


# Elucidation of the principles of angiogenesis focussed on endothelial stem cells

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## Purpose and Background of the Research

### ●Outline of the Research

- ★ Blood vessels are mainly composed with endothelial cells that form the lumen.
- ★ Traditionally, the main function of blood vessels has been thought to be to deliver oxygen and nutrient to tissue cells and collect carbon dioxide and waste product. However, it is becoming clear that factors secreted from endothelial cells (angiocrine factors) play an important role in the development and maintenance of organ cells.
- ★ In the Scientific Research (S)(2020~2024), we found that within cancer tissue, endothelial cells can either induce or suppress the malignant transformation of cancer cells by context dependent manner.
- ★ In this study, we focus on endothelial stem cells, which localize in the preexisting blood vessels and have a high ability to regenerate blood vessels, and elucidate the mechanism of self-renewal, differentiation, and proliferation of endothelial cells to clarify the process of angiogenesis specific to cancer and how angiocrine factors secreted by these vascular cells are involved in cancer growth (Figure 1).

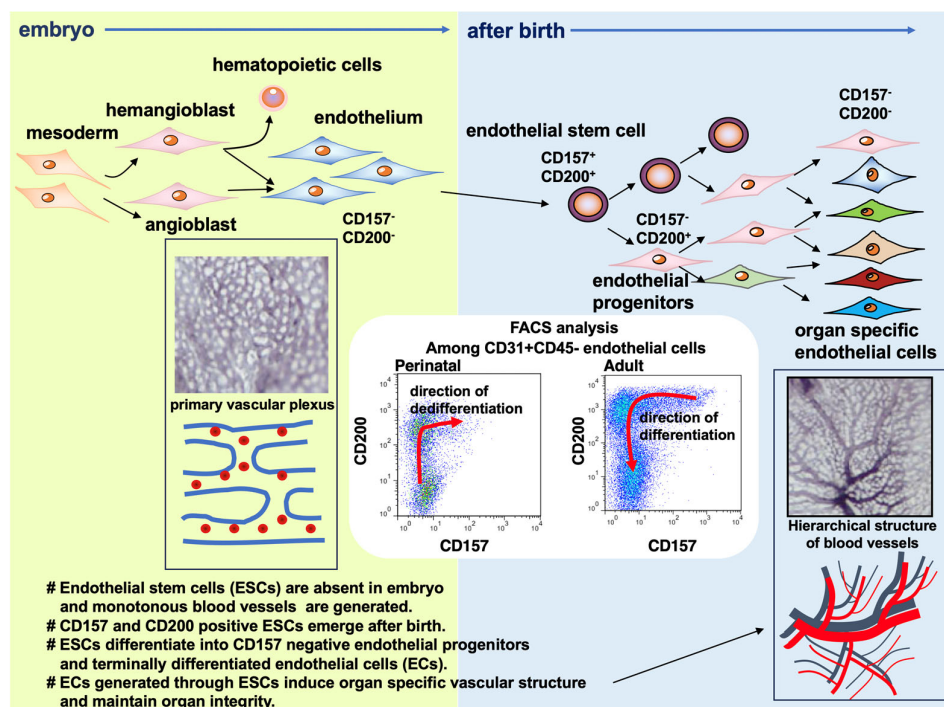
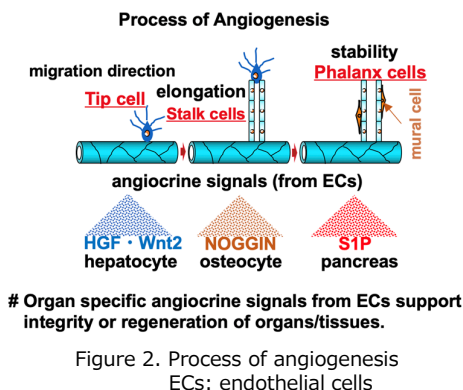


Figure 1. Illustration of endothelial stem cells and angiogenesis, which are the core of this research proposal

### ●Angiogenesis and angiocrine

- ★ New blood vessel formation from pre-existing blood vessels is called angiogenesis(Figure 2).
- ★ In angiogenesis, Tip cells decide the migration direction of new vessels and Stalk cells elongate new vessels, and finally phalanx cells induce maturation of blood vessels, resulting in finalization of angiogenesis.
- ★ New blood vessels not only deliver O<sub>2</sub> and nutrient but also supply angiocrine signals to tissue and organ to induce organ specific tissue regeneration and maintenance.
- ★ Different from the process in physiological angiogenesis, angiogenesis is continuously induced in tumor microenvironment.

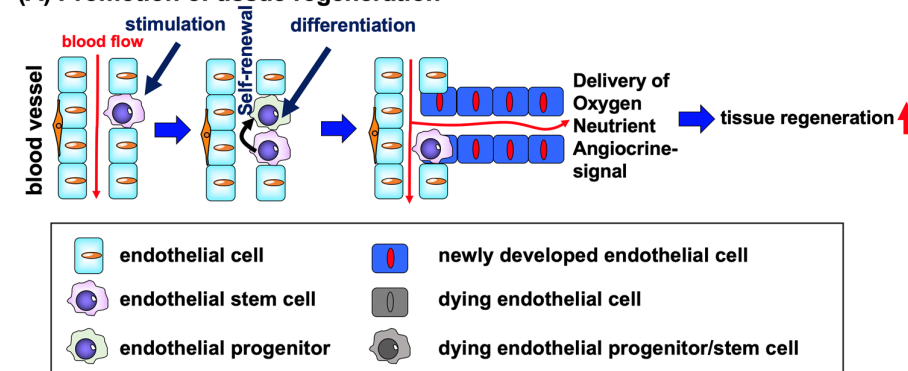


## Expected Research Achievements

### ●Suppression of tumor angiogenesis by the regulation of endothelial stem cells

Previously therapeutic drugs have been developed to suppress the proliferation of endothelial cells within tumor, and have actually been used clinically. However, simply controlling the growth factors involved in the proliferation of endothelial cells has limited therapeutic effect against cancer. In this study, we will elucidate a new principle of angiogenesis by examining how self-renewal and differentiation of endothelial stem cells are induced both physiologically (Figure 3A) and pathologically (Figure 3B). Finally, we create a new therapeutic concept that suppresses tumor growth by controlling vascular endothelial stem cells within tumors.

#### (A) Promotion of tissue regeneration



#### (B) Suppression of tumor growth

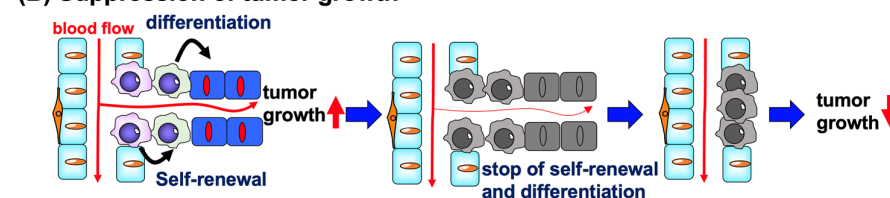


Figure 3. Image of the research plan for this research proposal