



Group A Strep – Immune Correlates of Protection

The Challenge

Group A streptococci give rise to a broad range of clinical conditions, from uncomplicated infections such as pharyngitis and impetigo to invasive disease. Millions of people are affected every year, and it is estimated that Group A streptococcal (GAS) infections account for 500,000 deaths worldwide, mostly from invasive infections and complications resulting from GAS infections such as rheumatic heart disease.

Despite the large global burden of disease, there are no licensed vaccines for GAS, although significant efforts are ongoing. Vaccine development efforts are guided by knowledge of the immune response needed to combat the infection, yet the immune correlates of protection against GAS infection remain largely unknown. The finding that adults show lower GAS pharyngitis and carriage rates compared to children and adolescents suggests that immunity to GAS develops over time, but the mechanism remains unexplained. A better understanding of the innate, humoral, and cellular immune responses that confer protection against GAS infection could inform vaccine development efforts and might yield insights into the pathogenesis of acute rheumatic fever and rheumatic heart disease.

The Goal

The challenge for the applicants is to characterize the protective immune response to GAS infection that occurs in humans over the life course.

What we are looking for

This call seeks to fund a collaborative, interdisciplinary, and scientifically rigorous research network to identify the correlates of the protective immunity that develops to GAS infection over the life course. Efforts might include studies of prospectively collected or pre-existing samples, humoral and cellular immune responses, characterization of mucosal immunity, appropriately justified animal models, human challenge models, transmission studies and/or longitudinal studies and studies of genetic susceptibility. Attention should be given to the multiple clinical syndromes caused by Group A Strep, including carrier states, superficial infections, and invasive infections.

Successful applicants will design an innovative research program that takes advantage of the interdisciplinary collaboration of the network members. Recognizing that innovation often arises at the intersection of different fields, we welcome the recruitment of investigators with diverse expertise who may bring new approaches to bear on this topic. It is not a requirement that all members of a proposed network have a track record of scientific accomplishment in GAS or rheumatic heart disease. In the assessment of the application, a track record of previous collaborative successes, either with prospective network members or with other investigators, will be considered a strength. For clarity, however, given the interdisciplinary character of the project, it is not necessary for members of the network to have collaborated with each other prior to the proposed network program.



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Winning proposals should:

- Provide a detailed scientific plan outlining the approach and its rationale. Although some aspects of the scientific approach may be exploratory and unbiased, a well-developed rationale for the specific proposed approach shall be part of the application.
- Clearly describe any prospective or pre-existing sample collections with attention to subject enrollment characteristics and sample sizes.
- Assure the integrity of any collected samples for the investigatory methods that will be employed.
- Describe the added synergistic value of the collaborative and interdisciplinary approach.
- Clearly delineate the role of each investigator.
- Address the following:
 - Relevant approvals from local authorities/institutions/government on the research methodology, sharing of data, and transfer of material (if applicable) among collaborators
 - Data analysis and adherence to relevant local laws/ policies pertaining to data sharing, hosting and data protection
 - Secure handling of personally identifiable information data and research results
 - Institutional Review Boards or equivalent human study regulation strategy
 - Protocols and capacity for sample collection and storage.

We will not consider funding for:

- Proposals that do not include an investigator from a rheumatic heart disease endemic country (N Engl J Med 2017; 377:713-722).
- Proposals aimed primarily at the creation of a biobank. While the use of human samples for this study is a necessity, proposals must go beyond the simple collection of human samples.
- Proposals that do not demonstrate a capacity to perform the research proposed; investigators should describe the capacity for human sample collection, processing and storage, transport if necessary, and characterization, including data analysis, follow-up strategies, and test validation. The use of well-phenotyped pre-existing sample collections is permitted.
- Network programs that are based exclusively or predominantly on high-throughput screening, or other techniques best pursued in a commercial/industrial context.



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Mechanism of Funding

- One application will be selected for funding in the first year of this RFA.
- The funding mechanism will be similar to that of the traditional Leducq International Network of Excellence
- One network coordinator will be responsible for directing the research team.
- The funding amount is 5M USD over a five-year funding period.
- Reporting requirements Leducq networks include:
 - A biannual call with the Chief Scientific Officer to update the foundation on progress
 - A year one written and in-person (or virtual) progress report
 - A written and in-person mid-term review
 - A year four written progress report
 - A final written progress report due at the end of the funding period

Application Process

- Letters of intent are due October 17, 2022
- Selected applicants will be asked to submit a full application due March 1, 2023
- Notification of funding decisions will be made in April 2023

Questions about the letter of intent, or about Leducq Foundation, should be directed to the Leducq Foundation office at contact@flcq.org.

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