血管マトリクス生物学（柳沢 裕美）
Vascular Matrix Biology (YANAGISAWA Hiromi)

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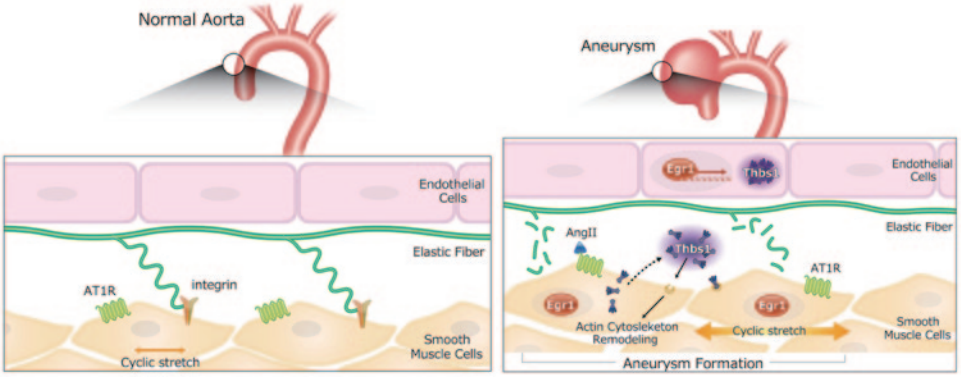
血管メカノトランスダクション機構の解明と疾患への応用

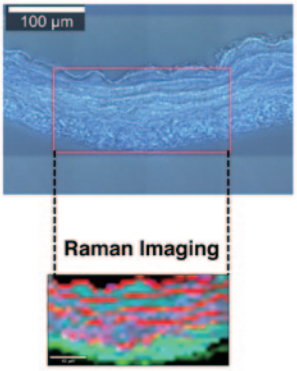
血管は心拍出による機械的刺激に常に晒されています。ではいかに機械的刺激が、血管細胞（内皮細胞、平滑筋細胞、線維芽細胞）に伝搬され、生化学シグナルに変換されるのでしょうか？解剖学的に異なる血管や、老化や炎症で性状が変化した血管では、シグナル伝達はどのように変わるのでしょうか？私たちは、循環器疾患(大動脈瘤や加齢性動脈硬化)のモデルマウスと、ストレッチアッセイ・ライブイメージング・ゲノムエディティングなどの技術を組み合わせ、メカノトランスダクション機構の解明と診断や治療への応用に取り組んでいます。バイオエンジニアリング・ラマンイメージング・バイオマテリアル・心臓血管外科などの研究室との共同研究も進めています。

Elucidating the molecular mechanism of mechanotransduction in blood vessels and its application to vascular diseases

Blood vessels are constantly exposed to the mechanical stress caused by cyclic pumping of the heart. However, 1) how vascular cells (endothelial cells, smooth muscle cells, and fibroblasts) sense stress and convert to biochemical signals, 2) whether anatomically different vascular systems have distinct signaling pathway(s), and 3) how damaged/aged extracellular matrix of the vessels affects mechanotransduction, are largely unknown. We utilize mouse models of cardiovascular diseases such as aortic aneurysms and elucidate the molecular mechanism of mechanotransduction in the vessel wall by combining *in vitro* stretch assays, live imaging, and genome editing. We are currently collaborating with bioengineering, biomaterials, and clinical laboratories.



Molecular dissection of mechanotransduction in normal (left) and aneurysmal wall (right). Mechanosensitive molecules, Egr1 and Thbs1, are highly upregulated in the aneurysm.



Label-free imaging of the aorta.

Recent publications

- Y. Yamashiro, et al. Abnormal mechanosensing and cofilin activation promote the progression of ascending aortic aneurysms in mice. *Science Signaling*. 8(399):ra105 (2015).
- Y. Yamashiro, B. Q. Thang, S. Shin, C. A. Lino et al. Role of thrombospondin-1 in mechanotransduction and development of thoracic aortic aneurysm in mouse and humans. *Circ. Res.* 123(6):660-672 (2018)