



<u>Université de Paris</u>

Institut Necker-Enfants Malades

Inserm U1151 / CNRS UMR 8253 - Head: Fabiola Terzi

Unit of Pathogenic and Systemic Infections, Team 07

Postdoc position in microbiology and physiology

Deciphering the role of endothelial microparticles in cardiovascular dysfunctions in bacterial sepsis

The Research Project:

Sepsis is a severe form of organ dysfunction, with high morbidity and mortality rates, worldwide. Cardiac dysfunction is one of the most common and severe complications of sepsis and directly affects patient mortality, as normal cardiac function is crucial for adequate organ perfusion. How sepsis induces acute cardiomyopathy is complex and characterized by numerous inter- and intra-cellular dysfunctions. The underlying mechanisms leading to cardiomyocyte acute dysfunction in the context of sepsis remains largely elusive. With the emergence of antibiotic-resistant bacteria, the number of individuals affected by bacteria-induced sepsis is bound to increase dramatically, representing an unmet medical need.

The overall objective of our project is to better understand cardiomyocyte death and/or dysfunction and therefore acute cardiac insufficiency in the context of bacterial sepsis, with a focus on *N. meningitidis* infection. For this, we leverage a consortium expertise in microbiology, vascular biology, cardiac biology, and critical care medicine.

Our main objectives are: (1) to identify factors specifically released by endothelial cells during meningococcal infection that will be involved in lethal sepsis. Will focus on endothelium-derived extracellular vesicles produced as a result of N. *meningitidis* interaction with endothelial cells, a specific feature of this infection; (2) to define the molecular and cellular impact of meningococcal infection on vascular and cardiac dysfunction, which ultimately leads to animal death.

Research keywords: Cardiovascular Dysfunctions; Endothelium-Derived Microparticles; Host-Pathogen Interactions; Sepsis; Mouse models

The Applicant:

The applicant should be a highly motivated postdoctoral candidate with a PhD degree in "Cardiac physiology" or "Bacteria associated sepsis and mouse physiology" and a high-quality track record. He/she should have a strong background in performing research in mouse and *in vitro* models.

The Research Environment:

The research Unit is Institut Necker Enfants Malades (INEM), a biomedical research center aiming at fundamental discoveries with the potential of leading to therapeutic progress, focusing on incurable chronic diseases. Our faculty includes 20 teams with an international background in: Cell Biology, Immunology, Hematology and Infection.

INEM shares a unique research campus with the IMAGINE institute and the Hôpital Necker-Enfants Malades, which, supported by state-of-the-art core facilities, together provide a rich and vibrant environment for basic research and translational innovation. The INEM teams collaboratively address multiple facets of diseases.

To apply: The candidate should send a curriculum with a brief statement of research experience, technical expertise and interests, and one or two references to Mathieu Coureuil or Anne-Sophie Armand.

Postdoc fellowship:

24 months (12+12) starting March 2025, 2024-ANR founded project (EMPCARD)

Contact :

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Selected references from the PIs, relevant to this application:

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Barnier JP, Euphrasie D, Join-Lambert O, Audry M, Schonherr-Hellec S, Schmitt T, Bourdoulous S, <u>Coureuil M</u>, Nassif X, El Behi M. Type IV pilus retraction enables sustained bacteremia and plays a key role in the outcome of meningococcal sepsis in a humanized mouse model. *PLoS Pathog.* 2021 Feb 16;17(2):e1009299.

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De Majo F, Martens L, Hegenbarth JC, Rühle F, Hamczyk MR, Nevado RM, Andrés V, Hilbold E, Bär C, Thum T, de Boer M, Duncker DJ, Schroen B, <u>Armand AS</u>, Stoll M, De Windt LJ. Genomic instability in the naturally and prematurely aged myocardium.

Proc Natl Acad Sci U S A. 2021. 118 : e2022974118.