Barry S. Coller, M.D.

PHYSICIAN IN CHIEF • VICE PRESIDENT FOR MEDICAL AFFAIRS • DAVID ROCKEFELLER PROFESSOR,
ALLEN AND FRANCES ADLER LABORATORY OF BLOOD AND VASCULAR BIOLOGY

When blood vessels break, platelets stop the bleeding by adhering to the damaged vessel walls. Coller's research focuses on molecular interactions between blood cells and blood vessels, and on new therapies for thrombotic diseases such as heart attack and stroke.

Because platelets play a vital role in blood coagulation, deficiencies in their numbers or function can result in excessive bleeding. But when platelets adhere to and aggregate on blood vessels narrowed by atherosclerosis, they can close off the blood vessel and cause a myocardial infarction (heart attack) or stroke.

By studying the receptors responsible for platelet aggregation and patients who genetically lack the receptors, Coller established the platelet αIIbβ3 (GPIIb/IIIa) receptor as an important target for antithrombotic therapy. This led him to develop monoclonal antibodies to the platelet αIIbβ3 receptor that inhibit platelet aggregation. Working with scientists at Centocor, Coller helped develop a derivative of one of these antibodies into the drug abciximab, which was approved in 1994 to prevent ischemic complications of percutaneous coronary interventions, such as stent placement in patients with myocardial infarction and related conditions. More than five million patients worldwide have been treated with abciximab.

Current research in Coller's lab focuses on multiple areas of platelet physiology. Among them is the genetic disorder Glanzmann thrombasthenia, which produces hemorrhage as a result of an abnormality of the platelet αIIbβ3 receptor. Coller and his lab members are studying the precise genetic and protein abnormalities responsible for the disease, as well as variants in the genes for the receptor (ITGA2B and ITGB3) identified in the general population by next-generation sequencing.

Other areas of blood and platelet physiology that the lab studies include:

Integrin structure and activation. Integrins, including platelet αIIbβ3 and αVβ3, are transmembrane glycoprotein receptors. Through site-directed mutagenesis, molecular dynamics, cryo-electron microscopy, hydrogen-deuterium exchange, and x-ray crystallography studies, the lab studies the mechanisms by which the receptors undergo a transition from an inactive to an active conformation with high affinity for ligands. Most recently, cryo-EM has led to atomic-level, three-dimensional reconstructions of the complex between αIIbβ3 and abciximab and a monoclonal antibody that activates the receptor.

High-throughput screening and structure-guided design of a novel antiplatelet drug. The Coller lab identified a compound, RUC-1, that inhibits ligand binding to platelet αIIbβ3. Structure-guided modifications of it led to the development of another compound, RUC-4, that is approximately 100 times more potent and has a novel mechanism of action as a pure antagonist. RUC-4 (generic name zalunfiban) is currently in Phase 3 human testing for prehospital therapy for myocardial infarction.

Platelet TGF-β1.The Coller lab discovered that platelet TGF-β1can be activated by shear forces, and studies are under way to assess the biological significance of this finding in several model systems.

Integrin αVβ3. The Coller lab is developing pure antagonist anti-αVβ3 drugs with the goal of studying their impact on a variety of pathological processes, including sickle cell disease, osteoporosis, and herpes virus infection.

EDUCATION

B.A., 1966
Columbia University

M.D., 1970
New York University School of Medicine

MEDICAL TRAINING

Internship in medicine, 1970–1971
Residency in medicine, 1971–1972
Bellevue Hospital

POSITIONS

Clinical Associate, 1972–1974
Staff Physician, 1974–1976
National Institutes of Health

Assistant Professor, 1976–1978
Associate Professor, 1978–1982
Professor, 1982–1993
Associate Director for Biomedical Research, 1992–1993
Distinguished Service Professor, 1993
State University of New York at Stony Brook

Professor, 1993–2001
Mount Sinai School of Medicine

Professor, 2001–
Vice President for Medical Affairs, 2001–
Director, Maurice R. and Corinne P. Greenberg Center for Studies in Inflammation, Microbiome, and Metabolism, 2019–
Co-director for Clinical Studies, Stavros Niarchos Foundation Institute for Global Infectious Disease Research, 2023–
The Rockefeller University

Physician in Chief, 2001–
Director, Center for Clinical and Translational Science, 2001–
The Rockefeller University Hospital

AWARDS

National Research Achievement Award, American Heart Association, 1998

Warren Alpert Foundation Award, 2001

Pasarow Award, 2005

Karl Landsteiner Memorial Award, 2013

Gill Award, University of Kentucky Gill Heart Institute, 2016

Grant Medal, International Society on Thrombosis and Haemostasis, 2021

HONORARY SOCIETIES

National Academy of Sciences

National Academy of Medicine

National Academy of Inventors

American Academy of Arts and Sciences

SELECTED PUBLICATIONS

Rikken, S. et al. Prepercutaneous coronary intervention Zalunfiban dose-response relationship to target vessel blood flow at initial angiogram in st-elevation myocardial infarction – A post hoc analysis of the cel-02 phase IIa study. *Am. Heart J.* 262, 75–82 (2023).

Sen, S. et al. Structure-based discovery of a novel class of small-molecule pure antagonists of integrin αVβ3. *J. Chem. Inf. Model.* 62, 5607–5621 (2022).

Buitrago, L, et al. Platelet binding to polymerizing fibrin is avidity driven and requires activated αIIbβ3 but not fibrin cross-linking. *Blood Adv.* 5, 3986–4002 (2021).

Nešić, D. et al. Cryo-electron microscopy structure of the αIIbβ3-abciximab complex. *Arterioscler. Thromb. Vasc. Biol.* 40, 624–637 (2020).

Li, J. et al. Novel pure αIIbβ3 integrin antagonists that do not induce receptor extension, prime the receptor, or enhance angiogenesis at low concentrations. *ACS Pharmacol Transl Sci.* 2, 387–401 (2019).