

PHRM-BE-570
Vascular biology, medicine and engineering
Directors Vlad Muzykantov and Tilo Grosser
Monday-Wednesday-Friday 2-3pm
Smilow Translational Research Center, 11th floor, Seminar room 11-146

				Department & School
		Section 1: Cardiovascular system (CVS) and blood	Vlad Muzykantov	Pharmacology SOM
1	Wed 1/16	Introduction to the course, CVS and blood. An overview of the cardiovascular system (heart, blood vessels and blood). The structure of blood vessels (tunica intima, tunica media and tunica adventitia). The unique features of pulmonary and cerebral circulation. Overview of the course assignments: Students will learn how to critically review scientific journal articles in the cardiovascular field. First assignment for the entire group (paper to be selected). To be completed by 2/11/19.	Vladimir Muzykantov	Pharmacology SOM
2	Fri 1/18	Blood elements and hemodynamics. Rheological parameters of blood (viscosity, heterogeneity, shear stress, plasma and cellular elements, hematocrit, margination effect of RBC), and their biomedical relevance in physiology (effects of food and exercise) and pathology (diseases altering blood fluidity).	David Eckmann	Anesthesiology PSOM/SEAS
	Mon 1/21	MLK day – no class		
3	Wed 1/23	Unique transporting features of red blood cells. Features of RBC providing extended circulation: elasticity, durability of the membrane. Mechanisms of elimination of senescent and damaged RBC (phagocytosis in the RES, complement). Role of CD47 in recognition of self RBC. Other mechanisms of RBC protection against elimination (DAF and complement inhibitors).	Dennis Discher	Pharmacology SOM
		Section 2: Coagulation and platelets	Adam Cuker & Timothy Stalker	Pathology-Hem PSOM
4	Fri 1/25	Blood coagulation. Hemostasis, its regulation and role in pathology. Key elements and pathways of the coagulation cascade: abnormal cell membranes, tissue factor, thrombin, fibrinogen etc. Basic enzymology of thrombin, its substrates and inhibitors.	Sriram Krishnaswamy	Hematology CHOP/PSOM
5	Mon 1/28	Platelets Platelet biogenesis, structure and functions in hemostasis and beyond. The role of platelets in the phases of the hemostatic response. Molecular mechanisms of platelet signaling and activation (shape change, release of agonists, TxA ₂ formation, α ₂ β ₃ integrin activation and aggregation). PARs.	Timothy Stalker	Hematology PSOM
6	Wed 1/30	Bleeding disorders, hemophilia and its therapy. The genetic and molecular mechanisms of common coagulation disorders predisposing to bleeding, their clinical presentation, complications and responses to treatment. Treatment of hemophilia, replacement biotherapeutic and gene therapy.	Valder Arruda	Hematology CHOP/PSOM

7	Fri 2/1	Platelet disorders and their management. Mechanisms controlling the number of platelets in blood. Thrombopenia and thrombophilia. Overview of clinical manifestation and genetic and molecular mechanisms of common platelet disorders (Glanzmann's thrombasthenia, Bernard Soullier syndrome).	Michele Lambert	Hematology SOM
8	Mon 2/4	Antiplatelet drugs. The antiplatelet drugs and mechanisms of their action: aspirin, purinergic receptor antagonists (clopidogrel, prasugrel) and $\alpha_2\beta_3$ integrin inhibitors (abciximab, eptifibatide, tirofiban). Pros and contras of antiplatelet drugs in clinical management of thrombosis.	Tilo Grosser	Pharmacology PSOM
9	Wed 2/6	Thrombosis and anti-thrombotic drugs. Arterial and venous thrombosis, PE, DVT, AMI and stroke. Therapeutic and prophylactic control of coagulation and fibrinolysis. Basic pharmacology, mechanism of action, pros and contras of heparin, warfarin, and target-specific oral anticoagulants. Plasminogen activators and fibrinolysis. DIC.	Katie Theken	Pharmacology PSOM
10	Fri 2/8	Blood fluidity: flow, dynamics and modeling. The role of rheology in clotting in arterial, venous and microvascular vessels. Kinetic parameters of clotting. Effect of shear stress on Fr VIII-vW functions. Approaches to quantitative analysis and computational modeling.	Maurizio Tomaiuolo	Hematogolgy PSOM
11	Mon 2/11	Course Assignment (1) – Review of Journal Articles We will discuss general principles of a critical evaluation of a scientific manuscript prior to publication (manuscript review process). We will go over the reading assignment from lecture 1 together – figure by figure. We will identify strengths and weaknesses of the paper. Assignment following the class: Prepare a shared document with recommendations for editors and authors.	Vlad Muzykantov Tilo Grosser	
		Section 3: Blood vessels, endothelial function and vasoregulation	Shampa Chatterjee & Tilo Grosser	Physiology SOM
12	Wed 2/13	Vascular contractility. Blood pressure and its control. Contractility of cardiomyocytes and smooth muscle cells. The central and peripheral mechanisms involved in the regulation of vascular tone. Sympathetic and parasympathetic systems. Second assignment (paper to be selected). Groups of ~3 students will evaluate the paper together (manuscript review) and prepare short recommendations for editors and authors (in writing, to be shared with the other groups). To be completed by 3/15/19.	Tilo Grosser	Pathology
13	Fri 2/15	Vasoactive eicosanoids. COX and vasoactive eicosanoids as a class of signaling mediators that regulate vascular tone. Role of platelets.	Tilo Grosser	Physiology, PSOM
14	Mon 2/18	Endothelium. The structure, functions and heterogeneity of the endothelium and its transport and signaling mechanisms.	Peter Davies	Pharmacology, PSOM

15	Wed 2/20	Endothelial sensing and reaction to flow. Flow and shear stress as biological signals. Mechanisms and outcomes of endothelial sensing of flow vascular changes in response to abnormal flow.	Shampa Chatterjee	Pharmacology SOM
16	Fri 2/22	The multifunctional vascular interfaces. Cellular surfaces as interface templates for protective (endothelial thrombomodulin-EPCR-PAR) and pathological multimolecular assemblies (coagulation on activated platelets and apoptotic cells).	Vlad M	Pharmacology SOM
17	Mon 2/25	Endothelial control of vascular contractility Renin-angiotensin system and ACE. Nitric oxide: signaling. Pharmacological applications of drugs affecting NO signaling (organic nitrates, phosphodiesterase inhibitors, inhaled nitric oxide).	Vlad Muzykantov	Pharmacology SOM
18	Wed 2/27	Control of blood pressure & hypertension treatment. Renal control of renin-angiotensin system and blood volume. Drug classes used to treat hypertension and their mechanisms of action (<u>A</u> CE inhibitors, <u>B</u> etablockers, <u>C</u> alcium channel blockers, <u>D</u> iuretics).	Ray Townsend	Medicine SOM
19	Fri 3/1	Angiogenesis. Factors triggering and regulating of blood vessel growth. Processes of angiogenesis. Vasculogenesis vs. angiogenesis.	Georgios Paschos	Pharmacology, PSOM
Spring break (March 2-10)				
20	Mon 3/11	Modeling of blood vessels and microfluidics Endothelial heterogeneity in the circulatory system. Challenges of studies of vascular functions in vivo and in vitro. Models from static multi-well to flow-adapted perfusion chambers and microfluidics	Vlad M	Pharmacology, PSOM
21	Wed 3/13	Intercellular adhesion and the mechanics of the vessel wall The roles of cellular adhesion and extracellular matrix (ECM) and its stiffness in vascular signaling and mechanical properties of blood vessels in the context of cardiovascular physiology and pathology.	Rick Assoian	Pharmacology, PSOM
22	Fri 3/15	Course Assignment – Review of Journal Articles (2) <i>We will go over the reading assignment from lecture 12 (2/13/19) together – figure by figure. We will identify strengths and weaknesses of the paper.</i>	Vlad Muzykantov Tilo Grosser	Pharmacology SOM
Section 4: Inflammation			Cindy Otto	Vet Med
23	Mon 3/18	Inflammation. Inflammation: medical significance, cardinal signs, phases, cellular and molecular mechanisms. Initiation of the inflammatory response to bacterial lipopolysaccharide. Pro-inflammatory and anti-inflammatory cytokines.	Cindy Otto	Vet Med
24	Wed 3/20	Vascular permeability, edema and leukocyte traffick. Pericellular and transcellular mechanisms of endothelial barrier and permeability. Role of bradykinin and VEGF in vascular edema. Leukocyte adhesion and traffick in inflammation.	Vlad Muzykantov	Pharmacology SOM
25	Fri 3/22	Bioengineering aspects of blood cell adhesion. Interactions of leukocytes with cell adhesion molecules: rolling, firm arrest and transmigration. Rheological and biomechanical factors. Cellular plasticity. Quantitative analysis and modeling.	Ravi Radhakrishnan	BE SEAS
26	Mon 3/25	Ischemia/reperfusion and acute oxidative stress. The injurious mechanisms of ischemia/reperfusion injury. Distinction between hypoxia and ischemia. The cellular effects of ischemia.	Vlad Muzykantov	Pharmacology SOM

		Reactive oxygen species (ROS): genesis, reactions and role in vascular pathology. Antioxidant interventions.		
27	Wed 3/27	<p>Anti-inflammatory agents. The prototypes, mechanisms, pros and contras of major classes of anti-inflammatory drugs: nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids and of TNFα and IL-1β antagonists.</p> <p>Third assignment. Each student will select a paper to review. Papers will be provided, but this can also be one you select yourself. They will relate to the themes covered in the preceeding lectures. Students will evaluate the papers as a home work assignment. At the end of the course each student will give a 7-10 minute presentation to discuss strength and weaknesses of the paper she/he selected. Presentations will on 4/19 and 4/22/19.</p>	Tilo Grosser	Pharmacology SOM
		Section 5: Atherosclerosis & vascular pathology	Marina Cuchel	Mol Medicine
28	Fri 3/29	<p>Atherosclerosis The major cellular and molecular events and spatiotemporal characteristics that distinguish the mechanisms of development of atherosclerosis vs restenosis following percutaneous coronary interventions (PCI).</p>	Mike Parmacek	Medicine
29	Mon 4/1	<p>Hemodynamic basis of atherosclerosis Factors of local hemodynamics predispose to atherosclerotic lesion development. Endothelial and sub-endothelial abnormalities caused by pathological hemodynamics.</p>	Peter Davies	Pathology/SEAS
30	Wed 4/3	<p>Atherosclerosis pathophysiology: metabolism of lipids and lipoproteins. The regulation of cellular cholesterol homeostasis (synthesis, absorption and excretion), the physiological function of cholesterol in the cell membranes. Lipoproteins and their receptors.</p>	Marina Cuchel	Mol Medicine
31	Fri 4/5	<p>Blood fluidity: flow, dynamics and modeling. The role of rheology in clotting in arterial, venous and microvascular vessels. Kinetic parameters of clotting. Effect of shear stress on Fr VIII-vW functions. Approaches to quantitative analysis and computational modeling.</p>	Scott Diamond	Bioengineering SEAS
32	Mon 4/8	<p>Atherosclerosis: therapeutic management. The role of lipids and lipoproteins in the formation of foam cells within the arterial wall. Approaches to lowering LDL levels and raising HDL levels. The molecular mechanisms of action of statins, ezetimibe, bile acid sequestrants, PCSK9 inhibitors and niacin.</p>	Marina Cuchel	Mol Medicine
		Section 6: Novel approaches and therapies	David Cormode	Radiology SOM
33	Wed 4/10	<p>Vascular imaging An overview of vascular imaging technologies, current modalities for imaging with untargeted and targeted agents and the use of imaging techniques in clinical drug trials.</p>	David Cormode	Radiology SOM
34	Fri 4/12	<p>Biomaterials for vascular medicine & angiogenesis Polymeric and natural materials for slow drug release, vascular stents, vascular wall implants and patches against aneurism, cardiac implants. Vascular reparative interventions using scaffolds for cells and growth factors. Biocompatibility, degradation and surface features of biopolymers for these applications.</p>	Vlad or Jacob	Pharmacology SEAS
35	Mon 4/15	<p>Vascular gene delivery and gene therapies. The concepts, challenges and prerequisites for safe and effective transfer of therapeutic genes in the vasculature, therapeutic applications and vectors for vascular gene transfer and current</p>	Michael Chorny	Cardiology CHOP

		strategies for targeted vascular gene therapy and their challenges.		
36	Wed 4/17	Invited Keynote Lecture	Professor Colleen Brophe	Vanderbilt University
37	Fri 4/19	Course Assignment – Review of Journal Articles (3) Student presentations	Vlad Muzykantov Tilo Grosser	
38	Mon 4/22	Course Assignment – Review of Journal Articles (4) Student presentations	Vlad Muzykantov Tilo Grosser	