# AUREUS: wAll teichoic acids as immUnogenic and conseRved altErnative targets for therapies versUs S. aureus

## AUREUS Consortium: Call for 15 PhD (Doctoral Training) positions within the Marie Skłodowska-Curie Doctoral Network (MSCA-DN)

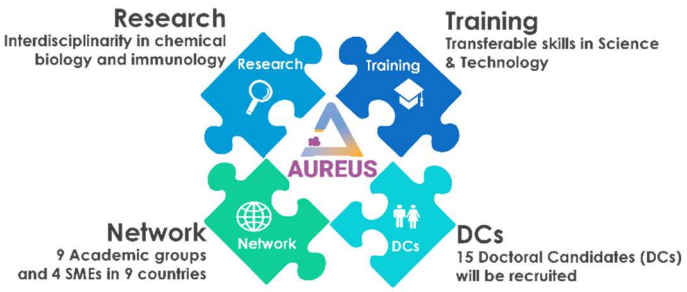
LINK to Euraxess

## Offer Description

### The Project

**AUREUS** is a multidisciplinary European Training Network built to counteract multidrug resistant *S. aureus* infections.

The aim of **AUREUS** is to **train a new generation of researchers as a response to the increasing need for highly qualified work force in the field of chemical biology.**

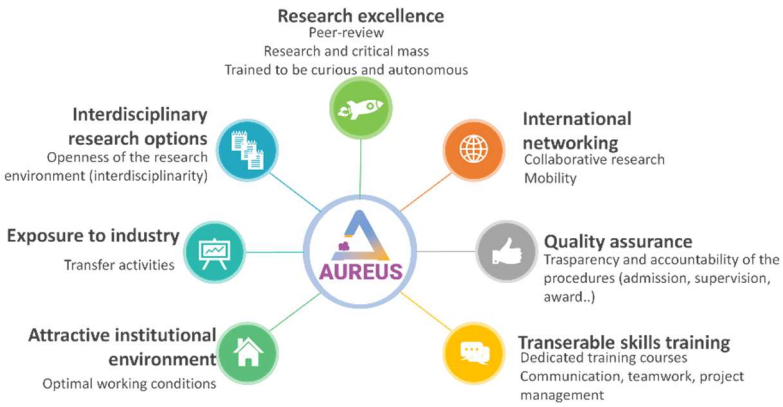



**AUREUS** intersectoral program is based on a unique international team, including **11 academic groups and 5 companies, c**ombining expertise in different fields including **chemistry**, **(micro-)biology** and **immunology**. Under their guidance, the Doctoral Candidates (DCs) will acquire complementary skills to exploit and develop different and innovative strategies to:

**i) unveil the biosynthesis and structure of unique S. aureus cell wall glycopolymers, the so-called WTA (wall teichoic acids)**

**ii) gain greater insights into the molecular basis of the human immune responses to S. aureus WTA**

**iii) harness the acquired knowledge to rationally design and develop effective immune-based therapies against *S. aureus* and related bacterial species.**




Moreover, DCs will be **trained in transferable skills** and will have the opportunity to take part in **research training** (secondments) in other consortium member's labs.

**Pursuing a PhD within the AUREUS network is an excellent starting point for a career at both top European research institutions as well as the healthcare/biotech job market.**

**Do you want to be a DC trained with broad, top-class scientific and professional competencies and skills, thereby expanding the pipeline of future leaders for both industry and academia?**

**Are you open-minded, curious, and ready to explore new ways, and do you like the challenge of working with 14 PhDs at leading academic research institutes and companies? Then apply!**

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## Requirements for all applicants

- Appreciation for interdisciplinary work, proactive drive to collaborate and excellent communication skills.
- Proficient speaking and writing in English.
- Applicants must be eligible to work in the European Union.
- Applicants should be available to start their project from **October 1st 2025**, onwards.
- Applicants are expected to demonstrate a strong interest in the specific research area of the PhD project they are applying for (see descriptions below).

**Important note!**

Candidates must meet the specific requirements of the University where they will be enrolled.
Information about these requirements, if applicable, can be found via the link indicated in the relevant PhD project description section 'Contacts for info'.

## Scientific Requirements

**Research Field**: Organic Chemistry, Analytical Chemistry, Biochemistry, Physical and Structural Biology, Immunology, Microbiology, Molecular Biology, Pharmacy or a related discipline
**Education Level**: Master's Degree or equivalent that fits the research area(s) of the DC position(s) of your interest.

## Benefits

- Highly **competitive salary and working conditions** following the MSCA-DNs guidelines (EU guidelines) and the general regulations of each host institution.
- **Challenging research projects** to lead to a dissertation PhD thesis at high-profile universities.
- **Participation in network-wide training activities, courses, workshops and conferences**.
- **Employment contract for 36 months** by the host institution entitled to full employee benefits and inclusion in social security schemes of the host country.
- Although the standard length for the PhD positions is a 3-year MSCA-DN contract, for some DCs positions, in the AUREUS DN funding for an additional 4th year will be provided by the host institution.

# Eligibility criteria

- **Following the strict MSCA-DN rules, you must meet the following two eligibility criteria** (please do not apply if you are not eligible):
- **1. Supported researchers**: applicants must be doctoral candidates, i.e., not already in possession of a doctoral degree at the date of recruitment.
- **2. Mobility rule**: researchers must not have resided or carried out their main activity (e.g., work, studies) in the country of the recruiting host institution for more than 12 months in the 36 months immediately before their recruitment date.
- Other eligibility criteria may apply depending on the recruiting beneficiary.

# Application and Selection Process

**Step 1: CALL FOR APPLICANTS**
**Applications (in English) must include:**
1) a **cover letter**, which includes the motivation for the position and should emphasize the candidate's strengths regarding the project and the requirements (max 3 pages, font size 12 and single spacing, with figures if necessary). **In the cover letter, the applicant should clearly indicate which other project(s), e.g. Project_DC#, the candidate applied to.**
2) an **updated CV** (max 2 pages)
3) the **scanned copy of the diploma** (usually the Master's Degree), which formally entitles the applicant to embark on a doctorate degree. In case the Master's Degree has not been obtained yet at the closing date for application, the candidate has to send a declaration signed by his/her supervisor or from the University stating that the degree will be obtained before the start date of PhD enrollment.

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4) **Letter of Recommendation** from two appropriate referees or contact details of two references.
5) **Transcripts of records.**

Candidates can apply for **maximum three PhD projects** and the applications need to be submitted separately to each institution.
The **PhD project number and name of the applicant** needs to be mentioned in the **header of the application file and to be used also as the name of the file** (the application when sent by email to be one single pdf (< 3 MB) using the following format: *Project_DC#_Name_of_the_candidate*.

## How to apply (please see information for individual projects):

1. **If the application is required to be sent by email** (please see email address in individual project descriptions), prepare the application in a **single pdf file** (< 3 MB), and name it following this format: *Project_DC#_Name_of_the_candidate* ).
The **subject line of the email** must be in the following format: *"AUREUS application for Project_DC#".*

2. **If the application is required to be sent through a recruitment platform/application system** (link provided in individual project description), please follow the instructions valid for the application system

**Step 2: ELIGIBILITY AND ADMISSIBILITY**
The eligibility check will be carried out based on the candidates' CV and cover letter by the Evaluation Committee, which will be established for each of the 15 PhD projects. The Committee may ask applicants for additional information or clarifications.
Selected applicants will be invited for an interview by email. In the email the candidate will receive specific guidance about the interviewing process.

**Step 3: INTERVIEWS**
All interviews will be conducted remotely by the Evaluation Committee with the aim to evaluate the adequacy to the project of the candidate. The applicant will be informed well in advance about technical requirements needed for the interview.

**Step 4: FINAL RANKING**

Those applicants who were selected for Step 3 will be duly informed of the results and the selected candidates will be asked to provide a written acceptance of the PhD position (i.e., a confirmation by email). If a successful candidate declines the offer, the PhD position will be offered to the next ranked candidate.

**The closing date for applications is: 25th May 2025 - 23:00 (Europe/Brussels) – unless otherwise specified in the DC project description**

## Individual Research Projects Overview

| Project | Project title & Application deadline | Contact for info and email where application is to be sent or link to recruitment | Host Institution & Country |
|---|---|---|---|
| **DC1** | Targeting WTA biosynthesis enzymes: enzymatic synthesis, probes and inhibitors<br>**11th May 2025** | **Prof. dr Jeroen Codée**<br>jcodee@chem.leidenuniv.nl<br>**Application to be sent to:**<br>https://www.universiteitleiden.nl/vacatures/2025-nl/q1/15528phd-design-and-synthesis-of-wall-teichoic-acid-biosynthesis-enzyme-inhibitors | **Universiteit Leiden**<br>(ULEI)<br>The Netherlands |
| **DC2** | Characterisation and inhibition of enzymes involved in ribitol-phosphate modification of wall teichoic acid<br>**12th May 2025** | **Prof. Lianne Willems** lianne.willems@york.ac.uk<br>**Application to be sent to:**<br>https://jobs.york.ac.uk/vacancy/marie-curie-early-stage-researcher-583912.html | **University of York**<br>(UY)<br>United Kingdom |

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| **DC3** | Bacterial glycoconjugates as targets for new therapeutics and diagnostics<br>**25th May 2025** | **Prof. Roberta Marchetti**<br>roberta.marchetti@unina.it<br>**Application to be sent to:**<br>marchetti.unina@gmail.com | **Università degli Studi di Napoli Federico II**<br>(UNINA)<br>Italy |
| **DC4** | D-Alanylated teichoic acids and their interaction with host receptors<br>**11th May 2025** | **Prof. dr Jeroen Codée** jcodee@chem.leidenuniv.nl<br>**Application to be sent to:**<br>https://www.universiteitleiden.nl/vacatures/2025-nl/q1/15529phd-automated-synthesis-of-well-defined-bacterial-wall-teichoic-acids | **Universiteit Leiden**<br>(ULEI)<br>The Netherlands |
| **DC5** | Probing the Immune Recognition of Staphylococcus aureus Teichoic Acids by Microarray Analysis<br>**25th May 2025** | **Dr Yan Liu**<br>yan.liu2@imperial.ac.uk<br>**Dr Antonio Di Maio**<br>a.di-maio@imperial.ac.uk<br>**Application to be sent to:**<br>Description \| Jobs \| Imperial College London | **Imperial College of Science Technology and Medicine**<br>(ICL)<br>United Kingdom |
| **DC6** | Investigating S. aureus Recognition by Receptor Proteins<br>**25th May 2025** | **Prof. Franck Fieschi**<br>franck.fieschi@ibs.fr<br>**Application to be sent to:**<br>franck.fieschi@ibs.fr | **Universite Grenoble Alpes**<br>(UGA)<br>France |
| **DC7** | Unveiling the structural features for bacterial surface glycopolymers recognition by host immune response<br>**25th May 2025** | **Prof. Roberta Marchetti**<br>roberta.marchetti@unina.it<br>**Application to be sent to:**<br>marchetti.unina@gmail.com | **Università degli Studi di Napoli Federico II**<br>(UNINA)<br>Italy |
| **DC8** | C-type lectin receptors in recognition and response to S. aureus WTA structures<br>**11th May 2025** | **Prof. Nina van Sorge**<br>n.m.vansorge@amsterdamumc.nl<br>**Application to be sent to:**<br>Vacatures - PhD (x2) in Staphylococcus aureus immune interaction - Amsterdam UMC | **Amsterdam UMC**<br>(AMC)<br>The Netherlands |
| **DC9** | Biophysical and cellular characterization of PRR-WTA interaction<br>**22nd March 2025**<br>**CLOSED** | **Prof. Dr. Christoph Rademacher**<br>Christoph.Rademacher@unvie.ac.at<br>**Application to be sent to:**<br>Christoph.Rademacher@unvie.ac.at | **Universitat Wien**<br>(UNIVIE)<br>Austria |
| **DC10** | Studying bacterial surface glycopolymers-proteins interactions<br>**25th May 2025** | **Dr. Ludovic Landemarre**,<br>landemarre@glycodiag.com<br>**Application to be sent to:**<br>landemarre@glycodiag.com or<br>admin@glycodiag.com | **Glycodiag**<br>(GLYD)<br>France |
| **DC11** | Structural biology of teichoic acid binding proteins<br>**25th May 2025** | **Prof. Mark J. van Raaij** mjvanraaij@cnb.csic.es<br>**Application to be sent to:**<br>mjvanraaij@cnb.csic.es | **Agencia Estatal Consejo Superior de Investigaciones Cientificas**<br>(CSIC)<br>Spain |
| **DC12** | Generating and characterizing anti-WTA mAb from human memory B cells using synthetic S. aureus WTA structures<br>**11th May 2025** | **Prof. Nina van Sorge**<br>n.m.vansorge@amsterdamumc.nl<br>**Application to be sent to:**<br>Vacatures - PhD (x2) in Staphylococcus aureus immune interaction - Amsterdam UMC | **Amsterdam UMC**<br>(AMC)<br>The Netherlands |
| **DC13** | Glycosylation-dependent interaction of Staphylococcal WTA with immunoglobulins and scavenger receptor LOX1<br>**11th May 2025** | **Prof. Andreas Peschel**<br>andreas.peschel@uni-tuebingen.de<br>**Application to be sent to:**<br>janes.krusche@uni-tuebingen.de | **Eberhard Karls Universitaet Tuebingen**<br>(UT)<br>Germany |

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| **DC14** | MS toolbox to understand the molecular basis of WTA/protein interaction<br>**25th May 2025** | **Dr. Jonathan Bones,**<br>jonathan.bones@nibrt.ie<br>**Dr. Sara Carillo**<br>sara.carillo@nibrt.ie<br>**Application to be sent to:**<br>https://www.nibrt.ie/careers/vacancies / | **National Institute for Bioprocessing Research and Training Limited**<br>(NIBRT)<br>Ireland |
| **DC15** | MGL binding to S. aureus cell surface WTA/LTA by integrated structural biology<br>**11th May 2025** | **Dr. Cedric Laguri**<br>cedric.laguri@ibs.fr<br>**Application to be sent to:**<br>cedric.laguri@ibs.fr | **Universite Grenoble Alpes**<br>(UGA)<br>France |

# Description of the Individual Projects

## Project_DC #1: Targeting WTA biosynthesis enzymes: enzymatic synthesis, probes and inhibitors

**Main Supervisor: Jeroen Codée** (ULEI) **Co-Supervisor:** Lianne Willems (UY)

**Location: Universiteit Leiden (ULEI), The Netherlands –** **https://www.universiteitleiden.nl/en/science/chemistry/biosyn** **-** (duration of the PhD: 4 years)

**Objectives:** The aim of AUREUS is to explore and exploit *S. aureus* wall teichoic acids and establish their role, mode of action and interactions with the host immune system at the molecular level. Molecular tools will be developed to probe these interactions as a function of the large structural diversity encountered in these glycopolymers and WTA biosynthesis will be studied with the aim to interfere with the bacterial synthesis of these crucial protective cell wall polymers.

This subproject of the AUREUS consortium will focus on the design, synthesis and exploitation of well-defined molecular tools and inhibitors to study and interfere with bacterial WTA biosynthesis enzymes. The ultimate goal of this work will be to open new routes to develop a new class of antibiotics.

**Expected Results:** Training: Expertise in bio-organic chemistry; Design and synthesis of bio-active compounds; Research: Identifying new WTA-biosynthesis enzymes inhibitors; Unveiling the structural requirements for inhibitor binding.

**The doctoral candidate will work in collaboration with Universite Grenoble Alpes (UGA), France; University of York (UY), United Kingdom and Iceni Glycoscience Limited (ICENI), United Kingdom.**

**Details on the terms of employment** can be found on the website of Universiteit Leiden: https://www.staff.universiteitleiden.nl/human-resources

**Link to the application/recruitment system**: https://www.universiteitleiden.nl/vacatures/2025-nl/q1/15528phd-design-and-synthesis-of-wall-teichoic-acid-biosynthesis-enzyme-inhibitors

**Internal Deadline**: May 11th, 2025

**Subject area**: not applicable

**Contacts for info:** Prof. dr Jeroen Codée (jcodee@chem.leidenuniv.nl)

**Project-specific selection criteria**: We are looking for a candidate with a strong synthetic organic chemistry background with a keen interest in (chemical) biology and structural biology, who is a real team player and open to collaborating in an intersectoral, international and interdisciplinary manner.

**Additional advantageous skills:** Interest in structural enzymology.

**Recommended literature:**

1. (Automated) Synthesis of Well-defined Staphylococcus Aureus Wall Teichoic Acid Fragments – Chem. Eur. J. 2021, 27, 10461-10469. doi.org/10.1002/chem.202101242
2. Do not discard Staphylococcus aureus WTA as a vaccine antigen – Nature 2019, 572, E1–E2. doi.org/10.1038/s41586-019-1416-8
3. Antibody Recognition of Different Staphylococcus aureus Wall Teichoic Acid Glycoforms - ACS Centr. Sci. 2022, 8, 1383-1392. doi.org/10.1021/acscentsci.2c00125

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## Project_DC#2: Characterisation and inhibition of enzymes involved in ribitol-phosphate modification of wall teichoic acid

**Main Supervisor:** Lianne Willems (UY) **Co-Supervisor:** Jeroen Codée (ULEI)

**Location: University of York (UY), United Kingdom – https://www.york.ac.uk/** (duration of the PhD: 3 years)

**Objectives:** Wall teichoic acids (WTAs) are glycoconjugates on the surface of gram-positive bacteria such as *Staphylococcus aureus*, which play important roles in, for example, cell growth, division and biofilm formation. They consist of polymers of either glycerol- or ribitol-phosphate which are further decorated with *N*-acetylglucosamine and alanine modifications to finetune their functions. Since WTAs are essential for pathogenesis and also implicated in antibiotic resistance of *S. aureus*, their biosynthesis has been proposed as a potential target for novel antibacterial agents. In this project, we aim to produce some of the enzymes responsible for biosynthesis and glycosylation of *S. aureus* WTA in order to explore the potential for inhibition of these enzymes with synthetic small molecules. For this purpose, we will express and purify the recombinant enzymes and develop *in vitro* assays to test their activity. Using the established platforms, we will then evaluate the inhibitory potency of putative small molecule inhibitors synthesized by others in the consortium. Additionally, we will apply the enzymes produced in chemoenzymatic synthesis strategies, allowing the generation of large WTA polymers with various modification patterns. The candidate will collaborate with several others across the consortium including DC1 for enzyme inhibition, DC3 for enzymatic WTA synthesis, DC6 and DC11 for structural characterization of the purified proteins and inhibitor complexes.

**Expected Results:** Training will be provided in gene expression and protein purification; biochemical analyses including enzyme activity assays; biophysical analyses. Training in synthetic chemistry can also be provided depending on the candidate's interests and experience. Research outputs will include the purification of recombinant enzymes; generation of active-site mutants; development of enzyme assays and x-ray structures; inhibition and co-crystallisation studies; chemoenzymatic synthesis of WTA.

**The doctoral candidate will work in collaboration with Università degli Studi di Napoli Federico II (UNINA), Italy; Universiteit Leiden (ULEI), The Netherlands and Biopox Srl (BIOPOX), Italy.**

**Details on the terms of employment** can be found on the website of the University of York: https://www.york.ac.uk/study/postgraduate-research/

**Entry requirements:** Applicants should have, or be expecting to achieve, a 2:1 undergraduate degree in Chemistry or a relevant, related discipline or a higher qualification such as MSc or Masters by Research. International equivalent qualifications are accepted; you can check requirements of your country here.

**Link to the application/recruitment system**: https://jobs.york.ac.uk/vacancy/marie-curie-early-stage-researcher-583912.htm

**Internal Deadline**: May 12th, 2025

**Subject area**: glycobiology, molecular biology, biochemistry, enzymatic synthesis

**Contacts for info:** Prof. Lianne Willems (lianne.willems@york.ac.uk)

**Project-specific selection criteria:** Experience and skills in molecular biology techniques, including (bacterial) gene expression and protein purification, and enthusiasm for the chosen project area.

**Additional advantageous skills:** Interest in carbohydrate chemistry and chemical glycobiology research; strong communication skills; ability to work independently and as a team player in a multidisciplinary environment. Knowledge of, and experience in, organic synthetic chemistry are also advantageous.

**Recommended literature:**


1. Swoboda JG, Campbell J, Meredith TC, Walker S. Wall teichoic acid function, biosynthesis, and inhibition. Chembiochem. 2010;11(1):35-45. doi:10.1002/cbic.200900557
2. Brown S, Meredith T, Swoboda J, Walker S. Staphylococcus aureus and Bacillus subtilis W23 make polyribitol wall teichoic acids using different enzymatic pathways. Chem Biol. 2010;17(10):1101-1110. doi:10.1016/j.chembiol.2010.07.017
3. Guo Y, Pfahler NM, Völpel SL, Stehle T. Cell wall glycosylation in Staphylococcus aureus: targeting the tar glycosyltransferases. Curr Opin Struct Biol. 2021;68:166-174. doi:10.1016/j.sbi.2021.01.003



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## Project_DC#3: Bacterial glycoconjugates as targets for new therapeutics and diagnostics

**Main Supervisor:** Roberta Marchetti (UNINA) **Co-Supervisor:** Lianne Willems (UY)

**Location: Università degli Studi di Napoli Federico II (UNINA), Italy – https://www.unina.it/en_GB/home-** (duration of the PhD: 3 years)

**Objectives:** This project will focus on the investigation of underexplored steps of WTA biosynthesis with the aim to design inhibitors of WTA-biosynthesis enzymes Computational studies will be used to identify new small-molecule ligands of the selected enzyme. Published 3D structures, as derived by NMR or X-ray crystallography, will be used for molecular docking calculations; otherwise, homology modelling and/or prediction with AlphaFold will be performed starting from known structures of homologous enzymes. The molecular basis of the interaction between potential inhibitors and enzymes will be disclosed by taking the advantage of state-of-the-art biophysical techniques. In particular, versatile NMR spectroscopy experiments, including STD NMR, tr-NOE, CPMG experiments, WaterLOGSY, DOSY etc., allow to explore the inhibitor binding and will provide key information on the enzyme mode of action. Additional atomic-level information on protein side will be obtained by NMR analysis of ligands bound to isotopically labelled proteins. The candidate will work closely with DC2, DC6 and DC11 to rationalize the design and to propose new compounds for optimization.

**Expected Results:** Training will be provided in computational studies (e.g. docking, MM and MD simulations), organic and carbohydrate chemistry. Research outcomes will include insights on the mode of action of selected WTA biosynthesis enzymes and on the structural requirements for inhibitor binding. As well as the identification new WTA-biosynthesis enzymes inhibitors.

**The doctoral candidate will work in collaboration with Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC), Spain; University of York (UY), United Kingdom and Iceni Glycoscience Limited (ICENI), United Kingdom**

**Details on the terms of employment:** not applicable
**Internal Deadline**: May 25th, 2025
**Subject area**: Computational and structural biology; Bioinformatics, Organic Chemistry, Carbohydrate chemistry,
**Contacts for info:** Prof. Roberta Marchetti (roberta.marchetti@unina.it)
**Email address where the application to be sent:** marchetti.unina@gmail.com

**Project-specific selection criteria:** Background in structural biology
**Additional advantageous skills:** Proven experience for computational methods, including Docking, MD and virtual screening; Biochemical lab skills including cell culture, protein expression and purification; Knowledge in NMR-based structural biology. Excellent communication skills; Interest in carbohydrate chemistry and chemical glycobiology research; Ability to work independently and as a team player in a multidisciplinary environment.

**Recommended literature:**


1. Swoboda JG, Campbell J, Meredith TC, Walker S. Wall teichoic acid function, biosynthesis, and inhibition. Chembiochem. 2010;11(1):35-45. doi:10.1002/cbic.200900557
2. Nieto-Fabregat et al.; Beilstein J. Org. Chem. 2024, 20, 2084–2107. https://doi.org/10.3762/bjoc.20.180



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## Project_DC#4: D-Alanylated teichoic acids and their interaction with host receptors

**Main Supervisor:** Jeroen Codée (ULEI) **Co-Supervisor:** Cristoph Rademacher (UNIVIE)

**Location: Universiteit Leiden (ULEI), The Netherlands – https://www.universiteitleiden.nl/en/science/chemistry/biosyn -** (duration of the PhD: 4 years)

**Objectives:** The aim of AUREUS is to explore and exploit S. aureus wall teichoic acids and establish their role, mode of action and interactions with the host immune system at the molecular level. Molecular tools will be developed to probe these interactions as a function of the large structural diversity encountered in these glycopolymers and WTA biosynthesis will be studied with the aim to interfere with the bacterial synthesis of these crucial protective cell wall polymers.

This subproject of the AUREUS consortium will focus on the development of effective synthesis methodology for the automated solid phase synthesis of well-defined WTA oligomers with a predetermined substitution pattern. This will enable the determination of WTA structure-activity relationships for interactions with antibodies and immune receptors.

**Expected Results:** Training: Expertise in bio-organic chemistry; Design and synthesis of bio-active compounds; Research: Automated solid phase synthesis methodology; libraries of teichoic aicds; detailed structure-activity relationships for teichoic acid binding receptors and antibodies.

**The doctoral candidate will work in collaboration with Glycodiag (GLYD), France; Universite Grenoble Alpes (UGA), France and Universitat Wien (UNIVIE), Austria.**

**Details on the terms of employment** can be found on the website of Universiteit Leiden: https://www.staff.universiteitleiden.nl/human-resources

**Link to the application/recruitment system**: https://www.universiteitleiden.nl/vacatures/2025-nl/q1/15529phd-automated-synthesis-of-well-defined-bacterial-wall-teichoic-acids

**Internal Deadline**: May 11th, 2025

**Subject area**: not applicable

**Contacts for info:** Prof. dr Jeroen Codée (jcodee@chem.leidenuniv.nl)

**Project-specific selection criteria:** We are looking for a candidate with a strong synthetic organic chemistry background with a keen interest in (chemical) biology/immunology, who is a real team player and open to collaborating in an intersectoral, international and interdisciplinary manner.

**Recommended literature:**


1. (Automated) Synthesis of Well-defined *Staphylococcus Aureus* Wall Teichoic Acid Fragments – Chem. Eur. J. 2021, *27*, 10461-10469. doi.org/10.1002/chem.202101242
2. Do not discard Staphylococcus aureus WTA as a vaccine antigen – Nature 2019, 572, E1–E2. doi.org/10.1038/s41586-019-1416-8
3. Antibody Recognition of Different Staphylococcus aureus Wall Teichoic Acid Glycoforms - ACS Centr. Sci. 2022, 8, 1383-1392. doi.org/10.1021/acscentsci.2c00125



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## Project_DC#5: Probing the Immune Recognition of Staphylococcus aureus Teichoic Acids by Microarray Analysis

**Main Supervisor:** Yan Liu (ICL) **Co-Supervisor:** Franck Fieschi (UGA)
**Assisting Supervisor**: Antonio Di Maio (ICL)

**Location: Imperial College of Science Technology and Medicine (ICL), United Kingdom – https://www.imperial.ac.uk/-** (duration of the PhD: 3 years)

**Objectives:** Carbohydrate microarrays have emerged as essential tools in glycobiology over the last two decades and are revolutionizing the molecular dissection of glycan-mediated endogenous recognition systems and microbe-host interactions. The neoglycolipid-based microarray system developed at ICL is one of the leading array platforms worldwide. The clustered and flexible presentation of non-covalently immobilized lipid-linked probes in a liposomal formulation renders this array system uniquely sensitive.

This project focuses on the development of a novel Staphylococcus WTA array to display the largest library to date of structurally defined synthetic TAs fragments of *S. aureus,* as well as WTA macromolecular isolated from *Staphylococcus* bacterial cells. The overarching aim is to establish a comprehensive recognition profile for *S. aureus* WTA with the host immune system. Screening analyses will be conducted to assess the interactions with a range of pattern recognition receptors (PRRs), including C-type lectin receptors, soluble pattern recognition molecules of the complement system, as well as relevant scavenger receptors. These screening analyses are expected to uncover preferred WTA fragments recognized by different immune receptors that serve as potential targets for follow-on investigations, including STD NMR and affinity measurement using SPR and BLI, as well as cellular model studies.

The DC will play an active role, engaging with a dynamic research network, including receiving custom synthetic TA fragments from DC4, collaborating with DC6 and DC9 on immune lectin preparation for microarray studies, and leading follow-up investigations on promising WTA fragments to thoroughly characterize target interactions. These investigations will include STD-NMR (with DC7), SPR and BLI for affinity measurements (with DC14), and cellular model studies (with DC9).

**Expected Results:** Training: Glycobiology, Glycan microarray technologies, Glyco-analytical chemistry, Molecular biology, Microbiology, Glycoinformatics. Research: Method development for arraying WTA fragments; Assay condition optimization for microarray binding studies with immune lectin receptors; Construction of a focused array of the synthetic TA fragment compound library; High throughput recognition studies with lectins (potentially also antibodies); Validation of microarray findings using complementary micro-techniques.

**The doctoral candidate will work in collaboration with Universite Grenoble Alpes (UGA), France; Universitat Wien (UNIVIE), Austria and Biopox Srl (BIOPOX), Italy.**

**Details on the terms of employment** at of Imperial College of Science Technology and Medicine will be provided after the offer is made.

**Link to the application/recruitment system**: Description | Jobs | Imperial College London

**Internal Deadline**: May 25th, 2025

**Subject area**: glycan microarray, glycobiology, molecular interactions

**Contacts for info:** Dr Yan Liu (yan.liu2@imperial.ac.uk), Dr Antonio Di Maio (a.di-maio@imperial.ac.uk)

**Project-specific selection criteria:** Background in Chemistry, Biochemistry, Glyco-Chemistry, Glycobiology or a closely related discipline.

**Additional advantageous skills:**

- Experience with glycan microarray or other array technologies
- Knowledge of glycan interactions, glycan binding systems, and ideally immune lectin receptors
- Some experience in small-scale organic synthesis
- Ability to work independently
- A collaborative mindset in a multidisciplinary and international environment
- Flexibility to travel and work in network laboratories across the EU

**Recommended literature:** PMID: 36313161, 24508828, 25670804, 39271664, 35352122

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## Project_DC#6: Investigating S. aureus Recognition by Receptor Proteins

**Main Supervisor:** Franck Fieschi (UGA) **Co-Supervisor:** Sara Carillo (NIBRT)

**Location: Universite Grenoble Alpes (UGA), France – https://www.univ-grenoble-alpes.fr/english/ - Institut de Biologie Structurale - https://www.ibs.fr** (duration of the PhD: 3 years)

**Objectives:** This project aims to study in depth the recognition of S. aureus by specific receptor proteins, including C-type lectin receptors (CLRs) to obtain more in-depth information on the critical molecular motifs recognized that could be used in certain potential therapeutic strategies. The capacity of CLRs to recognize molecular motif from S. aureus has been already documented but only for a limited number of CLR and thus it is still a poorly understood aspect of host-pathogen interactions. We have developed expertise in the production of a library of CLRs and the characterization of their interaction with carbohydrate-based motifs from pathogens. Thus, in this project, the recruited PhD will: 1) produce and engineer different proteins, including lectins at different oligomeric states ; 2) screen and identify the diversity of receptor proteins able to recognize selectively molecular component of S. aureus cell wall (in collaboration with other PhDs, DC1 and DC5 within the European network); 3) characterize proteins interaction with identified ligand investigating their binding affinity and kinetics through biophysical assays, such as ITC, SPR ( and/or BLI.

In collaboration with DC4, DC7 and DC11, the structural basis of receptor/ligand complexes will be elucidated. Cryo-electron microscopy for larger complexes will be considered. The fine characterization of binding modes, at the atomic level, will drive the future design of potential drugs that could be used in anti-adhesive and vaccine strategies.

**Expected Results:** Training: Recombinant protein production (bacterial expression, protein refolding and purification); Biophysical interaction studies (SPR, ITC, BLI, Cryo-EM). Research: Generation of recombinant proteins, including lectins, with and without engineered modifications; Lectin array and glycan made with our library of ligands from other consortium members; Biophysical characterizations of ligand identified with determination of affinity/avidity, kinetics of thermodynamic parameter of interactions ; Structural characterizations of relevant complexes by CryoEM.

**The doctoral candidate will work in collaboration with Universiteit Leiden (ULEI) in the Netherlands; National Institute for Bioprocessing Research and Training Limited (NIBRT), Imperial College of Science Technology and Medicine (ICL),United Kingdom, Ireland and Glycodiag (GLYD), France.**

**Details on the terms of employment** can be found on the website of Universite Grenoble Alpes: https://emploi.univ-grenoble-alpes.fr/english/

**Internal Deadline**: May 25th, 2025

**Subject area**: Host -Pathogen Interaction, Biochemistry, Immunology, Glycobiology, Structural biology

**Contacts for info:** Pr. Franck Fieschi (franck.fieschi@ibs.fr), Institut de Biologie Structurale, Université Grenobel Alpes, Grenoble, France

**Email address where the application to be sent:** franck.fieschi@ibs.fr

**Project-specific selection criteria:** Prior experience in recombinant protein production, biochemistry, biophysics of interaction study (SPR, BLI or ITC) and/or background on structural biology

**Additional advantageous skills:** Organizational skills, fluency in English, ability to work independently and as a team player in a multidisciplinary environment. Good communication skills (in the context of a multi-partner project on a European scale).

**Recommended literature:**


1. https://pubs.acs.org/doi/10.1021/acscentsci.2c01136
2. https://pubs.rsc.org/en/content/articlelanding/2024/sc/d4sc02980a
3. https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1009576



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## Project_DC#7: Unveiling the structural features for bacterial surface glycopolymers recognition by host immune response

**Main Supervisor:** Roberta Marchetti (UNINA) **Co-Supervisor:** Jonathan Bones (NIBRT)

**Location: Università degli Studi di Napoli Federico II (UNINA), Italy -https://www.unina.it/en_GB/home-** (duration of the PhD: 3 years)

**Objectives:** Understanding the molecular basis of bacterial glycopolymers function and recognition in many pathogen-related diseases remains a major challenge. That is why, although promising, the exploitation of many relevant pathologically protein-carbohydrate interactions has not yet reached its full potential. To fill this gap, DC7 will disclose pivotal molecular mechanisms that underpin pathogen recognition and subsequent orchestration of the immune response. The project will focus on S. aureus WTA in their interaction with PRRs and mAbs. An integrated approach based on state-of-the-art biophysical techniques combined with computational studies will be employed to unravel the conformation, dynamics and recognition features of WTA. The main goals of this research project will be: 1) studying WTA binding to selected PRRs; 2) studying WTA binding to selected mAbs; 3) investigating the conformational behaviour of WTA when interacting with PRRs and mAbs.
Detailed understanding of these complex interactions can provide new insights toward future immune-stimulatory therapeutics against infection.

**Expected Results:** Training will be provided in biophysical methods, particularly in NMR spectroscopy techniques (including ligand and protein-based approaches) devoted to the study of protein-ligand interaction; organic and carbohydrate chemistry; computational methods for building 3D glycoconjugates structures. Research outcomes will include structural requirements for the specific recognition of different WTA glycoforms by PRRs/mAbs; knowledge at the atomic level on the impact of WTA modifications on S. aureus-host interaction.

**The doctoral candidate will work in collaboration with Amsterdam UMC (AMC), The Netherlands; National Institute for Bioprocessing Research and Training Limited (NIBRT), Ireland and University of York (UY), United Kingdom.**

**Details on the terms of employment:** not applicable
**Internal Deadline**: May 25th, 2025
**Subject area**: Structural biology; Bioinformatics, Organic Chemistry, Carbohydrate chemistry
**Contacts for info:** Prof. Roberta Marchetti (roberta.marchetti@unina.it)
**Email address where the application to be sent:** marchetti.unina@gmail.com

**Project-specific selection criteria:** Background in structural biology
**Additional advantageous skills:** Proven expertise in NMR methods for the study of protein-glycan interactions; Biochemical lab skills including cell culture, protein expression and purification; Knowledge in computational techniques including Docking and MD. Excellent communication skills; Interest in carbohydrate chemistry and chemical glycobiology research; Ability to work independently and as a team player in a multidisciplinary environment.

**Recommended literature:**

**1.** Di Carluccio C. et al. ACS Central Science, 2022, 8, 10, 1383–1392.
**2.** Di Carluccio C. et al. Carbohydrate Research 503 (2021) 108313

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## Project_DC#8: C-type lectin receptors in recognition and response to S. aureus WTA structures

**Main Supervisor:** Nina van Sorge (AMC) **Co-Supervisor:** Cristoph Rademacher (UNIVIE)

**Location: Amsterdam UMC (AMC), The Netherlands-**
**https://www.amsterdamumc.org/en/organization/amsterdam-umc.htm -** (duration of the PhD: 4 years)

**Objectives:** Antigen-presenting cells (APCs) in the skin are critical to initiate local host defense responses and induce appropriate adaptive immunity for long-term protection. The skin contains different subsets of APCs that express different innate receptor repertoires, including CLRs. We have demonstrated that S. aureus is sensed by the CLR langerin (CD207), which is expressed on skin epidermal Langerhans cells (LCs) and interacts with specific S. aureus WTA glycoforms, resulting in different immunological outcomes.
However, when S. aureus invades deeper into the skin tissue, recognition by dendritic cells (DCs) becomes important. Using the synthetic WTA molecules (ULEI), recombinant CLR collection (UGA, UNIVIE) and characterized S. aureus WTA wild-type and mutant strains, DC8 will 1) identify recognition of S. aureus glycosylated WTAs by DC-expressed CLRs; 2) determine human DCs immunological responses in response to S. aureus glycotypes, and 3) based on the structural requirements for CLR-WTA interaction (DC5, DC6 and DC7), human genome databases will be interrogated to identify whether single-nucleotide polymorphisms in critical residues occur in the population. If this is the case, the SNP-CLR variant will be expressed as recombinant protein and in cell line models to assess their impact on S. aureus detection.

**Expected Results:** Training: Expertise in lectin-receptor biology, Flow cytometry, Molecular biology, Tissue culture, Lentiviral transduction, Microbiology, Immunological assays, Human cell isolation. Research: Identifying new CLRs that recognize S. aureus WTA-glycan patterns; Determining the impact of CLR interaction for DC immunological responses; Studying the impact of CLR SNP variation on S. aureus interaction.

**The doctoral candidate will work in collaboration with Universite Grenoble Alpes (UGA), France; Universitat Wien (UNIVIE), Austria and Iceni Glycoscience Limited (ICENI), United Kingdom.**

**Details on the terms of employment** can be found on the website of Amsterdam UMC: cao nfu umc

**Link to the application/recruitment system**: Vacatures - PhD (x2) in Staphylococcus aureus immune interaction - Amsterdam UMC

**Internal Deadline**: May 11th, 2025

**Subject area**: Microbiology, host-pathogen interaction

**Contacts for info:** Prof. Nina van Sorge (n.m.vansorge@amsterdamumc.nl)

**Project-specific selection criteria:** not applicable

**Additional advantageous skills:** You have experience with molecular (micro-)biology techniques and/or flow cytometry, and cell culture. Affinity with bioinformatics analysis and glycobiology is preferred. You can work independently as well as in a team in a multidisciplinary and international environment.

**Recommended literature:** PMID 32733813, 31088921, 31141812, 31219660

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## Project_DC#9: Biophysical and cellular characterization of PRR-WTA interaction

**Main Supervisor:** Christoph Rademacher (UNIVIE) **Co-Supervisor:** Nina van Sorge (AMC)

**Location: Universitat Wien (UNIVIE), Austria- https://www.univie.ac.at/en/ -** (duration of the PhD: 4 years)

**Objectives:** S. aureus host interaction is governed by many PRRs depending on the immune cells they encounter. UNIVIE has a long-standing expertise in mammalian C-type lectins and has previously reported on the structural basis of langerin S. aureus interactions. Furthermore, other PRRs are available to UNIVIE (DC-SIGN, dectin-1, dectin-2, MCL, mincle, CLEC2, CLEC14A, SP-D) and this collection can be expanded based on the discoveries of new PRRs . In this project, we will build up our insights into PRR epitope interaction from atomistic insights coming from biophysical studies to cell lines with individual receptors, singling out their individual contributions and synergies. Firstly, we will study the molecular details of the interaction by biophysical means (NMR, GCI, ITC, TSA ). Importantly, the insight generated from these biophysical studies will then be taken to the cellular level. A large panel of PRRs are available expressed on U937 or THP-1 NFkB reporter cells. These are either single receptor expressed, or multiple e.g. langerin/dectin-1 double positive cells, which will be applied to study the synergistic recognition of multiple epitopes present on S. aureus. However, since for most PRRs epitopes need to be present either on bacteria or at least on larger particles to activate the cells, synthetic structures will be used to generate suitable stimulants. These well-defined structures will either be formulated as liposomes (100 nm), by conjugation to PEGylated lipids using microfluidics formulation, or by reconstitution of supported lipid bilayers on plastic beads. Mixing epitopes and altering their density, in combination with investigating receptor mixture on U937 cells, resembling innate immune cells will give rise to a bottom-up approach to understand host-pathogen interactions.
Besides NFkB activation, these cells have been used to study further upstream signalling events such as phosphorylation of Erk in flow cytometry. Finally, UNIVIE has access to primary Langerhans cells from mice and human and can perform cell uptake and stimulation assays using these liposomes and particles to transfer cell line-based findings to more relevant primary cells. This will generate a picture of the complexity of differential epitope recognition by a large panel of involved PRRs.

**Expected Results:** Training: Viral transduction to generate reporter cell lines, Flow cytometry, Microscopy, Quantification of cellular signalling, Immunological assays. Research: Cellular interaction studies with S. aureus strains; Quantification of signal integration from multiple PRRs; Biophysical studies into protein ligand interactions.

**The doctoral candidate will work in collaboration with Amsterdam UMC (AMC), The Netherlands; Eberhard Karls Universitaet Tuebingen (UT), Germany and Glycodiag (GLYD), France.**

**Details on the terms of employment** can be found on the website of Universitat Wien:
https://jobs.univie.ac.at/content/Employer-UniVie/?locale=en
**Link to the application/recruitment system**: https://jobs.univie.ac.at/job/University-assistant-predoctoral/1179256201/
**Link on EURAXESS:** https://euraxess.ec.europa.eu/jobs/323853
**Internal Deadline**: 23rd March 2025
**Subject area**: Immunology, Biochemistry, Cell Biology
**Contacts for info:** Prof. Dr. Christoph Rademacher (Christoph.Rademacher@unvie.ac.at), Department of Pharmaceutical Sciences, University of Vienna, Vienna, Austria.
**Email address where the application to be sent:** Christoph.Rademacher@unvie.ac.at

**Project-specific selection criteria:** Background in cell culture, formulation of nanoparticles, flow cytometry, working with primary cells
**Additional advantageous skills:** not applicable

**Recommended literature:** https://elifesciences.org/articles/69415

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## Project_DC#10: Studying bacterial surface glycopolymers-proteins interactions

**Main Supervisor:** Ludovic Landemarre (GLYD) **Co-Supervisor:** Jeroen Codée (ULEI)

**Location: Glycodiag (GLYD), France - https://www.glycodiag.com/-** (duration of the PhD: 3 years)

**Objectives:** The interactions between carbohydrates and glycans-binding proteins play essential roles in cell adhesion, communication and endocytosis; hence, the development of new methods allowing better understanding of glycobiological interaction between host and pathogens is prime importance. The lectin glycoprofiling platform developed by GLYcoDiag is intended to determine interaction profiles with lectins allowing to identify "glycans signatures" on the surface cells or conversely to study the interactions with carbohydrate-binding proteins expressed by cells. During AUREUS DN, DC10 will be trained in the specific knowledge and expertise of the laboratory regarding “glycosciences interactions” in order to decipher WTA-glycans binding proteins interactions through the following tasks: i) Glycoprofiling of various strains of S. aureus on lectin arrays with a specific focus on WTA allowing to identify reference and/or specific glyco-signatures according to pathology/environment ; ii) Studying WTA interactions with glycans binding proteins identified as PRRs; iii) Synthesis of WTA glycoconjugates (neoglycoproteins) as reference standard used for interaction studies and avidity comparison among WTA glycoforms; iv) Selection of glycan binding proteins PRR with the goal of feasibility development of lectins/lectins-like arrays also intended for the screening of WTA glycoforms.

**Expected Results:** Training: Expertise in the field on glycans-proteins interactions and glycans pathogen recognition involved in immunological responses; Basis in organic chemistry for the synthesis of glycoconjugates. Research: Identification of S. aureus associated specific glycoprofiles; Determination of correlations between strains associated glyco-signatures and PRRs recognitions. Synthesis of WTA neoglycoproteins and feasibility of a lectin array dedicated to the screening of WTA profiles and more generally “Pathogen Associated Glycans Pattern”.

**The doctoral candidate will work in collaboration with Universiteit Leiden (ULEI), The Netherlands; National Institute for Bioprocessing Research and Training Limited (NIBRT), Ireland and Universite Grenoble Alpes (UGA), France.**

**Details on the terms of employment** can be found on the website of Glycodiag:
https://www.glycodiag.com/news/
**Internal Deadline**: May 25th, 2025
**Subject area**: Biochemistry, Glycobiology
**Contacts for info:** Dr. Ludovic Landemarre (landemarre@glycodiag.com), CEO/CSO GLYoDiag
**Email address where the application to be sent:** landemarre@glycodiag.com or admin@glycodiag.com

**Project-specific selection criteria:** Knowledge and experience in proteins purification and characterization methods, proteins linkage and labelling, ELISA and more generally binding methods. Background in Glycobiology would be a plus. Ability to work independently in a multidisciplinary environment.
**Additional advantageous skills:** Curiosity and interest for applications projects, small company R&D environment working and entrepreneurship.

**Recommended literature:** not applicable

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## Project_DC#11: Structural biology of teichoic acid binding proteins

**Main Supervisor:** Mark J. van Raaij (CSIC) **Co-Supervisor:** Roberta Marchetti (UNINA)

**Location: Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC), Spain- https://www.csic.es/en-** (duration of the PhD: 3 years)

**Objectives:** X-ray crystallography represents one of the methods of choice to obtain high-resolution structural information on protein-ligand interactions. In this project, DC11 will employ X-ray crystallography to: i) unravel the binding of WTA analogues/inhibitors with enzymes involved in the biosynthesis of teichoic acids; ii) analyze the molecular interaction between selected PRR proteins and WTA fragments; iii) study the interaction of FAb fragments of monoclonal antibodies in the free state and in the presence of WTA fragments. For example, to complement the NMR spectroscopic and computational studies of Fab-TA interactions (DC7), DC11 will co-crystallize selected FAbs with TA analogues, collect high-resolution data on these crystals and resolve their structures. In a similar manner to the FAb-TA studies, DC11 will crystallize PRR-TA and WTA-biosynthesis enzymes-TA complexes and solve their structures. The combination of the aforementioned projects will provide DC11 with a very thorough training in structural biology of proteins and glycans, expose him/her to a myriad of complementary biophysical techniques and in return, DC11 will provide the other members of the consortium with high-quality structures of protein-TA complexes which can be used for mutational analyses, conformational analyses via molecular dynamics, leading to valuable biological understanding.

**Expected Results:** Training: Expertise in protein structure prediction, expression and purification; Molecular modelling; Structure resolution by X-ray crystallography. Research: Co-crystallization of WTA-biosynthesis enzymes and inhibitors; Structural studies of PRR – WTA complexes; Structural studies of Fab – WTA complexes.

**The doctoral candidate will work in collaboration with Universita degli Studi di Napoli Federico II (UNINA), Italy; Imperial College of Science Technology and Medicine (ICL), United Kingdom and Biopox Srl (BIOPOX), Italy.**

**Details on the terms of employment** can be found on the website of Agencia Estatal Consejo Superior de Investigaciones Cientificas: https://www.csic.es/en/training-and-employment

**Internal Deadline**: not applicable

**Subject area**: May 25th, 2025

**Contacts for info:** Prof. Mark J. van Raaij (mjvanraaij@cnb.csic.es)

**Email address where the application to be sent:** mjvanraaij@cnb.csic.es

**Project-specific selection criteria:** not applicable

**Additional advantageous skills:** not applicable

**Recommended literature:**


1. https://doi.org/10.1128/microbiolspec.gpp3-0044-2018;
2. https://doi.org/10.1016/j.tim.2020.05.017;
3. https://doi.org/10.1021/acscentsci.2c00125;
4. https://pmc.ncbi.nlm.nih.gov/articles/PMC1186895/



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## Project_DC#12: Generating and characterizing anti-WTA mAb from human memory B cells using synthetic S. aureus WTA structures

**Main Supervisor:** Nina van Sorge (AMC) **Co-Supervisor:** Andreas Peschel (UT)

**Location: Amsterdam UMC (AMC), The Netherlands-**
**https://www.amsterdamumc.org/en/organization/amsterdam-umc.htm -** (duration of the PhD: 4years)

**Objectives:** Of the IgG antibodies that are directed against the S. aureus surface, 70% recognizes glycosylated WTA, underlining the immunodominant nature of these structures. ULEI has developed a limited set of completely synthetic WTA structures with defined linkages and numbers of GlcNAc epitopes that represent different WTA glycotypes that we have used to perform WTA antibody profiling studies using plasma from healthy donors and patients with S. aureus bacteremia. Data indicate that WTA-specific
IgM is correlated with protection from S. aureus sepsis, disclosing a previously unrecognized role for IgM in defense against S. aureus. In this project, we will isolate WTA-specific human memory IgM B cells using synthetic WTA structures to produce and characterize naturally occurring WTA-specific IgM antibodies from 1) healthy donors and 2) S. aureus sepsis patients. In addition, we will use the same technique 3) to identify human memory B cells with specificity for the uniform WTA backbone, which could possibly an ideal therapeutic agent against >95% of the S. aureus population. Functionality of the antibodies will be assessed in complement deposition assays and neutrophil killing assays as a proxy for their in vivo protective capacity. Fab fragments of these mAbs will be used for STD-NMR (with DC7) and X-ray crystallography (with DC11) and inform further antibody engineering studies to optimize their functional capacity.

**Expected Results:** Training: Expertise in antibody biology, human B cell sorting, molecular biology and microbiology, protein expression and purification, bacterial culture. Research: Identifying and cloning WTA-specific IgM mAbs and WTA-backbone IgG mAbs; Comparing mAb functionality in microbiological assays; Generating Fab fragments for biophysical studies; Optimizing mAb functionality through structure-inspired antibody engineering.

**The doctoral candidate will work in collaboration with Eberhard Karls Universitaet Tuebingen (UT), Germany; Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC), Spain and National Institute for Bioprocessing Research and Training Limited (NIBRT), Ireland.**

**Details on the terms of employment** can be found on the website of Amsterdam UMC: cao nfu umc
**Link to the application/recruitment system**: Vacatures - PhD (x2) in Staphylococcus aureus immune interaction - Amsterdam UMC
**Internal Deadline**: May 11th, 2025
**Subject area**: microbiology, pathogen-antibody interactions, B cell immunology
**Contacts for info:** Prof. Nina van Sorge (n.m.vansorge@amsterdamumc.nl)

**Project-specific selection criteria**: not applicable
**Additional advantageous skills:** Experience with protein expression, flow cytometry/cell sorting, molecular (micro-)biology and cell isolation/culture. Background in antibody functionality or glycobiology would be a plus. You can work independently as well as in a team in a multidisciplinary and international environment

**Recommended literature:** PMID 39293400, 31367020

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## Project_DC#13: Glycosylation-dependent interaction of Staphylococcal WTA with immunoglobulins and scavenger receptor LOX1

**Main Supervisor:** Andreas Peschel (UT) **Co-Supervisor:** Mark J. van Raaij (CSIC)

**Location: Eberhard Karls Universitaet Tuebingen (UT), Germany- https://uni-tuebingen.de/en/-** (duration of the PhD: 4years)

**Objectives:** WTA represents one of the most abundant and largely invariant surface epitopes of Firmicutes including the genus Staphylococcus. WTA backbones are usually species-specific, with poly- RboP or poly-GroP repeating units in S. aureus or S. epidermidis, respectively. We recently discovered the WTA glycosylation pathway of the opportunistic pathogen S. epidermidis but its relevance for immune recognition remains to be assessed. S. aureus WTA was shown to play a critical role in endovascular infections because it mediates attachment to endothelial cells via the scavenger receptor LOX1. The impact of different WTA backbones and glycosylation patters has also remained unknown. We propose to assess the impact of different WTA glycosylation patterns on the capacity of human serum antibodies (IgG and IgA) and of mAbs (from DC12) to bind to S. aureus or S. epidermidis.
Using our panels of WTA glycosylation mutants, we will achieve comprehensive knowledge on the specificity of serum immunoglobulins in humans with important implications for the immunogenicity of different WTA types and for their potential use as vaccine antigens. Using the same set of mutants, we will also elucidate if S. aureus or S. epidermidis cells with different WTA glycosylation patterns differ in their capacity to bind endothelial cells via LOX1. Soluble LOX1 and specific LOX1 inhibitors are available for NMR and X-ray crystallographic analysis (in collaboration with DC7 and DC11) allowing to further substantiate findings based on bacterial binding to cell lines.

**Expected Results:** Training: Expertise in bacterial genetics, glycobiology cell biology. Research: Analyzing WTA mutants for binding to immunoglobulins; Studying impact of WTA variation on LOX-1 mediated endothelial binding.

**The doctoral candidate will work in collaboration with Amsterdam UMC (AMC), The Netherlands; Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC), Spain and Biopox Srl (BIOPOX), Italy.**

The doctoral candidate will work in collaboration with Stichting Amsterdam UMC (AMC), The Netherlands; Agencia Estatal Consejo Superior de Investigaciones Cientificas (CSIC), Spain, and Biopox Srl (BIOPOX), Italy.
**Details on the terms of employment** can be found on the website of Eberhard Karls Universitaet Tuebingen: https://uni-tuebingen.de/en/research/support-for-junior-researchers/graduate-academy/information-platform/interested-in-doing-a-phd/
**Internal Deadline**: May 11th, 2025
**Subject area**: Molecular Microbiology, Infection Biology, Biochemistry
**Contacts for info:** Prof. Andreas Peschel (andreas.peschel@uni-tuebingen.de), LINK to additional contacts
**Email address where the application to be sent:** janes.krusche@uni-tuebingen.de

**Project-specific selection criteria:** MA in a discipline related to biomedical science; strong practical and theoretical background in molecular biological, microbiological, biochemical methodology.
**Additional advantageous skills:** Working in an international team

**Recommended literature:** https://pubmed.ncbi.nlm.nih.gov/32540314/

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## Project_DC#14: MS toolbox to understand the molecular basis of WTA/protein interaction

**Main Supervisor:** Jonathan Bones (NIBRT) **Co-Supervisor:** Yan Liu (ICL)

**Location: National Institute for Bioprocessing Research and Training Limited (NIBRT), Ireland- https://www.nibrt.ie/ -** (duration of the PhD: 4 years)

**Objectives:** Mass spectrometry (MS) techniques have been at the forefront of the investigation of protein/ligand interaction mechanisms. It can be employed to monitor protein complexes in native states (nativeMS), to understand the molecular basis of the interaction (hydrogen deuterium exchange mass spectrometry, HDX-MS) and to investigate mechanisms of action (MoA) elicited upon recognition of ligand and receptor on cellular surface. In this project, we aim to evaluate S. aureus WTA and PRRs interaction using native MS and HDX-MS to enable the understanding of the molecular features necessary to design suitable inhibitors of the WTA-PRR interaction, or effective monoclonal antibodies (mAbs) that could target WTA as pathogen associated molecular pattern (PAMP). Initial screening, supported by the results obtained by the other AUREUS partners, will be followed by more depth study of selected WTA/protein systems, including differential proteomic studies to highlight elicited pathways upon recognition of the WTA structures from the host immune cells.

**Expected Results:** Training: Expertise in MS techniques, and native MS enabled structural biology; Monoclonal antibodies LCMS based bioanalytics; Proteomics workflows. Research: Understanding the protein features necessary for the recognition between WTA and candidate PRR; Highlighting and understanding MoA elicited upon WTA/PRRs interaction; Evaluating interaction of WTA and candidate monoclonal antibodies.

**The doctoral candidate will work in collaboration with Universita degli Studi di Napoli Federico II (UNINA), Italy; Imperial College of Science Technology and Medicine (ICL), United Kingdom and Iceni Glycoscience Limited (ICENI), United Kingdom.**

**Details on the terms of employment** can be found on the website of National Institute for Bioprocessing Research and Training Limited: www.nibrt.ie/careers/

**Link to the application/recruitment system**: https://www.nibrt.ie/careers/vacancies/

**Internal Deadline**: May 25th, 2025

**Subject area**: Mass spectrometry, Structural Biology, Analytical Chemistry

**Contacts for info:** Jonathan Bones (jonathan.bones@nibrt.ie), Sara Carillo (sara.carillo@nibrt.ie)

**Email address where the application to be sent:** careers@nibrt.ie (as indicated on website https://www.nibrt.ie/careers/vacancies/ )

**Project-specific selection criteria:** not applicable

**Additional advantageous skills:** Experience in proteins characterization by mass spectrometry and in the use of Orbitrap-based instruments.

**Recommended literature:** not applicable

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## Project_DC#15: MGL binding to S. aureus cell surface WTA/LTA by integrated structural biology

**Main Supervisor:** Cedric Laguri (UGA) Co-Supervisor: Roberta Marchetti (UNINA)

**Location: Universite Grenoble Alpes (UGA), France- https://www.univ-grenoble-alpes.fr/english/- Institut de Biologie Structurale - https://www.ibs.fr** (duration of the PhD: 3 years)

Objectives: Macrophage Galactose Lectin (MGL) is among the host immune receptors involved in the recognition of S. Aureus Teichoic Acids glycoconjugates (TA). However, little insights on the mechanism of recognition are known. Recognition however depends on the arrangement of the teichoic acids at the bacterial surfaces and conformational dynamics of the Carbohydrate Recognition Domain (CRDs) with respect to the oligomerization coiled-coil domain of the MGL. This topological variation could have great impact on the selectivity of recognition. Our group is able to produce on a routine basis the CRD and ECD of the MGL. The recognition of TA at the surface of S. aureus will be adressed through an integrated structural biology approach, from cells to molecular details at atomic resolution.
We will employ fluorescently labelled MGL to probe the interaction at the surface of S. aureus, either wild type or mutated in TA biosynthetic enzymes as controls, by confocal and super-resolution microscopy. Isolated wall-TA (or synthetic WTA) and Lipo-TA (in detergent micelles or native nanodiscs) MGL interaction will be characterised by Surface Plasmon Resonance, NMR and small-angle X-ray scattering (in collaboration with DC6). Co-crystallization of MGL with WTA ligands and X-ray crystallography could be also envisioned if required.

**Expected Results:** Training – Expertise in recombinant protein production (bacterial expression, protein refolding, purification); Confocal and Super-Resolution microscopy; Biophysical interactions studies (SPR, ITC); NMR spectroscopy and SAXS experiments. Research: Characterization of of binding specificity on S. Aureus surface and towards isolated WTA and LTA, determination of affinity and selectivity. Fine characterizations of WTA/LTA binding mode towards MGL.

**The doctoral candidate will work in collaboration with Universita degli Studi di Napoli Federico II (UNINA), Italy; National Institute for Bioprocessing Research and Training Limited (NIBRT), Ireland and Imperial College of Science Technology and Medicine (ICL), United Kingdom.**

**Details on the terms of employment** can be found on the website of Universite Grenoble Alpes:
https://emploi.univ-grenoble-alpes.fr/english/
**Internal Deadline**: May 11th, 2025
**Subject area**: Biochemistry, Biophysics, Structural biology, Host-pathogen interactions
**Contacts for info**: Dr Cedric Laguri (cedric.laguri@ibs.fr)
**Email address where the application to be sent:** cedric.laguri@ibs.fr

**Project-specific selection criteria:** Strong interest in integrated structural biology and biophysics
**Additional advantageous skills:** Organizational skills, fluency in English, ability to work independently and as a team player in a multidisciplinary environment. Good communication skills (in the context of a multi-partner project on a European scale).

**Recommended literature:**


1. https://doi.org/10.1093/pnasnexus/pgad310
2. https:/doi.org/10.1101/2025.02.05.636646



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