PhD student positions in quantitative biology (Zampieri Lab)

The Zampieri group offers multiple research opportunities for PhD candidates in the context of systems pharmacology, cancer and microbiology, computational biology and metabolic regulation. These positions will be based in the Department of Biomedicine (https://biomedizin.unibas.ch/en/) in Basel, one of the world's leading locations for life sciences, home to several companies and institutions.

The mission of the group is to understand fundamental mechanisms regulating short- and long-term metabolic adaptation to genetic and chemical perturbations to find new and unconventional therapeutic strategies, ranging from antibacterial to anticancer drugs. To this end, we develop new ways to combine state-of-the-art technologies in metabolomics with mathematical modeling.

The PhD students will exploit some of the cutting-edge experimental and computational methods, comprising high-throughput metabolomics, time-lapse microscopy, constraint-based and kinetic modeling, to investigate how to pharmacologically interfere with fundamental mechanisms in the regulation of metabolism. Available resources at the department include a mouse facility, high-end FACS, IT and microscopy facilities, the Life Sciences Training Facility (for gene expression and proteome profiling) and much more.

The candidates are expected to have a strong background and interest in quantitative disciplines, excellent teamwork and communication skills in English. They will have the opportunity to develop the following projects with a lot of academic freedom and strong support from senior members in the lab, and at the same time to play an active role in shaping and in creating inspiring research and working environment.

Project 1) Investigate the role of metabolism in mediating functions of tumor suppressor and oncogenes.

Project 2) Uncover the role of the central metabolism in mediating antibiotic tolerance.

Project 3) Study how bacterial susceptibility to antibiotics depends on the metabolic and physiological states of bacteria.

Project 4) Find new and unconventional antibacterial compounds to treat Tuberculosis.

In line with our and Uni Basel values (https://www.unibas.ch/en/Research/Values-Ethics/Diversity.html), we are committed to sustain and promote an inclusive culture, ensure equal opportunities and value diversity and respect in our working and learning environment.

Please send your application to mattia.zampieri@unibas.ch, by submitting the following requested documents: A) a cover letter, in which you also indicate for which project you wish to apply, B) a complete curriculum vitae C) the PhD application form (https://imsb.ethz.ch/research/zampieri-group.html) D) names and email addresses of at least two referees.

Project 1 description

We are looking for a highly motivated doctoral researcher to investigate the role of metabolism in mediating functions of tumor suppressor and oncogenes (60% wet lab and 40% computational).

Your main tasks will be:

- Adapting existing and developing improved experimental protocols for the high-throughput metabolomics analysis of CRISPR engineered cell lines.
- Mapping the metabolic adaptome of cancer cell lines to genetic perturbations of tumor suppressor and oncogenes
- Determining the underlying mechanisms that link modulation of gene expression to metabolic phenotypes
- Developing network-based approaches to investigate and predict response to genetic perturbation in an *in vivo* context
- Support and preparation of scientific reports and journal articles

What we offer:

- You will have access to state-of-the-art research equipment in metabolomics, cell biology, time-lapse microscopy.
- You will work in a dynamic and highly interdisciplinary team including computer scientists and experimentalists.
- You will be involved in cross-disciplinary collaborations and have training opportunities to further develop and grow your scientific interests.
- Opportunity to work in close contact with other basic- and clinical-research groups at the Department of Biomedicine in Basel
- Support from highly competent, experienced team members and potential to lead projects with a high degree of academic freedom

Your profile:

Essential:

- Master's degree in (Bio)Physics, (Bio)engineering, Biological Sciences, Microbiology, Biochemistry, Systems Biology, Molecular Biology, Bioinformatics/Computational Biology, or related fields.
- Basic experience of designing and running experiments with cell cultures (cell lines) in the laboratory
- Hands-on experience with key biochemical and molecular biological methods
- Motivation to work in an international research environment

Highly desirable:

- Experience with and/or motivation to learn systems biology approaches, high-throughput methodologies
- Experience with and/or motivation to learn programming language (e.g. Matlab, R or Python)
- Good communication skills

Any of the following will be a plus:

- Proficiency in data analysis using Matlab, R or Python
- Interest in mathematical modeling of metabolic and regulatory/signaling network

Key References:

Ortmayr, K. and Zampieri M. "Sorting-free metabolic profiling uncovers the vulnerability of fatty acid β-oxidation in in vitro quiescence models". To appear in *Molecular Systems Biology* 2022

Anglada-Girotto, M., Handschin, G., Ortmayr, K. *et al.* Combining CRISPRi and metabolomics for functional annotation of compound libraries. *Nat Chem Biol* **18**, 482–491 (2022).

Ortmayr, K., Dubuis, S. & Zampieri, M. Metabolic profiling of cancer cells reveals genome-wide crosstalk between transcriptional regulators and metabolism. *Nat Commun* **10**, 1841 (2019).

Dubuis, S., Ortmayr, K. & Zampieri, M. A framework for large-scale metabolome drug profiling links coenzyme A metabolism to the toxicity of anti-cancer drug dichloroacetate. *Commun Biol* **1**, 101 (2018).

Project 2 description

In the framework of the NCCR AntiResist (https://www.nccr-antiresist.ch/en/), we are looking for a highly motivated doctoral researcher to uncover the role of the central metabolism in mediating antibiotic tolerance. This project will be conducted in collaboration with Prof. Sarah Tschudin Sutter at the University hospital of Basel and Prof. Urs Jenal at the Biozentrum (60% wet lab and 40% computational).

Your main tasks will be:

- Developing new strategies to combine high-throughput metabolomics with single cell analysis of metabolic and transcriptional reporters.
- Investigating if variations in metabolic activity can act as metabolic mediators of antibiotic tolerance
- Determining the underlying mechanisms that link regulation of respiro-/fermentative metabolism to phenotypic heterogeneity and antibiotic tolerance.
- Testing the relevance of metabolic tolerance in clinical strains
- Support and preparation of scientific reports and journal articles

What we offer:

- You will have access to state-of-the-art research equipment in metabolomics, cell biology, time-lapse microscopy and single cell analysis.
- You will work in a dynamic and highly interdisciplinary team including computer scientists, experimentalists and clinicians.
- You will be involved in cross-disciplinary collaborations and have training opportunities to further develop and grow your scientific interests.
- Access to a large consortium of experts in different disciplines, such chemistry, engineering, clinics, computational biology and (Micro- / Cell- / Immune-)Biology (https://www.nccr-antiresist.ch/en/about-us/organization-structure/principal-investigators).
- Opportunity to work in close contact with other basic- and clinical-research groups at the Department of Biomedicine and the Biozentrum in Basel
- Support from highly competent, experienced team members and potential to lead projects with a high degree of academic freedom

Your profile:

Essential:

- Master's degree in (Bio)Physics, (Bio)engineering, Biological Sciences, Microbiology, Biochemistry, Systems Biology, Molecular Biology, Bioinformatics/Computational Biology, or related fields.
- Basic experience of designing and running experiments with microbial cultures in the laboratory
- Hands-on experience with key biochemical and molecular biological methods
- Motivation to work in an international research environment
- Experience with and/or motivation to learn systems biology approaches, high-throughput methodologies, analysis of single cells imaging data

Highly desirable:

- Experience with and/or motivation to learn programming language (e.g. Matlab, R or Python)
- Good communication skills

Any of the following will be a plus:

- Proficiency in data analysis using Matlab, R or Python
- Interest in mathematical modeling of metabolic and regulatory/signaling network

Key References:

Anglada-Girotto, M., Handschin, G., Ortmayr, K. *et al.* Combining CRISPRi and metabolomics for functional annotation of compound libraries. *Nat Chem Biol* **18**, 482–491 (2022).

Fuentes, D.A.F., Manfredi, P., Jenal, U. *et al.* Pareto optimality between growth-rate and lag-time couples metabolic noise to phenotypic heterogeneity in *Escherichia coli*. *Nat Commun* **12**, 3204 (2021).

Øyås O., Borrell S., Trauner A., *et al.* Model-based integration of genomics and metabolomics reveals SNP functionality in Mycobacterium tuberculosis. PNAS 117 (2020)

Campos A. and Zampieri M. Metabolomics-Driven Exploration of the Chemical Drug Space to Predict Combination Antimicrobial Therapies. Molecular Cell 74, 1291-1303 (2020)

Project 3 description

In the framework of the NCCR AntiResist (https://www.nccr-antiresist.ch/en/), we are looking for a highly motivated doctoral researcher to study how bacterial susceptibility to antibiotics depends on the metabolic and physiological states of bacteria (40% wet lab and 60% computational).

Your main tasks will be:

- Adapting existing and developing improved experimental protocols for the high-throughput metabolomics analysis of drug-perturbed bacteria across different growth conditions.
- Unravel the hidden potential of apparently inactive molecules in hampering bacterial infection
- Determining the underlying mechanisms that link antibacterial efficacy to the metabolic or physiological state of bacteria.
- Testing their relevance in host-like environmental conditions
- Support and preparation of scientific reports and journal articles

What we offer:

- You will have access to state-of-the-art research equipment in metabolomics, cell biology, time-lapse microscopy.
- You will work in a dynamic and highly interdisciplinary team including computer scientists, experimentalists and clinicians.
- You will be involved in cross-disciplinary collaborations and have training opportunities to further develop and grow your scientific interests.
- Access to a large consortium of experts in different disciplines, such chemistry, engineering, clinics, computational biology and (Micro- / Cell- / Immune-)Biology (https://www.nccr-antiresist.ch/en/about-us/organization-structure/principal-investigators).
- Opportunity to work in close contact with other basic- and clinical-research groups at the Department of Biomedicine and the Biozentrum in Basel
- Support from highly competent, experienced team members and potential to lead projects with a high degree of academic freedom

Your profile:

Essential:

- Master's degree in (Bio)Physics, (Bio)engineering, Biological Sciences, Microbiology, Biochemistry, Systems Biology, Molecular Biology, Bioinformatics/Computational Biology, or related fields.
- Basic experience of designing and running experiments with microbial cultures in the laboratory
- Experience with and/or motivation to learn programming language (e.g. Matlab, R or Python)
- Hands-on experience with key biochemical and molecular biological methods
- Motivation to work in an international research environment

Highly desirable:

- Experience with and/or motivation to learn systems biology approaches, high-throughput methodologies, analysis of single cells imaging data

- Good communication skills

Any of the following will be a plus:

- Proficiency in data analysis using Matlab, R or Python
- Interest in mathematical modeling of metabolic and regulatory/signaling network

Key References:

Ortmayr, K., de la Cruz Moreno, R. & Zampieri, M. Expanding the search for small-molecule antibacterials by multidimensional profiling. *Nat Chem Biol* **18**, 584–595 (2022)

Anglada-Girotto, M., Handschin, G., Ortmayr, K. *et al.* Combining CRISPRi and metabolomics for functional annotation of compound libraries. *Nat Chem Biol* **18**, 482–491 (2022).

Zampieri, M., Hörl, M., Hotz, F. et al. Regulatory mechanisms underlying coordination of amino acid and glucose catabolism in Escherichia coli. Nat Commun 10, 3354 (2019)

Øyås O., Borrell S., Trauner A., *et al.* Model-based integration of genomics and metabolomics reveals SNP functionality in Mycobacterium tuberculosis. PNAS 117 (2020)

Campos A. and Zampieri M. Metabolomics-Driven Exploration of the Chemical Drug Space to Predict Combination Antimicrobial Therapies. Molecular Cell 74, 1291-1303 (2020)

Project 4 description

We are looking for a highly motivated doctoral researcher to find new and unconventional antibacterial compounds to treat Tuberculosis. This project will be conducted in collaboration with Prof. Michael Berney (https://www.berneylab.org/) at the Albert Einstein College of Medicine (50% wet lab and 50% computational).

Your main tasks will be:

- Using existing experimental protocols for the high-throughput metabolomics analysis of chemically and genetically perturbed *M. tuberculosis* strains.
- Profiling a large library of small molecules with attractive antituberculosis properties
- Determining the underlying drug modes of action.
- Testing their relevance in host-like environmental conditions
- Support and preparation of scientific reports and journal articles

What we offer:

- You will have access to state-of-the-art research equipment in metabolomics, cell biology, time-lapse microscopy.
- You will work in a dynamic and highly interdisciplinary team including computer scientists, experimentalists.
- You will be involved in cross-disciplinary collaborations and have training opportunities to further develop and grow your scientific interests.
- Opportunity to work in close contact with other basic- and clinical-research groups at the Department of Biomedicine and experts in the field of tuberculosis
- Support from highly competent, experienced team members and potential to lead projects with a high degree of academic freedom

Your profile:

Essential:

- Master's degree in (Bio)Physics, (Bio)engineering, Biological Sciences, Microbiology, Biochemistry, Systems Biology, Molecular Biology, Bioinformatics/Computational Biology, or related fields.
- Basic experience of designing and running experiments with microbial cultures in the laboratory
- Experience with and/or motivation to learn programming language (e.g. Matlab, R or Python)
- Hands-on experience with key biochemical and molecular biological methods
- Motivation to work in an international research environment

Highly desirable:

- Experience with and/or motivation to learn systems biology approaches, high-throughput methodologies, analysis of single cells imaging data
- Good communication skills

Any of the following will be a plus:

- Proficiency in data analysis using Matlab, R or Python
- Interest in mathematical modeling of metabolic and regulatory/signaling network

Key References:

Ortmayr, K., de la Cruz Moreno, R. & Zampieri, M. Expanding the search for small-molecule antibacterials by multidimensional profiling. *Nat Chem Biol* **18**, 584–595 (2022)

Anglada-Girotto, M., Handschin, G., Ortmayr, K. *et al.* Combining CRISPRi and metabolomics for functional annotation of compound libraries. *Nat Chem Biol* **18**, 482–491 (2022).

Zampieri M., *et al*. High-throughput metabolomic analysis predicts mode of action of uncharacterized antimicrobial compounds. Science Translational Medicine Vol 10, Issue 429 (2018)

Øyås O., Borrell S., Trauner A., *et al.* Model-based integration of genomics and metabolomics reveals SNP functionality in Mycobacterium tuberculosis. PNAS 117 (2020)

Campos A. and Zampieri M. Metabolomics-Driven Exploration of the Chemical Drug Space to Predict Combination Antimicrobial Therapies. Molecular Cell 74, 1291-1303 (2020)