



Division of Immunology

1 Blackfan Circle
Boston, MA 02115
(617) 919-2484

Title: Orthopox Immunization in patients with cancer or eczema

Principal Investigator: Ellis Rheinherz, MD

Researchers Involved: Robert Fuhlbrigge MD, PhD

Summary: The major goals of this Cooperative Center for Translational Research on Human Immunology and Biodefense project are to characterize the cutaneous immune response to vaccinia virus infection and develop preclinical models for safe and effective immunization to smallpox in at risk populations.

Funding Source(s): NIH

Contact Information:

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Title: Regulation of T Cell Migration to Melanoma Metastases

Principal Investigator: Robert Fuhlbrigge MD, PhD

Researchers Involved: Ahmed Gehad, PhD

Summary: Despite aggressive efforts over many years, metastatic malignant melanoma remains largely untreatable and is rising in incidence among US and world populations. Vaccination strategies have been shown to enhance autologous anti-tumor cytotoxic activity in peripheral blood T cells but have offered little improvement in survival. My lab has shown that the T cells generated by immunization with melanoma antigens express a normal complement of adhesion receptors, but that blood vessels within melanoma metastases are deficient in the counter-receptors for T cell migration leading to creation of an immune privileged site within the tumor. Studies of tumor angiogenesis include an intriguing observation that blood vessels in melanoma may not be formed by endothelial budding, but appear to be formed by de-differentiation of tumor cells to form channel structures- a process known as vascular mimicry. Using a xenotransplantation model of human metastatic melanoma tissue implanted in immune deficient mice, we are exploring the role of melanoma stem cells in forming these structures and the capacity of therapeutic interventions to induce expression of homing receptors on these channels in melanoma metastases and promote immune destruction of the tumors.

Funding Source(s): Children's Hospital Boston

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Title: Skin Disease Research Center: Leukocyte Migration Core Facility

Principal Investigator: Thomas S. Kupper, MD

Researchers Involved: Robert Fuhlbrigge MD, PhD - Sandy King, PhD

Summary: This core facility provides support for the study of leukocyte migration studies for members of the Harvard Skin Disease Research Center.

Funding Source(s): NIH

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Title: Skin Homing T Cells: Molecular Characterization of CLA

Principal Investigator: Thomas S. Kupper, MD

Researchers Involved: Robert Fuhlbrigge MD, PhD

Summary: The major goals of this project are to study the CLA glycoprotein on human T lymphocytes and its role in directing leukocyte migration in skin inflammatory disease.

Funding Source(s): NIH

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Title: Structure Function Analysis of T Cell E-Selectin Ligands

Principal Investigator: Robert Fuhlbrigge MD, PhD

Researchers Involved: Sandy King, PhD

Summary: T cells that home to skin are defined by expression of the Cutaneous Lymphocyte-associated Antigen (CLA), a carbohydrate epitope differentially expressed on a limited set of glycoproteins on T cells and other leukocytes involved in immune surveillance and immune responses in skin. The goals of this project are to define the molecular structures and characterize the functions of these ligands. A crucial step in this work has been the development, in collaboration with Dr. Robert Sackstein, of a novel assay method termed blot-rolling. Using this method, individual leukocyte glycoproteins separated by SDS-PAGE and transferred to paper as in a Western blot can be queried for selectin ligand function by direct observation of rolling adhesions in physiologic shear flow using a laminar flow chamber mounted directly on the blot and perfused with selectin bearing cells. This method allows for the functional identification and purification of selectin ligands from leukocyte lysates without prior knowledge of structure. These projects, conducted in my lab or in collaboration, have identified and characterized three independently regulated leukocyte E-selectin ligands (PSGL-1, CD43 and CD44) in both human and mouse and related expression of the CLA-related carbohydrate determinants on these protein scaffolds to the activity of specific fucosyltransferases.

Funding Source(s): NIH

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