatory substrate switch in fatty-acid oxidation defects
Host organisation: Universitätsklinikum Freiburg, DE
contact: zkj.sekretariat.prof.spiekerkoetter[at]uniklinik-freiburg.de

Challenge 4: Metabolic fluxes and metabolite homeostasis are regulated extensively through gene expression and signalling. Recently, the physiological importance of autophagy-like pathways for glycogen and lipid metabolism has become apparent. The challenge is to develop novel experimental and computational methodologies to follow polymers in the cell and to integrate this spatial regulation with classical levels of regulation, potentially identifying novel mechanisms for patient-to-patient variability.

PhD student 13: Multi-level regulation of metabolism in fatty-acid oxidation defects
Host organisation: University Medical Centre Groningen, NL
contact: b.m.bakker01[at]umcg.nl

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PhD student 14: Directing signal transduction pathways to establish novel therapies for glycogen storage disease type I
Host organisation: University Medical Centre Groningen, NL
contact: m.h.oosterveer[at]umcg.nl

PhD student 15: The role of autophagy and mTOR signalling in inborn errors of glycogen metabolism in hepatocytes
Host organisation: University Medical Centre Groningen (NL) and Carl von Ossietzky Universität Oldenburg (DE)
contact: kathrin.thedieck[at]uni-oldenburg.de

PhD student 5: Integration of genome-scale models with signalling networks
Host organisation: KTH Royal Institute of Technology, Stockholm SE
contact: adilm[at]kth.se

Challenge 5 A key challenge in Systems Medicine research is making the extremely diverse data FAIR. FAIR means Findability, Accessibility, Interoperability and Reusability of data. Within this project we base ourselves on the FAIRDOMHub, a platform for FAIR data, and explore improving the Findability of data using information retrieval methods. How can we enable users to store their results in a way that the results are most easily found, even if the query is imprecise?

PhD student 7: Data and model management and information retrieval
*Host organisation: HITS gGmbH, Heidelberg, DE**
contact: wolfgang.mueller[at]h-its.org

*If the host organisation is a company, the PhD will be employed and do the research at the company. In addition, the PhD will be registered at a university to obtain the PhD degree.

For detailed information about the specific PhD project please visit our website: polimer-itn.eu/vacancies

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Eligible candidates for a PhD position in the PoLiMeR training network should have the following qualifications:

- A(n) (almost) completed master's degree in a discipline relevant to the PhD position(s) for which you apply.
- Strong motivation for scientific research in an interdisciplinary and international environment
- Excellent English presentation and writing skills
- Good organizational and communication skills, being a team-player

Mobility rule by the EU

Successful candidates must fulfil the mobility criteria defined by the European Commission:

At the time of recruitment by the host organisation, researchers must not have resided or carried out their main activity (work, studies, etc.) in the country of their host organisation for more than 12 months in the 3 years immediately prior to the reference date.

The start of PhD projects is envisaged for April 2019, but it will be possible to start earlier or later, between October 2018 and September 2019.

Application and contact

You are invited to apply if you are interested in one or more of the PhD positions. Please submit your CV and motivation letter via the website: **polimer-itn.eu/vacancies**. Please indicate in your motivation for which PhD position(s) you are applying.

You can apply until **1 October 2018.**

For more information about a specific position please contact the person indicated for that position.