●平成 26 年度医学・生命科学セミナー／D1 “MEDICAL & LIFE SCIENCE SEMINAR, 2014” ●

Endothelial Cell Dynamics in Angiogenic Morphogenesis

＊演題が変更となりました。Title has been changed.

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・Date: September 17th (WED) from 17:30.　9 月 17 日（水）17:30～

・Place: Lecture Room 2, Medical Education & Library Building 3F.

医学教育図書棟 3 階 第 2 講義室

Angiogenesis is a vital biological reaction to maintain homeostasis of tissues, wherein a new vascular network emerges from pre-existing vessels in not only developmental stages but also various (patho)physiological settings such as ischemia, inflammation and tumorigenesis. In medical science, angiogenesis attracts attention as one of the potential therapeutic target for the diseased conditions. Also, angiogenesis is of extreme interest as a biological multicellular phenomenon driven by morphogenetic cell behaviours. Vascular endothelial cells (ECs) collectively behave in consort with mural cells in an orderly fashion to form dendrite structures through sprouting, elongating, branching and lumenisation processes. To date, a number of angiogenesis-related molecular players and signalling pathways have been identified, the first being vascular endothelial growth factor (VEGF), and their angiogenic functions have been extensively explored even at the single cell level. However, the underlying cellular mechanisms, which would bridge the gap in our understanding between molecules and angiogenic morphogenesis, remain largely unknown.

To gain further insights into morphogenesis, we developed a system combining time-lapse imaging with computer-assisted quantitative analysis, which enables us to comprehensively explore the EC behaviours driving angiogenic morphogenesis in an *in vitro* model [1]. We discovered EC behaviours to be much more dynamic and complex than previously thought. Individual ECs moved frequently changing their relative positions, including tip cell overtaking (“cell-mixing”) [1]. The ‘cell-mixing’ phenomenon was unexpected because angiogenic elongation was assumed to be a quasi-static phenomenon in which tip cells with filopodia lead to the way as pioneer cells and a chain of followers serves as stalk cells [2]. Quantitative and statistical analyses further uncovered how morphogenetic EC behaviours contributed to effective branch elongation. In this seminar, I will introduce EC dynamics driving angiogenic morphogenesis through self-organization-like processes and will discuss the underlying molecular and cellular mechanisms. Also, I will introduce a developing analytical framework using mathematical modeling to dissect the next question, i.e. how the movements of individual ECs are integrated into such a dynamic and complex multi-cellular process culminating in ordered architectures. Finally, I will present recent data obtained through the framework, showing stochastic and deterministic aspects of angiogenic EC movements (unpublished data).

References

[1] Arima, S*. Nishiyama, K*., Ko, T., Arima, Y., Hakozaki, Y., Sugihara, K., Koseki, H., Uchijima, Y., Kurihara, Y., Kurihara, H., 2011. * These authors contributed equally to this work. Angiogenic morphogenesis driven by dynamic and heterogeneous collective endothelial cell movement. *Development*, **138**: 4763–4776.

[2] Gerhardt, H., Golding, M., Fruttiger, M., Ruhrberg, C., Lundkvist, A., Abramsson, A., Jeltsch, M., Mitchell, C., Alitalo, K., Shima, D., Betsholtz, C., VEGF guides angiogenic sprouting utilizing endothelial tip cell filopodia, *J Cell Biol*, 161(6):1163-1177.

Inviter: Prof. Hisao Ogawa (Dep. of Cardiovascular Medicine)　小川久雄 教授（循環器内科学分野）

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