

Trans-NIH Working Group Meeting

Lymphatic Research

Executive Summary

The Working Group was convened September 6-7, 2007 in Washington, D.C. to provide recommendations to the NHLBI and other NIH Institutes for future directions in lymphatic research. This working group meeting responds to the NHLBI Strategic Plan Goals 1 and 2 to improve understanding of the molecular and physiologic basis of health and disease as well as the clinical mechanisms of disease, and thereby enable better prevention, diagnosis, and treatment. (<http://apps.nhlbi.nih.gov/strategicplan/>)

Discussion

Participants received brief state-of-the-art presentations including: Key Functional Roles of the Lymphatic Vasculature, Major Lymphatic Disorders, and Available Imaging Methods (S. Rockson); Development of the Lymphatic System, Animal Models, and Genetics (G. Oliver); Lymphangiogenesis in Health and Disease (D. McDonald); The Role of the Lymphatic System in Immune Function and Trafficking (N. Ruddle); and Tumor Related Lymphatic Biology and Lymphatic Disease (M. Skobe). These presentations provided the stimulus for discussions of the most pressing research imperatives meeting public health concerns surrounding lymphatic biology in health and disease.

The Working Group identified four Public Health needs that reflect the imperative for advances in lymphatic investigations:

- Lymphatic vascular pathologies. There is a need to improve comprehension, diagnosis, and treatment of congenital and hereditary lymphedemas and the broad array of lymphatic vasculopathologies (including lymphatic disorders such as protein-losing enteropathy, lymphangiomas and cystic hygroma, visceral lymphangiectasias). The incidence of acquired lymphedema after cancer treatment and other surgical interventions is unacceptably high. Prevention and enhanced therapeutics are required. Investigations suggest that pathological lymphangiogenesis plays a role in organ transplant rejection. A better understanding of the lymphatic component to rejection would facilitate the development of methods for therapeutically modulating it.
- Improvement of cancer outcomes. Cancer affects approximately 1.5 million people per year. Lymph node involvement and the implications for cancer metastasis have a profound negative impact on survival. Improving cancer outcomes requires a better understanding of the role of the lymphatic system in cancer metastasis as well as improved accuracy and enhanced methodology for Tumor-Node-Metastasis staging. Improved methods to predict and prevent lymphatic metastasis are also critical. The improved ability to modulate the impact of the lymphatic interface on cancer prognosis, treatment, and outcome could result from a better understanding of the lymphatic metastasis process.
- Inflammation. Diverse lines of evidence implicate a role for the lymphatic system in the initiation and propagation of inflammatory and the immune responses. The lymphatic vasculature and nodes are integrally involved in immune surveillance and immune cellular trafficking. In addition, it has been demonstrated that pathological lymphangiogenesis plays a role in chronic respiratory inflammation and infection as well as cornea and kidney transplant rejection, and that chronic inflammation is a central attribute of the cutaneous response to lymphatic vascular insufficiency (lymphedema). Many chronic inflammatory diseases have significant morbidity. More effective diagnosis and treatment could be achieved through advances in the understanding of the role of the lymphatic system in inflammation. Also, the efficacy of new vaccine development (including vaccines for cancer) must rely on a better understanding of the transport of antigen-presenting cells to the lymph nodes.
- Obesity. There is a global epidemic of obesity with profound consequences. Recent investigations suggest a potential link between lymphatic malfunction and obesity. Clinical data clearly correlate the presence of

edema with accumulation of adipose tissue. Characterization of the relationship of lymphatic function to obesity can impact strategies to prevent and treat obesity, as well as influence lipid absorption, storage and transport.

The Working Group concluded that advances in the above areas require additional research infrastructure consistent with the following recommendations.

Recommendations:

- Create centralized core facilities for: (a) experimental molecular and diagnostic lymphatic imaging; (b) the development and standardization of research reagents; (c) the generation of virtual networks to facilitate basic, translational, and clinical research
- Develop techniques for the quantitative and molecular imaging of lymphatic function, lymphatic malformations, and lymph nodes
- Create interdisciplinary programs to train new investigators in lymphatic research
- Create patient registries and a lymphatic disease tissue bank
- Generate and characterize animal models to foster and facilitate investigations in lymphatic biology
- Identify suitable panels of biomarkers for lymphatic disease
- Continue the interdisciplinary Trans-NIH Working Group on Lymphatic Research with focused sub-groups to be convened on an as-needed basis

Publication Plans:

A summary of the workshop proceedings and recommendations will be published in a peer-reviewed scientific journal.

Sponsors:

National Cancer Institute
National Eye Institute
National Heart, Lung and Blood Institute
National Institute of Allergy and Infectious Disease
National Institute of Nursing Research
Office of Rare Diseases, NIH

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