Roles of Stem Cell Antigen-1 in the Pulmonary Endothelium

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Keywords

Resident progenitor cell · Pulmonary vessels · Sca-1 · Angiogenesis

There is growing evidence that resident progenitor cell populations exist in murine lung tissues and differentiate into a mesenchymal cell lineage [1, 2]. Stem cell antigen-1 (Sca-1) is a cell surface glycoprotein, initially found in murine bone marrow-derived stem cell subtypes, such as hematopoietic stem cells. Some studies showed Sca-1 expression in the pulmonary vascular endothelium of adult murine lungs [3], while a subset of Sca-1-expressing cells formed vascular-like structures under specific conditions [1].

We previously performed DNA microarray analysis using murine lung cells positive for vascular endothelial marker, CD31, selected by fluorescence-activated cell sorting (FACS) at embryonic and postnatal stages. Sca-1 was found to be more robustly expressed in postnatal pups than in embryos (Uchida K, unpublished observation), suggesting that a subset of Sca-1-expressing cells may be related to the formation of the capillary network during later development.

First, we performed immunohistochemistry using eight-week-old murine lung sections where Sca-1 immunostaining was found in the vascular wall of pulmonary vessels and alveolar capillaries. Some of these Sca-1-positive cells showed overlapping expression with vascular endothelial marker, vWF. Cell populations were then

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Fig. 10.1. The tube formation assay. The tube formation (arrows) reflecting angiogenesis is more robustly observed in Sca-1 (–) CD31 (+) cells than in Sca-1 (+) CD31 (+) cells. Scale bars, 100 μ m

isolated from whole-lung cells by FACS, using antibodies for Sca-1 and CD31, following the depletion of CD45-positive cells. We investigated the tube formation ability of these sorted cells cultured in endothelial growth media and found that Sca-1 (–) CD31 (+) cells were more robust in tube formation than Sca-1 (+) CD31 (+) cells (Fig. 10.1).

These results suggest that though Sca-1 (+) CD31 (+) cells form vascular tube structures, they have lower tube formation activity than Sca-1 (–) CD31 (+) cells. Sca-1 may possibly repress angiogenesis activity in the endothelial cells and potentially make progenitor cell populations stay resident in adult murine lungs. Further analysis would delineate the physiological function of Sca-1 in developing lungs through embryonic to adult stages.

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