

2 PhD Studentships in Microbiology Available!

Positions in the project: PhD student, starting from 01.10.2024.

Scientific discipline: Life Sciences, Microbiology, Infection Biology

Stipend amount/month: 4000 PLN net; increased to 7000 net (~1500 EUR) upon successful application to the Doctoral School

Period of stipend agreement: 48 months

Institution: University of Warsaw

Laboratory: Laboratory of Infection Biology, Centre of Biological and Chemical Research

Projects leaders:

Dr Marta Zapotoczna (m.zapotoczna@uw.edu.pl) & Dr Jakub M. Kwieciński

Project titles:

1. The relevance of the interplay of staphylocoagulases and staphylokinase in the development of *Staphylococcus aureus* infections (abstract below).
2. Central role of the human hemostasis system in the formation of *Staphylococcus aureus* biofilms (abstract below).

Key responsibilities:

1. Co-design and execution of experimental laboratory procedures. Both projects will implement state-of-the-art microbiology methods, incl. cloning, mutagenesis, protein purification, protein-protein interactions, culture-based *in vitro*, *in vivo* and *ex vivo* assays as well as in silico modelling of protein structures.
2. Literature review, data and results analysis and interpretation.
3. Participation in seminars and scientific conferences.
4. (Optional) Readiness to research visit in a partner institution (e.g. Jagiellonian University, University of Leuven)
5. The successful candidate is expected to enroll in one of the Doctoral Schools of the University of Warsaw <https://szkolydoktorskie.uw.edu.pl/en/>

Profile of candidates/requirements:

1. At least 1 year of research experience in the field of microbiology, genetics, molecular biology.
2. Experience in presenting research results.
3. Scientific independence and team working skills.
4. Very good knowledge of English.
5. Willingness to gain new expertise.



Required documents:

1. Short motivation letter
2. Curriculum vitae including: a detailed description of the academic degrees, titles of theses, names and affiliations of supervisors, places of employment, list of scientific publications, conferences, awards and trainings.
3. Address details of at least one direct supervisor/scientist who may recommend the given candidate.
4. Copies of obtained diplomas.
5. For the purpose of the recruitment process, please attach a scan of signed, written permission for recruitment-related personal data processing, which states: „I give permission to the University of Warsaw, registered at the address of ul. Krakowskie Przedmieście 26/28, 00-927 Warszawa, to process my personal data for the purposes of carrying out the recruitment procedure, choosing the employee, and entering into an employment contract with the University of Warsaw, if applicable. I have been informed about my legal rights and obligations in relation to these actions. I acknowledge that providing the aforementioned personal data is done by me on a voluntary basis.“

Candidates are encouraged to contact the project leader to discuss the position scope and ask any questions they may have – m.zapotoczna@uw.edu.pl

Please submit the following documents to: m.zapotoczna@uw.edu.pl

Application deadline: 30.05.2024r.

For more details about the position, please visit:

Popular science summaries (PL):

Ad. Project 1 - <https://projekty.ncn.gov.pl/opisy/572567-pl.pdf>

Ad. Project 2 - <https://projekty.ncn.gov.pl/opisy/589166-pl.pdf>

NCN stipend offer: <https://www2.ncn.gov.pl/baza-ofert/?akcja=wyswietl&id=224267>

Euraxess stipend offer: <https://euraxess.ec.europa.eu/jobs/213442>

Projects' abstracts:

1. The relevance of the interplay of staphylocoagulases and staphylokinase in the development of *Staphylococcus aureus* infections.

Staphylococcus aureus is a leading cause of localized infections of skin and soft tissues, incl. abscesses and chronic wound infections, as well as bloodstream infections associated with life-threatening complications, such as infective endocarditis. A unique feature of *S. aureus* is



the combined production of factors of opposite functions which manipulate and hijack the human host hemostasis in order to evade host defenses and disseminate. These extracellular factors include two coagulases (von Willebrand factor binding protein and staphylocoagulase), which promote formation of a fibrin scaffold, and staphylokinase, which activates human plasminogen inducing fibrinolysis. Their individual roles, i.e. in development of fibrin enclosed abscesses, biofilm formation, evasion of immune responses and dissemination have been shown in various preclinical models but the relevance of their combined contribution remains unknown. *S. aureus* is a highly clonal pathogen with over 80% of the European (incl. Polish) bacteraemia isolates distributed across clonal complexes (CCs) of 5, 30, 45, 22, 8, 15 and 1. Unlike, staphylokinase (Sak) and von Willebrand factor binding protein (vWbp), staphylocoagulases (Coa) isoforms from those CCs are highly polymorphic yet only the Coa gene from CC8 has been investigated to date. We recently found that these Coa isoforms have different levels of amidolytic activity, which although not reflected in the total amount of the Coa-promoted fibrin, seems critical for the distinctive biophysical properties of the fibrin clots (incl. porosity and viscosity). To explore this phenomenon in the context of blood clot properties and their relevance for the efficacy of the host defenses we propose to use a range of novel ex vivo and in vitro methods, incl. experimental model of thromboelastometry - based assessment of hemostatic properties of human blood clotting and neutrophil migration and killing assays. We will produce recombinant Coa isoforms from the different clonal complexes to study their blood clotting properties, incl. K_d, clotting time, clot size and firmness, and susceptibility to lysis using thromboelastometry. We will also use this model to investigate the concentration dependent role of recombinant Sak and vWbp on citrated blood coagulation and clot fibrinolysis. Apart from revealing novel adaptive strategies of *S. aureus* pathogenicity this analytical approach will become a highly relevant platform for investigation of novel inhibitors against *S. aureus* interference with the hemostatic system. Moreover, we will investigate the relevance of the structural differences of staphylothrombin - induced fibrin to neutrophil migration and killing, known as the key defense mechanisms against *S. aureus* infection. Furthermore, we recently found that bacteraemia isolates from a representative Polish collection can be divided into functional subgroups based on their varying levels of Coa - mediated biofilm and Sak - induced fibrinolysis. The majority of the isolates (66%) produced Coa-dependent biofilm and had no detectable Sak activity, while ca. 20% were positive for both phenotypes. Interestingly, the subgroups were differentially associated with the infection foci of the patients. The Sak - negative isolates were more frequently isolated from patients with infective endocarditis, whilst Coa-negative isolates, or isolates characterized by high levels of both phenotypes were more frequently associated with pneumonia. Hereby we propose to address the hypothesis that *S. aureus* exploits different functional strategies to control the amount and structure of deposited fibrin required for adaptation to a specific niche. We will characterize and compare those functional strategies in respect to the individual and combined roles of Sak, Coa and vWbp for the disease development using the most relevant in vivo models of pneumonia, infective endocarditis and chronic wound infection in mice humanized for plasminogen (as Sak is exclusively specific for human plasminogen). The study will be performed using clinically - relevant *S. aureus* isolates representing different functional strategies and their isogenic deletion mutants, deficient of the respective genes. The project will yield novel insights on the mechanisms employed by *S. aureus* during bacteraemia development as well as provide knowledge of importance for the development of preventive measures and improved treatment against severe bacteraemia complications.

2. Central role of the human hemostasis system in the formation of *Staphylococcus aureus* biofilms

Staphylococcus aureus is a leading cause of chronic biofilm infections, and their treatment remain extremely challenging because of the biofilms' resistance to antibiotics and host immune responses. An increased understanding of *S. aureus* biofilms is therefore needed in order to design better therapies in the future. Biofilms are usually thought of as bacterial communities attached to surfaces and immersed in an extracellular matrix produced by the bacteria themselves. However, there is increasing number of evidence that *S. aureus* can incorporate host-derived compounds into its biofilm matrix, what leads to formation of biofilms with distinctly altered properties. A unique virulent feature of *S. aureus* is its ability to manipulating the host hemostasis (that is, the coagulation and fibrinolysis systems), creating or dissolving fibrin clots according to its infectious needs. Therefore, it is likely that this host-derived fibrin is also being used by *S. aureus* as a scaffold for its own biofilm. Indeed, we have observed, that when grown in presence of host plasma, *S. aureus* incorporates host-derived fibrin and fibrinogen in tis biofilm matrix, creating a biofilms with unusual structure and properties, distinct from the typical *S. aureus* biofilms studied in laboratories. Importantly, as plasma and/or coagulation proteins are almost always present at sites of *S. aureus* infection, this type of fibrin-containing biofilms is probably the default type of *S. aureus* biofilm in real-life scenarios. Therefore, it is impossible to understand *S. aureus* biofilm infections without first understanding how and why these fibrin-containing biofilms differ from "traditional" biofilms. In this project we will explore the unique features of fibrin-containing *S. aureus* biofilms, and will explain mechanisms behind this distinct types of biofilm formation. By combining state-of-the-art microscopy of laboratory biofilms, biophysical analyses of biofilm mechanics, insights from molecular biology and analysis of *S. aureus* mutant panels, large-scale genotyping and phenotyping of *S. aureus* clinical isolates from human infections, and analysis of biofilm samples from mouse infection models and human patients, we will reach three aims: 1. Characterize the distinct structural and mechanical properties of fibrin-containing *S. aureus* biofilms. 2. Identify the regulatory mechanisms controlling development of fibrin-containing *S. aureus* biofilms. 3. Elucidate the mechanism of interaction of *S. aureus* with host cells (phagocytes and platelets) in the context of fibrin-containing biofilms. Performed in collaboration between Jagiellonian University and University of Warsaw, this project will not only help establish a new interdisciplinary and intercollegiate *S. aureus* research group in Poland, but will also provide a new paradigm of "host-derived biofilm matrix components", which can initiate a new research avenue on multiple other biofilm-forming microorganisms.

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given and family name

Information on personal data processing

Controller

Controller of your personal data processed in connection with the recruitment process is the University of Warsaw, ul. Krakowskie Przedmieście 26/28, 00-927 Warszawa, as the Employer.

Contact with the controller:

- by traditional mail at: University of Warsaw, ul. Krakowskie Przedmieście 26/28, 00-927 Warszawa (name the organizational unit to which your letter is addressed);
- by phone: 22 55 20 355.

Data Protection Officer (DPO)

Controller has designated Data Protection Officer whom you may contact via email at iod@adm.uw.edu.pl. You may contact the DPO in all matters relating to your personal data processing by the University of Warsaw and the exercise of rights in relation to the processing of personal data.

The DPO, however, does not proceed other matters, like handling recruitment procedures, collecting recruitment documents, providing information on current recruitment process.

Purpose and legal grounds of data processing

Personal data of candidates for employment shall be processed for recruitment purposes only.

Your personal data shall be processed in the scope as indicated by employment law¹ (*given name (names) and family name, date of birth, contact information as provided, education, professional qualifications, previous employment*) for the purposes of this recruitment process², whereas other data³ shall be processed based on your consent which may take the following wording:

I agree to the processing of personal data provided in (e.g. CV, cover letter, and other submitted documents) by the University of Warsaw for realising my recruitment process.

¹ Art. 22¹ of the law of June 26, 1974 Labour Code (i.e. Journal of Laws 2019 item 1040 with subsequent changes);

² Art. 6 section 1 letter b of the Regulation of the European Parliament and the Council (EU) 2016/679 of April 27, 2016 on protection of individual persons with regard to the personal data processing and on the free flow of such data, and also repealing Directive 95/46/EC (general regulation on data protection) (Official Journal EU L 119 of 04.05.2016, page 1, with subsequent changes) (hereinafter as the GDPR);

³ Art. 6 section 1 letter a of the GDPR;

If your documents include data as mentioned in Art. 9 section 1 of the GDPR (special categories of personal data), processing shall be possible upon your consent to processing such data⁴ which may take the following wording:

I agree to the processing of special categories of personal data, as mentioned in Art. 9 section 1 of the GDPR, provided in (e.g. CV, cover letter, and other submitted documents) by the University of Warsaw for realising my recruitment process.

The University of Warsaw shall be also processing your personal data in future recruitment processes upon your consent⁵ which may take the following wording:

I consent to processing of my personal data for the purposes of any future recruitment processes at the University of Warsaw for the period of the next nine months.

You may revoke all such consents at any time by, for example, sending an email at (email address due for the recruitment process).

Be advised that the revocation of your consent does not affect legal compliance of processing which had been completed upon consent before its revocation.⁶

Data retention period

Your personal data collected in this recruitment process shall be stored over the period of three months from the date the recruitment process is completed.

In case you agree to process your data in future recruitments, your data shall be used over the period of nine months.

Data recipients

Officers authorized by the Controller shall have access to your personal data, the processing of which is in the scope of their duties.

Recipients of personal data may be other subjects obligated by the Controller to provide specific services involving data processing, like

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(name all recipients of data)

Data transfer outside the European Economic Area (EEA)

Your personal data shall be disclosed to subjects authorized by law. Signing-in is through Google Forms. Your personal data may be also processed by our provider of G-Suit for education by Google Company in their data processing centres.⁷ Your data shall be protected under the standards of the Privacy Shield, accepted by the European Commission.⁸ This shall guarantee an adequate level of data security.

⁴ Art. 9 section 2 letter a GDPR;
⁵ Art. 6 section 1 letter a GDPR;
⁶ Art. 7 section 3 GDPR;
⁷ <https://www.google.com/about/datacenters/inside/locations/index.html>
⁸ <https://www.privacyshield.gov>

Rights of the data subject

Under the GDPR data subjects have the following rights:

- to access data and to receive copies of the actual data;
- to correct (rectify) your personal data;
- to restrict processing of personal data;
- to erase personal data, subject to provisions of Art. 17 section 3 of the GDPR;
- to file a claim with the President of the Personal Data Protection Office, if you believe data processing violates law.

Information on the requirement to provide data

Providing your personal data in the scope resulting from law is necessary to participate in the recruitment process. Providing other personal data is voluntary.

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place and date

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applicant's signature