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Uncovering the molecular mechanisms of blood and lymphatic vessel formation

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Dr. Watabe graduated from the University of Tokyo and received his PhD at University of California. He became Assistant Professor (2001) and Associate Professor (2009) at the University of Tokyo, then Professor of School of Life Sciences, Tokyo University of Pharmacy and Life Sciences in 2013. He joined TMDU as Professor of Biochemistry in 2015. He has held the office of Special Advisor to the President since 2017.

Q Your research focuses on blood and lymphatic vessel formation. Why are these processes physiologically important?

A: Normal blood vessel development is required for the development of a functioning circulatory system during embryogenesis and also for tissue remodeling and repair in children and adults. In addition, the lymphatic system is necessary for tissue fluid homeostasis; disruption of functional lymphatic vessels results in lymph-edema. We are working with collaborators in Japan and internationally to uncover the molecular pathways that govern blood and lymphatic vessel development and maintenance, both under normal physiological conditions and in disease states such as cancer.

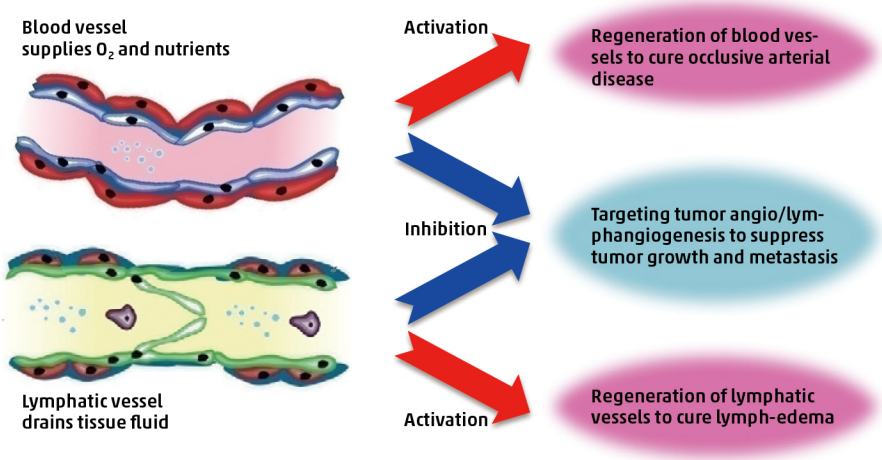
Q Can you tell us about your findings?

A: We have been investigating members of the transforming growth factor (TGF)-ß family. We have shown that TGF-ß inhibits blood vascular endothelial cell proliferation and increases endothelial permeability. We recently found that BMP-9 (bone morphogenetic protein) functions in both blood and lymphatic vessel formation. Activation of this signaling axis promotes blood vessel formation both *in vitro* and *in vivo* (e.g. tumor xenograft model). Conversely, it inhibits lymphatic vessel formation both during normal development and in tumors.

Q Why is an understanding of these molecular pathways important clinically?

A: Both blood and lymphatic vessel formation are of critical interest both in cancer research and regenerative medicine. Progression and metastasis of various types of tumors require growth of new blood and lymphatic vessels, since blood vessels supply oxygen and nutrients to cancer cells and both kinds of vessels provide a pathway for metastasis. We have reported that the inhibition of BMP-9 signals has effectively decreased tumor formation, suggesting that BMP-9 is a potential molecular target for therapeutic interventions. Furthermore, regeneration of blood and lymphatic vessels is urgently required for curing patients of occlusive arterial disease and lymph-edema. Since regulation of signals mediated by TGF-ß and BMPs improves the quality of newly formed blood and lymphatic vessels, a comprehensive overview of the signaling pathways is important for developing novel therapeutic strategies for cancer and regenerative medicine.

Bioengineering of blood and lymphatic vessels by TGF-ß family signals



Blood and lymphatic vessels play important roles not only in the maintenance of fluid homeostasis but also in cancer progression. We are trying to activate and/or inhibit angio/lymphangiogensis by modulating TGF-ß family signals for cancer therapy and regenerative medicine of occlusive arterial disease and lymph-edema.

Q How does your research align with TMDU's strengths and objectives?

A: TMDU has a strong tradition of translational research, so it is an excellent setting for pursuing this kind of basic research with clinical applicability. In particular, since TMDU recently launched a "Organ and Tissue Neogenesis Consortium", which emphasizes regenerative medicine, our efforts in the bioengineering of blood and lymphatic vessels align with TMDU's mission to contribute to people's well-being.

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