柳沢プロジェクト
H. Yanagisawa project

http://saggymouse.tara.tsukuba.ac.jp

血管マトリクス生物学

私たちの体を構成する細胞は、 細胞外環境（細胞外マトリクス、マトリクス分解酵素、機械的応力や低酸素）に応答して、細胞骨格や機能を変化させ、新たな転写を誘導して恒常性を保ちます。血管系を中心に、細胞と細胞外環境との相互作用から生命現象を捉えます。老化マトリクスによる幹細胞の機能変化や、マトリクス欠損疾患の病態などを研究しています。

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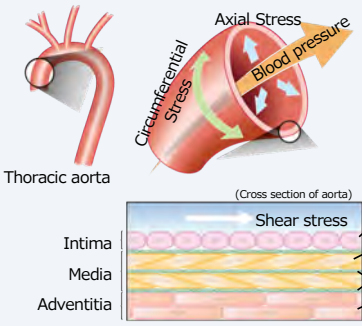
Elucidating the molecular mechanism of mechanotransduction in the blood vessels and its application to vascular diseases



Blood vessels are constantly exposed to the mechanical stress caused by cyclic pumping of the heart. The extracellular matrix (ECM) is fundamental to cellular and tissue structural integrity and mechanical cues that influence diverse biological functions. However, how vascular cells (ECs, SMCs, and fibroblasts) sense the stress and convert to biochemical signals and how ECM modulates these processes are largely unknown. We generate mouse models of cardiovascular diseases such as aortic aneurysms and age-related stiff vessels and try to elucidate the molecular mechanism of mechanotransduction by using cutting-edge techniques in genetic engineering and cellular & molecular biology. We intensively collaborate with laboratories of bioengineering, label-free imaging, and biomaterials.

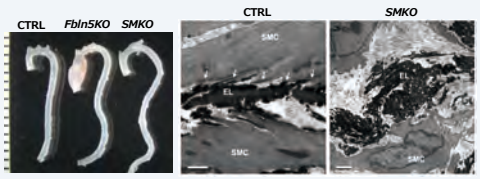
Our questions??

- How does the alteration of ECM affect integrity of the aortic wall?
- What is molecular signature(s) underlying aortic aneurysm formation and/or rupture?
- How do cells sense the mechanical stress and convert to biochemical signals?
- How can we control cell behavior and develop therapeutic techniques for vascular diseases?

Morphological analysis

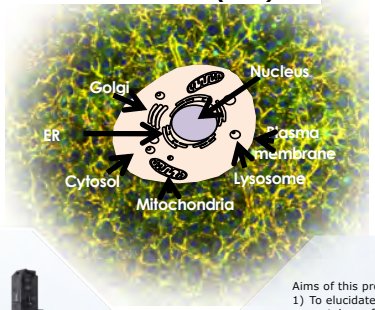
Characterize the pathological change(s) in mouse and human aortic aneurysms

Collaboration with Dr.Hiramatsu (University of Tsukuba)



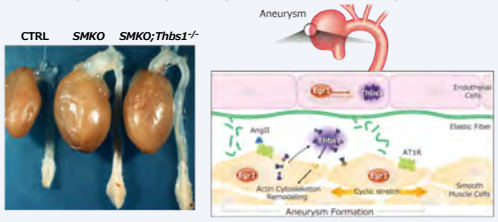
Huang et al. *Sci, Transl Med*, 2013, Yamashiro et al. *Sci. Signal.*, 2015

Cell is surrounded by extracellular matrix (ECM)



Thrombospondin-1 (Thbs1)

Thbs1 is a potential therapeutic target for thoracic aortic aneurysms



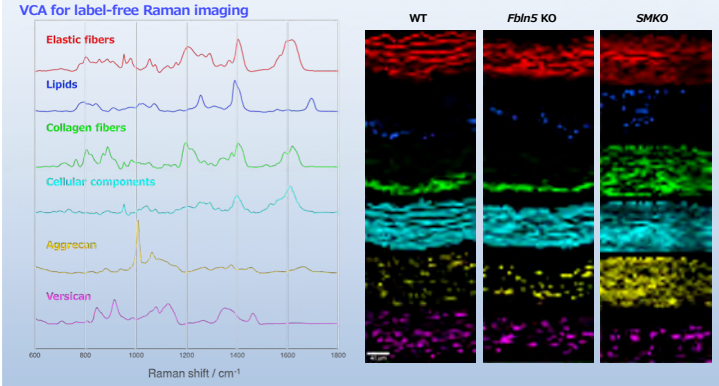
Yamashiro et al. *Circ. Res.*, 2018

Label-free Raman Imaging Project

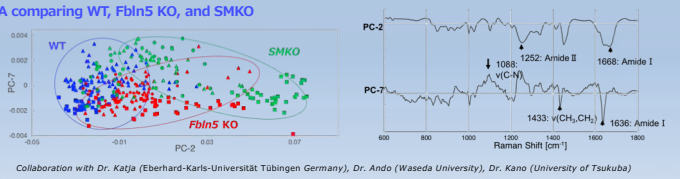
Aims of this project:
1) To apply label-free Raman imaging to examine mouse aortic tissues
2) To identify molecular signatures of the aortas with defective ECM and to compare with wild-type aortas by Raman microspectroscopy

We also utilize statistical methods to analyze the data such as VCA (vector component analysis), PCA (principle component analysis), and MCR-ALS (multivariate curve resolution alternating least square).

VCA for label-free Raman imaging



PCA comparing WT, Fbln5 KO, and SMKO

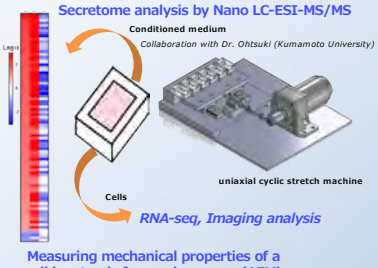


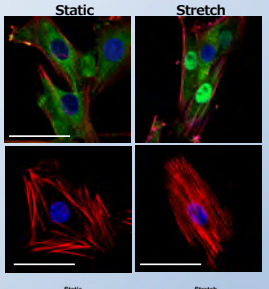
Collaboration with Dr. Katja (Eberhard-Karls-Universität Tübingen Germany), Dr. Ando (Waseda University), Dr. Kano (University of Tsukuba)

Matrix mechanotrasduction Project

Aims of this project:
1) To elucidate the molecular mechanism of mechanotransduction in the vessel wall, we analyze secreted protein profiles, RNA expression, intracellular signaling and cellular mechanical properties in response to mechanical stretch.
2) To establish a therapeutic strategy for vascular diseases caused by abnormal mechanotransduction, we find a way to alter cellular mechanics and control cell behavior by using nanotechnology.

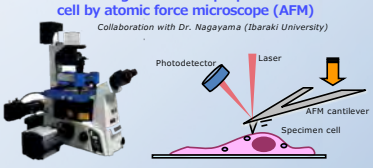
Secretome analysis by Nano LC-ESI-MS/MS

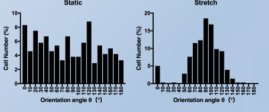


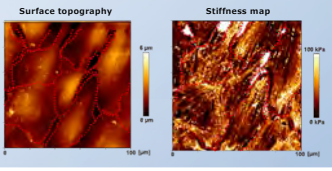


Measuring mechanical properties of a cell by atomic force microscope (AFM)

Collaboration with Dr. Nagayama (Ibaraki University)







Live imaging & Nano technology

Collaboration with Dr. Miyamoto (Tsukuba University)