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Description of the funded research project

1st Call for H.F.R.I. Research Projects to Support Faculty Members & Researchers and Procure High-Value Research Equipment

Title of the research project: **“Immune clock”: The deviation of immunological age in atopic individuals**

Principal Investigator: **Nikolaos Papadopoulos**

Reader-friendly title: **iClock**

Scientific Area: **Life Sciences (Medical and Health Sciences)**

Institution and Country: **National and Kapodistrian University of Athens, Greece**

Host Institution: **National and Kapodistrian University of Athens**

Collaborating Institution(s):

1. **University Hospital Giessen and Marburg GmbH, Campus Marburg, Germany**
2. **University of Manchester, United Kingdom**

Project webpage (if applicable):

Budget: **177999,3 €**

Duration: **24 months**

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Research Project Synopsis

Respiratory Allergic Diseases such as allergic rhinitis and asthma are a major and growing issue of public health in Europe. Studies into the pathogenesis of allergic asthma and rhinitis have highlighted the importance of pathways leading to Th2-mediated inflammation. Th2 responses predominate in neonatal life; the normal immune maturation process results into Th1 responses dominating after the first years of life. However, influenced by genetic predisposition as well as environmental triggers, Th2-mediated responses persist in allergic individuals, often manifesting as asthma and rhinitis later in life. The timelines of Th2 to Th1 transition, occurring in healthy but not in atopic individuals, have not yet been fully determined. Recent studies have shown that "biological" age may determine when the symptoms of a disease will occur. These observations have stimulated research towards new biomarkers (including epigenetic factors) that may potentially predict, monitor and provide additional information on age-related disease development. The aim of iClock is to determine epigenetic maturation, assessed through whole genome methylation, throughout the life cycle in healthy and atopic individuals. This information with be associated with clinical and immunological parameters, to develop a model of age-dependent immune maturation and reliably describe an immunological clock. This will also explore the hypothesis that allergic diseases result from epigenetically-mediated defects in early immune maturation that may be reversed. The findings of the study may have major prognostic and therapeutic implications.

Project originality

The current research project is expected to indicate the methylation levels of the respiratory epithelium and to correlate them with the biological age of healthy and atopic individuals. Age-dependent and allergy-dependent factors, at the transcriptional and metagenomic levels, will be combined to determine the “immune clock”, of healthy individuals and its differentiation in presence of atopy. The current research project aims to cover a significant gap of knowledge in the field of maturation of innate immunity in relation to age and the development of allergic diseases. A goal is to considerably deepen and extend our knowledge on the interactions between exposure and/or susceptibility to infection and the maturation of non-specific immunity throughout the life cycle, and to clarify the mechanisms of development and persistence of asthma and rhinitis. The development and maturation of the respiratory epithelium from birth to adulthood is a big gap in the global literature. Also, there is paucity of evidence on innate immune maturation mechanisms and their correlation with the development of asthma and rhinitis. Most importantly, potential epigenetic modulation of allergic diseases, such as methylation of the respiratory epithelium, although partially studied, has never been associated with maturation processes and age. Last but not least, it is the first time that a systems biology approach will be attempted using information at the regulatory (epigenetic modulation), translational (protein expression) and clinical levels, leading to a model that will be used to identify “biological age” at the personal level and therefore contributing to personalised medicine. The need for new diagnostic and prognostic markers is clearly urgent in the field of respiratory allergic diseases, taking into account the dynamic nature of these conditions .

Expected results & Research Project Impact

The proposal is expected to benefit significantly both society and European businesses by proposing innovative diagnostic and therapeutic strategies improving personalized patient care. The development of innovative biomarkers predicting the "immune age" will be an important tool for describing and determining the stage of the disease for the physician. The benefit of this program to coordinate research activities on allergies and asthma at national level will also be very important. Deliverables such as the epigenetic signature associated with susceptibility to infection and the risk of developing respiratory allergic diseases will provide the basis for future collaborations and maximize the chances of future funding.

Overall, this proposal will improve research on allergy and asthma, combine it with existing knowledge and provide solutions for clinical practice. In this respect, this proposal will be extremely beneficial for the whole national and European scientific community.

The importance of this funding

The present funding is of the outmost importance to conduct and complete iCLOCK study. Due to the high cost of the specific analyses and specialized staff, it is impossible to complete the study without funding. The research results will be a powerful tool for the subsequent development of a new personalized diagnostic approach to determine the immune age of each individual.

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