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 zalinuban) is currently in Phase 3 human testing for prehospital therapy for myocardial infarction.

- **Platelet TGF-β1.** The Coller lab discovered that platelet TGF-β1 can 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.

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**Selected Publications**


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).