This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under Marie-Sklodowska Curie grant agreement No 101034285

UNIVERSITY: Public University of Navarre (UPNA)

WIT PROGRAMME´S RESEARCH LINE NAME: CARDIOLOGY

DOCTORAL PROGRAMME:

Doctorate in Health Sciences https://www.unavarra.es/escuela-doctorado/doctorate-programs/current-plan/Health+Sciences/doctorate-in-health-sciences?languageId=1

Doctorate in Biotechnology https://www.unavarra.es/escuela-doctorado/doctorate-programs/current-plan/engineering-and-architecture/doctorate-in-biotechnology?languageId=1

COMPLETE DESCRIPTION OF THE LINE

The Microbial Pathogenesis Research Unit seeks to understand at the molecular level how pathogenic bacteria grow when adhered to the surface of medical devices and tissues, leading to infections that are resistant to antibiotics and tend to become chronic. In order to understand this form of bacterial growth, known as biofilm, genetic engineering strategies are used, along with omics approaches, synthetic biology and animal models.

The ultimate goal is to identify the critical elements in biofilm formation in order to prevent biofilm formation, eliminate already formed biofilms, improve existing treatments and favor the formation of non-pathogenic bacteria biofilm for therapeutic purposes.

Infective endocarditis (IE) is an inflammation of the inner tissues of the heart, the endocardium, usually of the valves. It is an uncommon infectious disease with an annual incidence ranging from 3 to 7 per 100 000 person-years. Although relatively rare, IE caused morbidity and mortality remains high and it is still the third or fourth most common life-threatening infection syndromes, after sepsis, pneumonia, and intra-abdominal abscess. This is partially due to the difficulty of treatment. Even prolonged courses of broad-spectrum antimicrobials often fail to eradicate the infection, making surgical intervention necessary in

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many cases with the subsequent risk of mortality. The current hypothesis that IE is a biofilm infection explains its resistance to antimicrobials and why surgical disruption and removal of the biofilm improves the chance of cure. *S. aureus* is one of the most frequent cause of infectious endocarditis (IE) (33). The great ability of *S. aureus* to adhere to and colonize damaged valves relays on several surface adhesins (microbial surface components recognizing adhesive matrix molecules, MSCRAMMs) that mediate attachment to extracellular host matrix proteins. Adhesins include both proteins and polysaccharides. In particular, the fibrinogen-binding protein, clumping factor A (ClfA) and the fibronectin-binding protein A (FnBPA) play a critical role in valve colonization and invasion, whereas other MSCRAMMs seem less implicated. Fibrinogen-binding mediates the primary attachment of the bacteria to nonbacterial thrombotic endocarditis, and subsequent binding of fibronectin triggers endothelial cell internalization, followed by local proinflammatory and procoagulant responses. Studies aimed to compare *S. aureus strains* isolated from nasal healthy carriers and patients with IE, a great variability in the *in vitro* capacity to adhere to fibrinogen and fibronectin was detected, which did not correlate with the *in vivo* infectivity. This result indicates that laboratory *in vitro* conditions cannot capture the differences in regulation and gene expression that very likely infection isolates carriage and develop to adapt to their respective colonization sites.

Hypothesis: Understanding how a pathogen redirects and fine-tunes its gene expression in response to the challenges of infection is central to the development of more efficient anti-infective therapies.

In this project, we will evaluate the transcriptional profile of *S. aureus* during a human endocarditis process. For that, we will used high-throughput RNA sequencing "dual RNA-seq" to simultaneously captured all classes of coding and noncoding transcripts in both S. aureus and host endothelial cells.

RESEARCH GROUP NAME: MICROBIAL PATHOGENESIS

COORDINATOR: Iñigo Lasa

- Last and first name; link to the "Portal of scientific production":

https://www.navarrabiomed.es/en/research/research-units/microbial-pathogenesis

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MEMBERS OF THE LINE RESEARCH:

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Carmen Gil
Begoña García
Pablo Iturbe
Carmen Gomez Arrebola
Liliana Laverde

ANOTHER RESEARCH LINES OF THE GROUP: list of them

- Characterization of the two-component signal transduction system in *Staphylococcus aureus*

- Analysis of the biological meaning of "noncontiguous operon" architecture in bacteria

- Entities involved in research lines and contact person:

✓ Academic entities:

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- José R. Penadés, MRC Centre for Molecular Bacteriology and Infection, Imperial College London, UK
- Jean Marc Ghigo, Institut Pasteur. Paris
- Jörg Vogel: Helmholtz-Center for Infection Research, Würzburg, Germany.
- Felipe Cava, Department of Molecular Biology, Umea University, Sweden
- Xianyang Fang: Tsinghua University, Beijing, China.
- Andreas F. Haag: University of Glasgow, Scotland, UK.

✓ Industrial entities:

Recombina S. L. (https://www.recombina.com/es/)

- Brief group overview

The Microbial Pathogenesis Research Unit seeks to understand at the molecular level how pathogenic bacteria grow when adhering to the surface of medical devices and tissues, leading to infections that are resistant to antibiotics and therefore tend to become chronic. In order to understand this form if bacterial growth, known as biofilm, genetic engineering strategies are used, along with omics approaches, synthetic biology and animal models.

The ultimate goal is to identify the critical elements in biofilm formation in order to prevent biofilm from forming, eliminate already formed biofilm, improve existing treatments and favoring the formation of non-pathogenic bacteria biofilm for therapeutic purposes.

The main areas of interest of the group focus on the study of bacterial adhesion to abiotic surfaces (implants) and tissues, signal transduction mechanisms in bacteria and the identification of new targets for the treatment of infections.

- Link of the group to the "Portal of scientific production"

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REQUIRED QUALIFICATIONS

- Biological Science
- Medical Science
- Computer Science

ADDITIONAL REQUIREMENTS:

Applicants should have a strong background un microbiology and/or cellular biology. Experience in molecular biology and bioinformatics is highly desirable, together with high degree of motivation and interest in the research project. Experience with animal models of infection would be an advantage.