Description of Funded Research Projects
1st Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers

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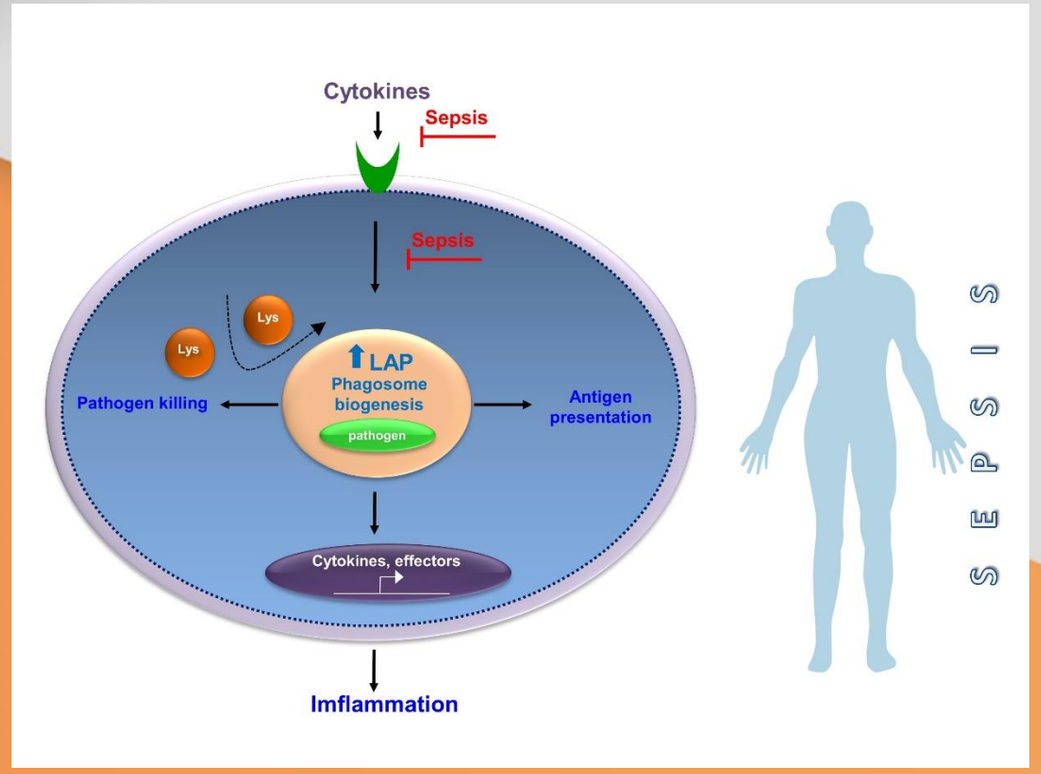
Research Project Title:

Delineating molecular mechanisms of PHAGOsome dysFUNction underlying Sepsis Immunosuppression: A Roadmap to Personalized Medicine in Sepsis

Principal Investigator:
Antonia Akoumianaki



Popular Title:
Dysfunction of phagocytes in sepsis results in increased susceptibility to secondary infections

Scientific Field:
Life Sciences

Host Institution:
University of Crete, Medical School

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Research Project Summary

Despite significant advances in life support of critically ill patients, sepsis remains a major cause of mortality worldwide. Recently, it has been realized that many patients who survive the initial sepsis episode, enter a prolonged state of immune deactivation, termed sepsis-induced immunosuppression, which accounts for treatment failure and death due to secondary infection(s) by opportunistic bacterial and fungal pathogens. While the clinical impact of sepsis immunosuppression is well recognized, the underlying mechanisms remain unknown. Furthermore, the failure of over 100 clinical trials on sepsis immunotherapy has been largely attributed to the complexity of the underlying molecular mechanisms of the disease in humans and the lack of reliable biological measures that discriminate patients with immune deactivation.

Sepsis immunosuppression is characterized by the inability of professional phagocytes (monocytes, macrophages, neutrophils) to eliminate pathogens. Due to the impairment of phagocyte immune responses, sepsis patients with underlying immunosuppression are more susceptible to secondary infections by fungal pathogens such as Aspergillus Fumigatus.

A non-canonical autophagy pathway termed LC3 associated Phagocytosis (LAP), regulates a wide range of physiological immune responses in phagocytes against specific opportunistic pathogens. We have extensively characterized the fundamental role of LAP in antifungal immunity (Kyrmizi et al., J Immunol 2013, Akoumianaki et al., Cell Host Microbe 2015). In view of the important role of LAP on phagocyte effector functions, I have decided to explore the molecular mechanisms of LAP defects in sepsis immunosuppression in order to comprehensively characterize them, with the ultimate goal to identify novel biomarkers mechanistically linked to sepsis immunosuppression and pave the way for personalized medicine approach based on immunophenotyping of individual sepsis.

Project Impact on Society

Despite significant improvements in clinical care of critically ill patients, sepsis remains a major healthcare problem, with huge impact on society and economy worldwide. Mortality of severe sepsis patients exceeds 50% and hospitalization cost is substantial. Furthermore, the failure of all immunomodulatory trials in sepsis coupled with the emerging problem of antimicrobial resistance, clearly reveals the unmet need to dissect fundamental mechanisms of underlying immune defects and implement these finding in clinical research.

Overall, PhD in SEPSIS will have an impact on: a) understanding of the complex pathophysiology of sepsis immunosuppression, a highly prevalent condition with enormous impact on patient morbidity and mortality, as well as on health care costs, b) identification of novel biomarkers and therapeutic targets in a condition where there is currently none available, and c) supporting a step toward personalized medicine in sepsis based on accurate immunophenotyping of each individual patient.

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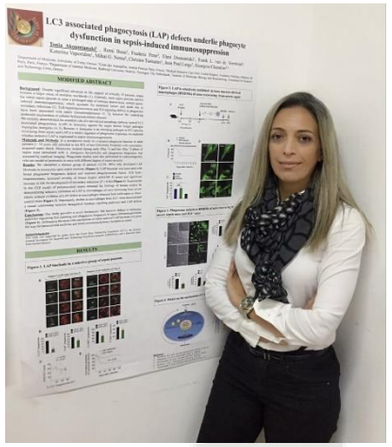
To me, H.F.R.I. funding would mean...



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Over the past few years I am interested in dissecting molecular mechanisms of host-pathogen interactions in the context of sepsis induced immunosuppression, with the ultimate goal to discover novel therapeutic strategies and personalized medicine approaches.

Because of the need of supporting young scientists and promoting research and innovation in the country, this grand will allow me to pursue my expectations and build up an independent career in the field. For the first time a Post-doc is responsible for a grant and can create a new research team. In addition, this funding will support new collaborations with internationally recognized scientists in the field, with the same strong interest for development and clinical validation of novel sepsis biomarkers and therapeutics. Collectively, this grant is my first important step that will pave the way to independency.

The Principal Investigator,

Antonia Akoumianaki

Funding

Amount: **180,000 €**

Duration: **36 months**

Foundation: **H.F.R.I.**

H.F.R.I.
Hellenic Foundation for Research & Innovation

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