

## Immunology

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### Other Faculty Members

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### Major Scientific Interests of the Group

The maintenance of a proper extracellular environment comprised of extracellular matrices (ECM), ECM degrading enzymes, cytokines/growth factors, and physical factors, is crucial for normal development and stem cell functions. The long-term goal of our research is to investigate the interactions between extracellular environment and various cell types and elucidate how they modulate intracellular signaling, cellular functions, and cell fate. In particular, we focus on the vessel wall and ECM. We aim to identify novel ECM proteins and characterize their biochemical properties, as well as to investigate pathophysiological functions by taking cellular, molecular biological, and genetic engineering approaches.

### Projects for Regular Students in Doctoral or Master's Programs

- 1) Identification of novel therapeutic targets for genetic aortic aneurysms
- 2) Molecular mechanism of mechanotransduction in vascular cells.
- 3) Novel ECM and renal calcification
- 4) Identification of novel niche for epidermal stem cells
- 5) Implication of epithelial stem cell aging in age-related diseases

### Study Programs for Short Stay Students (one week – one trimester)

- 1) Genetic and phenotypic identification of mutant mice with defective ECM
- 2) Preparation of histological sections and expression analysis by immunostaining

### Selected Publications

- 1) Y. Yamashiro, B. Q. Thang, S. Shin, C. A. Lino, T. Nakamura, J. Kim, K. Sugiyama, C. Tokunaga, H. Sakamoto, M. Osaka, E. C. Davis, J. E. Wagenseil, Y. Hiramastu, and H. Yanagisawa: Role of thrombospondin-1 in mechanotransduction and development of thoracic aortic aneurysm in mouse and humans. *Circ. Res.* 123 (6):660-672 (2018).
- 2) J. Tsunozumi, H. Sugiura, L. Oinam, A. Ali, B. Q. Thang, A. Sada, Y. Yamashiro, M. Kuro-O, and H. Yanagisawa: Fibulin-7, a heparin binding matricellular protein, promotes renal tubular calcification in mice. *Matrix Biol.* Dec;74:5-20 (2018).
- 3) Y. Yamashiro, C. L. Papke, J. Kim, L-J. Ringuette, Q-J. Zhang, Z-P. Liu, H. Mirzaei, J. E. Wagenseil, E. C. Davis and H. Yanagisawa: Abnormal mechanosensing and cofilin activation promote the progression of ascending aortic

aneurysms in mice. *Sci. Sig.* 8(399):ra105 (2015).

- 4) J. Huang, Y. Yamashiro\*, C. L. Papke\*, Y. Ikeda\*, Y. Lin, M. Patel, T. Inagami, V. P. Le, J. E. Wagenseil and H. Yanagisawa: Angiotensin converting enzyme-induced activation of local angiotensin signaling is required for ascending aortic aneurysms in fibulin-4 deficient mice. *Sci. Transl. Med.* 5, 183ra58 (2013). \* equal contribution second author
- 5) J. Huang, E. C. Davis, S. L. Chapman, L. Y. Budatha, M., Marmorstein, R. A. Word and H. Yanagisawa: Fibulin-4 deficiency results in ascending aortic aneurysms: a potential link between abnormal smooth muscle cell phenotype and aneurysm progression. *Circ Res.* 106(3):583-592 (2010).