Summary:
The vascular system development precedes the formation and functioning of virtually all organs. It provides necessary nutrients and oxygen to the organs. It also feeds growth factors required for the organ development. In converse, it is also known that developing organs feed the vascular system with growth and differentiation factors for the vasculature.

More than a decade ago, we have identified a novel class of receptors, Tie1 and Tie2, and shown that both of these receptors are required for the normal development of blood vessels during embryogenesis. Subsequently, in collaboration with Regeneron Pharmaceuticals, we discovered specific ligands for the Tie2 receptor. These ligands, angiopoietins, are also required for the normal vascular development.

In addition to angiopoietins/Tie system, VEGF/VEGF-receptors also play critical roles in vascular development. VEGF has been generally thought to be critical for the growth of blood vessels (i.e. angiogenesis). However, we have recently shown that VEGF also induces the specification of arterial type vascular endothelial cells (i.e. arteriogenesis). Furthermore, this VEGF-induced arteriogenesis can be modified differentially by two angiopoietins, angiopoietins-1 and angiopoietins-2. Most recently, we have also found genetic evidence for the involvement of Wnt signaling pathways in controlling angiogenesis and arteriogenesis mediated by VEGF and angiopoietins.

One of the main receptors for VEGF is KDR/Flk1. This receptor is required for the formation of the most primitive vascular system in embryos. Recently, we have discovered a novel gene, AlK (Albo of KDR/Flk1), as a modifying gene for the KDR/Flk1 function during embryonic vascular system.

In my talk, I will first summarize the current view of molecular mechanism of vascular development. I will then present our most recent findings discussed above.

In addition to our effort to understand how the vascular system develops, we have recently begun to study the mechanisms underlying stem cell differentiation. Towards this end, I will briefly present our new cell biology based post-genomic approach to find key proteins involved in stem cell differentiation.