

**The 592nd Kitasato Medical Society
Invitational Academic Lecture Series Abstract**

(H24.6.8)

**Pericytes - the unknown neighbor of
the endothelium**

Christer Betsholtz

(Professor, Department of Medical Biochemistry and
Biophysics, Karolinska Institutet, Stockholm, Sweden)

Pericytes, the mural cells of blood microvessels, have recently come into focus as regulators of vascular morphogenesis and function during development, cardiovascular homeostasis, and disease. Pericytes are implicated in the development of diabetic retinopathy and tissue fibrosis, and they are potential stromal targets for cancer therapy. Some pericytes are probably mesenchymal stem or progenitor cells, which give rise to adipocytes, cartilage, bone, and muscle. However, there is still confusion about the identity, ontogeny, and progeny of pericytes. In my seminar, I will review the history of these investigations, indicate emerging concepts, and point out problems and promise in the field of pericyte biology. I will specifically discuss our own work on the role of pericytes in regulation of the blood-brain barrier, and describe some novel tools for pericyte identification and imaging.

**The 595th Kitasato Medical Society
Invitational Academic Lecture Series Abstract**

(H24.6.14)

**Function and regulation of class VII/class X
myosin and actin cytoskeletal reorganization**

Mitsuo Ikebe

(Professor, Department of Microbiology and
Physiological Systems, University of Massachusetts
Medical School, Massachusetts, USA)

Motor proteins play a fundamental role in diverse cellular processes, such as muscle contraction, cytokinesis, chemotaxis, phagocytosis, secretion, exocytosis, endocytosis, vesicular trafficking, etc. We wish to clarify the function and regulation of motor proteins in these cellular processes.

The goal of the research in my laboratory is two fold. One is to understand the events responsible for linking stimuli to contractile activity in smooth muscle as well as non-muscle cells at the molecular level. It is well known that a number of cellular events are regulated by the protein kinases/phosphatases cascade. For vertebrate smooth muscle as well as non-muscle contractile machinery, the phosphorylation of myosin molecules is the predominant regulatory mechanism for contraction. While the protein kinases and phosphatases which catalyze these processes have been identified, the regulatory cascade of myosin phosphorylation/dephosphorylation is complex and has not been clarified. Although it is established that myosin phosphorylation is obligatory for initiation of smooth muscle contraction, it is not understood how myosin phosphorylation and the motility of non-muscle cells during cytokinesis, chemotaxis, etc. are interrelated. Our objective is to clarify these problems.

The second goal of my research is to clarify the physiological function and regulation of mammalian unconventional myosins. It has recently become clear that myosin forms a large and diverse group of molecular motors which have been hypothesized to play fundamental roles in various cellular processes such as cell locomotion, phagocytosis and vesicle transport. Our goal is to identify the physiological function of each unconventional myosin and clarify the regulatory mechanism of these motor proteins.

**The 596th Kitasato Medical Society
Invitational Academic Lecture Series Abstract**

(H24.7.3)

**Angiogenesis and lymphangiogenesis in
mouse airways**

Peter Baluk

(Professor, Cardiovascular Research Institute,
University of California, San Francisco, USA)

Changes in the blood and lymphatic vasculature contribute to many biological processes such development and pathological conditions including inflammation and cancer. Therefore, it is useful to have in vivo experimental preclinical models where blood vessels and lymphatics can be easily examined and subtle changes in them can be observed. The mouse trachea presents an ideal stage where these vascular actors can play very different roles depending on their developmental age, environment, and stimuli acting on them.

Tracheas of pathogen-free adult mice have a stereotyped two-dimensional network of blood vessels and lymphatics. Individual arterioles, capillary, venules, and accompanying pericytes and smooth muscle cells can all be recognized.¹ In newborn mice, the vascular network is much more primitive in appearance.² It is rapidly remodeled over the first few postnatal days into the hierarchical adult network. The changes involve vascular regression followed by angiogenesis and are driven by changes in hypoxia and mechanical forces. Transgenic over-expression of VEGF-A in epithelial cells of the adult mouse trachea induces the rapid growth of blood vessels by angiogenic sprouting, but no lymphangiogenesis.³ The newly formed blood vessels also rapidly regress when the stimulus is turned off. In contrast, chronic inflammation as a result of airway bacterial infection with *Mycoplasma pulmonis* induces more complex responses from blood vessels and lymphatics, probably resulting from the concurrent influx of leukocytes and induction of multiple inflammatory genes.^{4,5} An early change is vascular remodeling by lateral enlargement, whereby small capillaries gradually transform into venules capable of supporting leukocyte adhesion and plasma extravasation.^{4,5} At later stages, small blood vessels grow by angiogenic sprouting. Lymphatics also grow by sprouting, driven by VEGFR-3 signaling.⁵ A surprising feature of the newly formed lymphatics is their persistence when the stimulus that

originally induced them has been removed.^{5,6} We conclude that the blood vessels and lymphatics of mouse trachea display an extraordinary plasticity of response and are an excellent system for studying vascular biology.

1. McDonald DM, Yao LC, Baluk P. Dynamics of airway blood vessels and lymphatics: lessons from development and inflammation. *Proc Am Thorac Soc* 2011; 8: 504-7. (PubMed: 22052927)
2. Ni A, Lashnits E, Yao LC, et al. Rapid remodeling of airway vascular architecture at birth. *Dev Dyn* 2010; 239: 2354-66. (PubMed: 20730909)
3. Baluk P, Lee CG, Link H, et al. Regulated angiogenesis and vascular regression in mice overexpressing vascular endothelial growth factor in airways. *Am J Pathol* 2004; 165: 1071-85. (PubMed: 15466375)
4. Baluk P, Yao LC, Feng J, et al. TNF-alpha drives remodeling of blood vessels and lymphatics in sustained airway inflammation in mice. *J Clin Invest* 2009; 119: 2954-64. (PubMed: 19759514)
5. Baluk P, Tammela T, Ator E, et al. Pathogenesis of persistent lymphatic vessel hyperplasia in chronic airway inflammation. *J Clin Invest* 2005; 115: 247-57. (PubMed: 15668734)
6. Yao LC, Baluk P, Feng J, McDonald DM. Steroid-resistant lymphatic remodeling in chronically inflamed mouse airways. *Am J Pathol* 2010; 176: 1525-41. (PubMed: 20093490)