# 柳沢プロジェクト
# H. Yanagisawa project

https://www.saggymousehkytsukuba.com

# 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・骨軟骨系を中心に、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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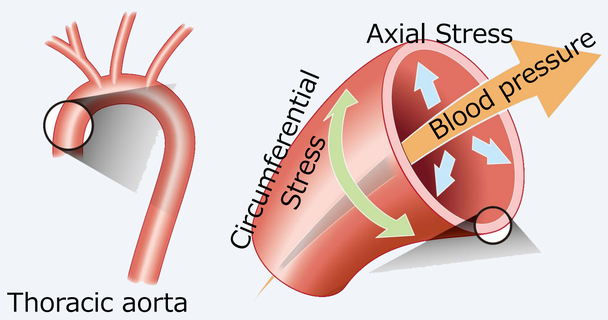
## Elucidating the molecular mechanism of mechanotransduction in the blood vessels and its application to vascular diseases



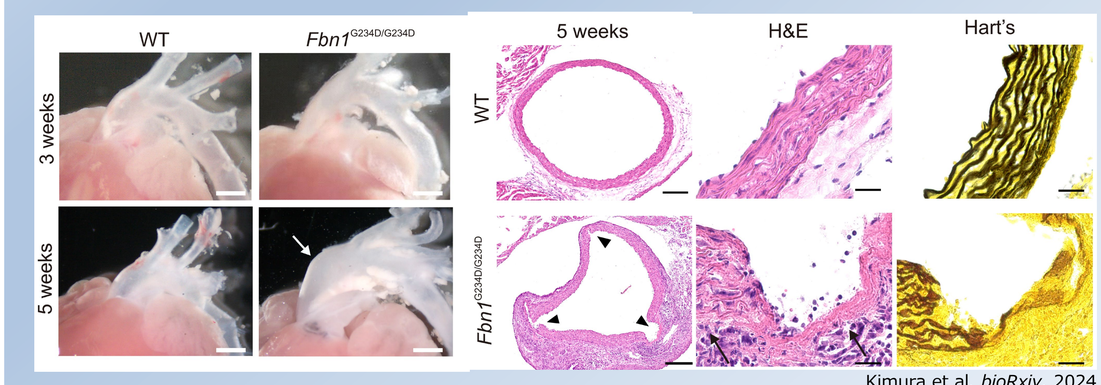

Blood vessels are constantly exposed to the mechanical stress caused by cyclic pumping of the heart. The extracellular matrix (ECM) is fundamental to cellular and tissue structural integrity and mechanical cues that influence diverse biological functions. However, how vascular cells (ECs, SMCs, and fibroblasts) 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?

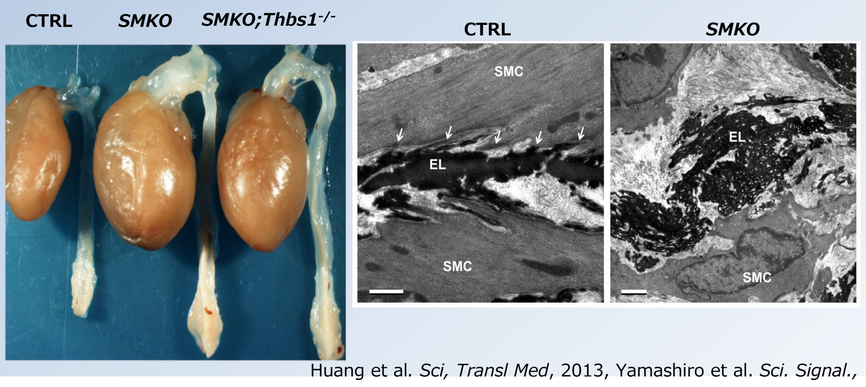
## Generation of a mouse model with defective extracellular matrix and searching for a novel therapeutic strategy

### Aortic dissection model



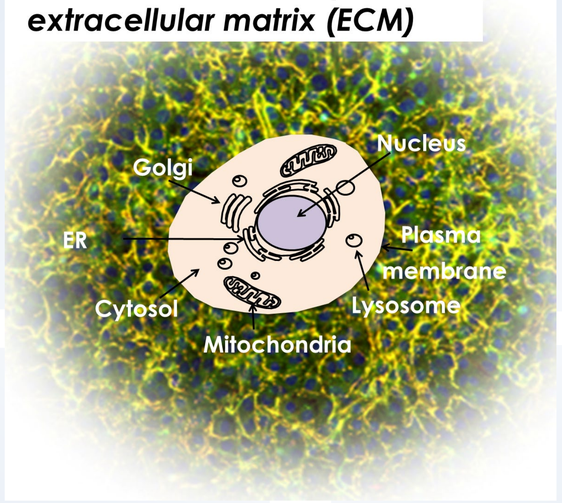

Kimura et al. *bioRxiv,* 2024

### Aortic aneurysm model

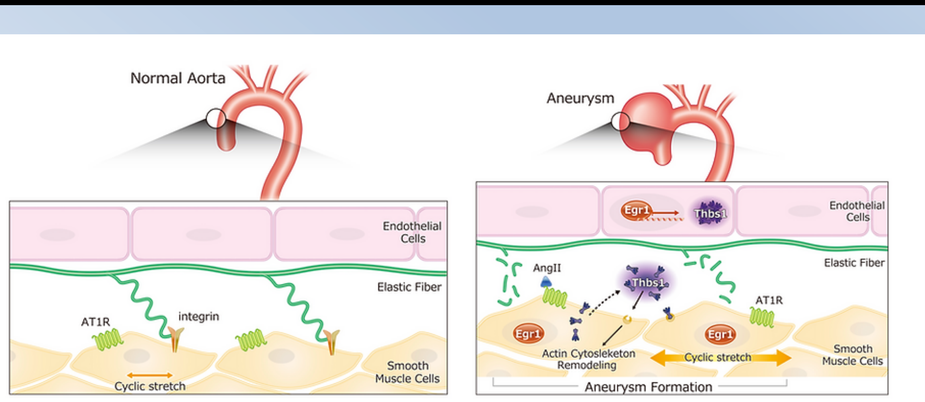



Huang et al. *Sci, Transl Med*, 2013, Yamashiro et al. *Sci. Signal.,* 2015

***Cell is surrounded by extracellular matrix (ECM)***

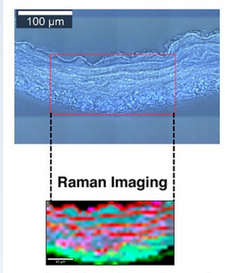



## Elucidating the molecular mechanism of mechanotransduction in blood vessels and its application to vascular diseases



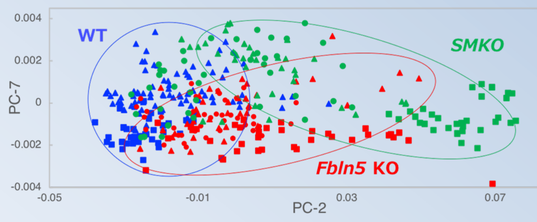

Molecular dissection of mechanotransduction in normal (left) and aneurysmal wall (right). Mechanosensitive molecules, Egr1 and Thbs1, are highly upregulated in the aneurysm.

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




Label-free imaging of the aorta.

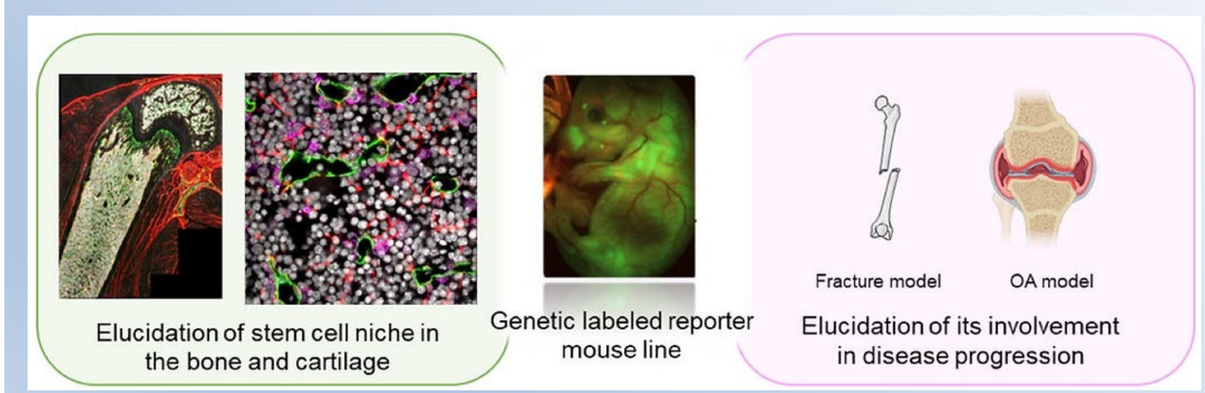
**PCA comparing WT, Fbln5 KO, and SMKO**




Sugiyama et al. *Cell Report Medicine.,* 2021

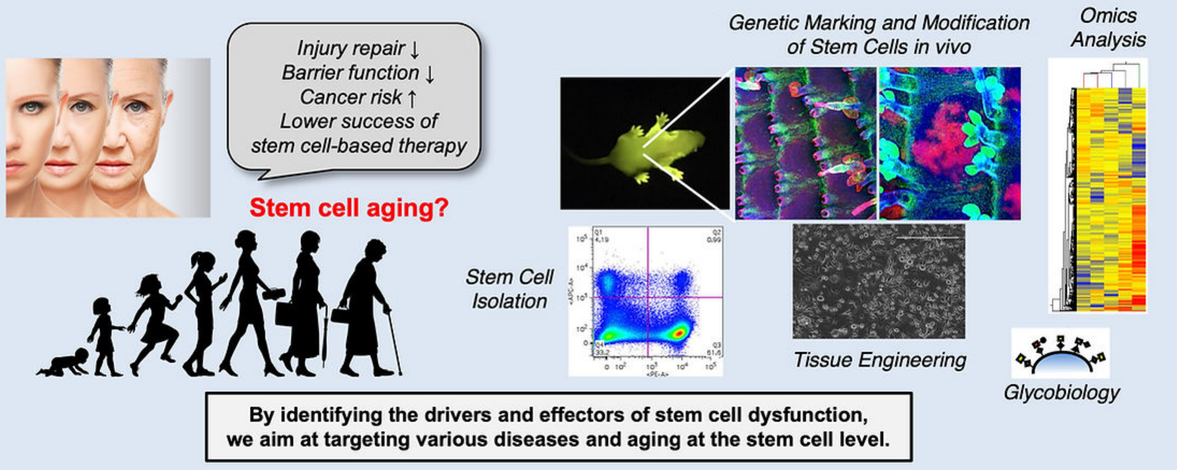
## Elucidating the functional properties of mesenchymal stem cells during homeostasis and disease

### Relationship between ECM and bone/cartilage homeostasis




Kimura et al. *Cell Stem Cell,* 2018, Kimura et al. *Bone Reports,* 2021

## Elucidating the mechanism of tissue regeneration and aging




Raja et al. *EMBO rep,* 2022