THE
DISCOVERY
LECTURE SERIES

TIMOTHY A. SPRINGER, Ph.D.

IMMUNOLOGY, MEDICINE, AND THE SOUL OF THE INTEGRIN MACHINE

FEBRUARY 8, 2024
4:00 P.M.
208 LIGHT HALL

SPONSORED BY:
BROCK FAMILY CENTER FOR APPLIED INNOVATION

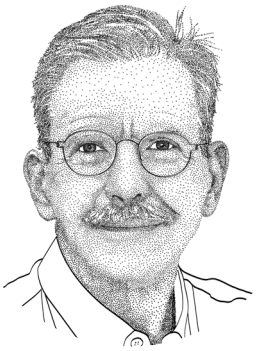
VANDERBILT UNIVERSITY
MEDICAL CENTER

IMMUNOLOGY, MEDICINE, AND THE SOUL OF THE INTEGRIN MACHINE

Integrins are mechano-adhesive receptors that allow cells to get a grip on ligands in their environment. Integrins also connect to the actin cytoskeleton. Integrins transmit tension between their ligands and the cytoskeleton that stabilizes tissues against deformation and provides traction for cell migration. Integrins are heterodimers of α and β subunits that come together to form many ligand binding specificities to recognize important components in the extracellular matrix / basement membranes and on cell surfaces. The functions they mediate are quite varied and include blood clotting, activation of TGF-β, emigration out of blood vessels into sites of inflammation, and antigen recognition in lymphoid organs.

Relevant to how integrins are activated are their three conformational states, and the ensemble model that enables understanding of their "average" affinity. Measurements of the basal ensemble affinity and the affinity in the presence of Fab fragments to stabilize specific states has been used to calculate integrin intrinsic affinity for ligand, populations on the cell surface, and free energies.

Dr. Springer will focus on integrins as machines - how do they transit among the three conformational states- what is the order of progression among the three states and how long does it take? We now can measure the kinetics of these transitions for single integrin molecules using FRET. Dr. Springer believes that you cannot understand a machine without seeing its parts move. With FRET, we can see into the "soul" of the integrin machine, which has some surprises and joys.



TIMOTHY A. SPRINGER, Ph.D.

LATHAM FAMILY PROFESSOR OF BIOLOGICAL CHEMISTRY AND MOLECULAR PHARMACOLOGY, HARVARD MEDICAL SCHOOL.

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Timothy A. Springer, Ph.D. is the Latham Family Professor at the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School and Senior Investigator at the Program of Cellular and Molecular Medicine at Boston Children's Hospital. Dr. Springer is a world leader in structural biology and immunology. He discovered many of the adhesion receptors in the immune system with monoclonal antibodies, then cloned and functionally and structurally characterized them. Dr. Springer was the first to demonstrate that lymphocytes and leukocytes had adhesion molecules. His work on these receptors has advanced to characterizing their interactions and allosteric transitions by x-ray crystallography, electron microscopy, and laser tweezers force spectroscopy. In recognition of this work, he received the Canada Gairdner International Award in 2019, the Lasker Basic Medical Research Award in 2022, and was recently awarded the Robert Koch Award in 2023. Dr. Springer is a founder and private investor in biopharmaceutical ventures, including LeukoSite, Scholar Rock, Morphic Therapeutic, Moderna Therapeutic, Editas Medicine, Selecta Biosciences, and Ab Initio Biotherapeutics. His research and company formation has led to six FDA-approved drugs, including antibodies for treating cancer and immune diseases. Notably, Dr. Springer also co-founded the Institute for Protein Innovation: a non-profit to advance entrepreneurship and innovation in protein therapeutics and open-source antibodies and small molecules.

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Upcoming Discovery Lecture:

VANESSA NORTHINGTON GAMBLE, MD, PhD

University Professor of the Medical Humanities
Professor of Medicine

Professor of Health Policy and American Studies
The George Washington University

April 18, 2024

208 Light Hall / 4:00 P.M.