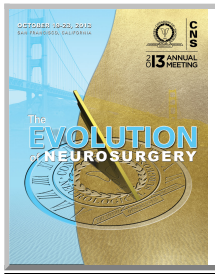

CD41 and CD45 Expression Marks the Angioformative Initiation of Neovascularization in Human Hemangioblastomas

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Introduction

The predominant theory proposed that VEGF secreted by stromal cells may bind to the corresponding receptors of endothelial cells, and thereby it triggers an intracellular signaling pathway in the endothelial cells that finally results in cell proliferation and vascular formation. This angiogenesis mediated by hypoxia induced factor, however, is unlikely to be a major factor of VEGF upregulation and hemangioblastoma (HB)-neovascularization, since this tumor is well vascularized and necroses do not occur. This attention has been shifted to embryonic hemangioblasts or identifying the transformed cell type (vasculogenesis). Therefore, the angioformative process of HB-neovascularization remains to be further elucidated.

Methods

We studied the cellular expression of some primitive hematopoietic progenitor markers and their progeny tracking in order to explicate the atypical vasculature.

Results

We firstly describe the cellular expression of CD41 and CD45, which are similar to human embryonic vasculogenesis by comparison. Culture of fluorescenceactivated cell sorter (FACS) purified cells from HBs showed that primitive hematopoietic progenitors were highly enriched in the CD41+ fraction, whereas endothelial cells also developed from CD41-cells. In vitro analysis showed that CD45-CD41+ subpopulation gave rise to occasional primitive erythroid activity and endothelial marker expression, meanwhile, the CD45+c-kit+ population was gained from CD41+ cells that lack definitive hematopoiesis. Furthermore, the kinetic investigation of CD41+CD45+ subpopulation showed couples of molecules, including Scl, Flk1 and c-kit, and are involved in vascular formation.

Conclusions

The present data suggested that CD41 and CD45 expression marked the onset of HB-neovascularization and CD45 expression implicated the divergence of primitive hematopoiesis from hemangioblasts during HB-neovascularization. Such findings also provide new insights into the mechanisms of HB-neovascularization and the underlying therapeutic targets of this tumor anti-angiogenic treatment.

Learning Objectives

1.Describe embryonic hematopoietic marker CD41 and CD45 expression in hemangioblasomas

2.Show vasculogenesis examples of in vitro and in vivo tracking the freshly harvested CD41+ and/or CD45+ cells

3.Discuss challenges in the development of validated biomarkers of vasculogenic activity, as well as their selective targeting of anti-vasculogenic treatment.

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