



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

Description of the funded research project
2nd Call for H.F.R.I. Research Projects
to Support Post-Doctoral Researchers

Title of the research project: EndotyPIng PreHospitAI de Novo acute hYpoxemic respiratory failure

Principal Investigator: Ilias Siempos

Reader-friendly title: EPIPHANY

Scientific Area: Life Sciences

Country: Greece

Host Institution: National and Kapodistrian University of Athens



Budget: 180.000 €

Duration: 36 months

Research Project Synopsis

The **acute respiratory distress syndrome** (ARDS), the most severe form of acute hypoxemic respiratory failure (AHRF), is a hallmark of intensive care medicine and (as highlighted in the COVID-19 pandemic) a serious public health problem with no available targeted pharmaceutical therapy.

We envision a change in the conceptual framework of ARDS by focusing to the simpler and more reliable phenotype of AHRF. Identifying what clinical, radiological, physiological and biological variables collected early in the course of AHRF correlate with subsequent mortality or persistent severe hypoxemia may better define ARDS. An agnostic, clinically unbiased approach may reveal new insights into the pathogenesis and may identify endotypes (distinct bio-subtypes likely to benefit from a specific drug) of AHRF.

We therefore carry out an innovative research program, which **links bioinformatics methods in electronic health record data (“big data”) to cutting edge biomarker science** using a **biorepository of residual blood**.

Project originality

Our research project has several innovations:

- i) **Change of the conceptual framework of acute respiratory distress syndrome:** This project directs the research focus away from the problematic phenotype of acute respiratory distress syndrome to the more reliable and straightforward phenotype of acute hypoxemic respiratory failure.
- ii) **Link of bioinformatics methods in electronic health record data (“big data”) to cutting edge biomarker science using a biorepository of residual blood:** This highly innovative precision medicine approach takes advantage from recent breakthroughs in the field of big data and the field of omics along with sophisticated statistical techniques to achieve a nuanced endotyping of critically ill patients presenting in the emergency department with de novo acute hypoxemic respiratory failure.
- iii) **Usage of a global, agnostic discovery approach to explore novel modified aptamer-based, proteomic biomarkers:** Using cutting edge high-throughput proteomic platform allows for quantification of approximately 5,000 unique human protein analytes in only 150 uL of plasma from each enrolled patient.

Expected results & Research Project Impact

Our research project is anticipated to have considerable **scientific impact** in the field of translational medicine, clinical trial design and genetic epidemiology of acute hypoxemic respiratory failure. Our proposed change in the conceptual framework of acute respiratory distress syndrome has a high likelihood of identifying novel endotypes that may be useful to generate new animal models, to use as clinical trial enrolment criteria, and for more refined genetic epidemiology.

Our proposed global, agnostic discovery approach to explore novel modified aptamer-based, proteomic biomarkers may reveal new insights into the pathogenesis of acute hypoxemic respiratory failure. We are committed to sharing the biological insights revealed from our discovery proteomics approach through collaborations with scientists who will investigate novel candidates in more traditional hypothesis-testing experiments.

The proposed creation of the registry and biobank of critically ill patients presenting in the emergency department with de novo acute hypoxemic respiratory failure may serve as a template for the organization of additional biobanks in Greece and will foster international collaborations.

Given the incidence, morbidity and mortality associated with acute hypoxemic respiratory failure and its more severe form, acute respiratory distress syndrome, which make it a serious public health problem, scientific advances (as those described above) will likely be translated in improved outcomes of patients and, thus, will have considerable **social impact**.

The importance of this funding

This grant from the Hellenic Foundation for Research and Innovation consolidates my academic transition from USA to Greece and facilitates further development of my career as **clinician-scientist**.

As I strongly believe that the safest legacy of an investigator are their mentees, I am committed to **mentoring** and I consider the career development of my research team as my high priority. This grant catalyzes the building of my research program in Athens with the recruitment of talented Greece-based scientists and clinician-scientists as members of my research team. It provides me with protected time and resources (creation of the registry and biobank) to mentor pre- and post-graduate trainees in high quality patient-oriented research.



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