論　文　内　容　の　要　旨
Synopsis of Thesis

氏　　名 Ｎａｍｅ	WANG MAN
論文題名 Title	APJ Regulates the Balance Between Self-Renewal and Differentiation of Vascular Endothelial Stem Cells（APJは血管内皮幹細胞の幹細胞性維持と分化のバランスを調節する）

論文内容の要旨

〔目　的(Objective)〕

CD157 marks a population of tissue-resident vascular endothelial stem cells (VESCs) in mice which play key roles in EC homeostasis and liver vascular regeneration. However, the mechanisms regulating postnatal VESC behavior under physiological and pathological conditions remain unclear. This study investigates the role of the endothelial G protein coupled receptor APJ in regulating VESCs homeostasis and regenerative potential.

〔方法ならびに成績(Methods/Results)〕

Using an APJ knockout (KO) mouse model, we examined how APJ deficiency impacts VESCs function. Flow cytometry revealed that APJ KO led to a significant accumulation of VESCs in adult mice, which displayed enhanced colony-forming capacity but delayed differentiation into mature ECs. APJ KO mice exhibited impaired vascular regeneration following partial hepatectomy, linked to compromised VESC differentiation. Gene expression analysis revealed upregulation of transcription factors Egr1 and Egr2 and downregulation of Ccnd1 in APJ KO VESCs, consistent with disrupted cell cycle regulation. Additionally, APJ deletion reduced Collagen IV levels, weakening the basement membrane and contributing to the maintenance of VESCs in an undifferentiated state.

〔総　括(Conclusion)〕

Our findings demonstrate that APJ signaling is essential for coordinating the balance between self-renewal and differentiation of VESCs. APJ deficiency alters cell cycle regulation and extracellular matrix composition, thereby maintaining VESCs in an undifferentiated state. These results highlight the apelin/APJ pathway as a key regulator of the VESC niche and a potential target for modulating vascular stem cell behavior in regenerative medicine.

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

This thesis elucidates the role of the Apelin receptor (APJ) in regulating the homeostasis and regenerative capacity of vascular endothelial stem cells (VESCs). Using APJ knockout mouse, the author demonstrated that loss of APJ promotes VESC expansion and maintains these cells in an undifferentiated state, characterized by enhanced proliferative potential but impaired differentiation. This, in turn, compromises vascular regeneration following partial hepatectomy. The study further reveals that APJ deficiency disrupts both cell cycle progression and basement membrane composition, thereby uncovering a novel mechanism by which APJ regulates VESC behavior through intrinsic and extrinsic cues.

These findings underscore the importance of APJ signaling in maintaining the balance between self-renewal and differentiation in VESCs and highlight its potential as a therapeutic target in regenerative medicine.

This research is worth being granted a doctoral degree(medicine).