Reviewer’s report

Title: Elevated expression of VEGFR-3 in lymphatic endothelial cells from lymphangiomas

Version: 2 Date: 17 November 2006

Reviewer: Janice Nagy

Reviewer’s report:

General
The authors set out to begin to address an important clinical question: the etiology of lymphangiomas. Specifically, the authors compared the expression pattern of known vascular and lymphatic molecular markers on lymphatic endothelial cells (LECs) obtained from healthy skin versus LECs that they isolated from lymphangioma tissue obtained from two pediatric patients. The authors also compared these expression patterns on LECs with that found on BECs from umbilical vein, aorta and myometrial microvessels.

The authors found that LECs from foreskin and lymphangioma had an almost identical pattern of some lymphatic endothelial markers such as podoplanin, Prox1, reelin, cMaf and integrin-alpha1 and -alpha9; however, LYVE-1 was down-regulated and VEGFR-2 and VEGFR-3 were up-regulated in lymphangiomas. Moreover the authors found that Prox1 was constantly expressed in LECs but not in any of the BECs, and thus the authors suggest that prox-1 expression can be used to distinguish LECs from BECs. Finally the authors report high levels of VEGFR-3 and –2 on the LECs from lymphangioma patients and suggest that these receptors may contribute to the etiology of lymphangiomas.

This is a well-written, paper that presents clear data to support the conclusion that Prox-1 is the only definitive lymphatic marker. This is an important finding that should help to sort out much confusion in the field of lymphatic research. Moreover, the authors have performed a careful side-by-side comparison using FACS, immunofluorescence and ELISA and provide new data on lymphangioma LEC from expression profiling with micro chips.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) The authors report the “surprising” finding that the LECs isolated from the lymphangioma tissue at least from patient are express high levels of VEGFR-2. However this finding is not new. Huang et al reported in Lab Investigation 81:1729-1734, 2001, the co-expression of VEGF-C and both of its receptors, i.e, VEGFR-3 and VEGFR-2, in endothelial cells in lymphangiomas. Therefore this present work confirms the findings of this earlier reference and this reference should be cited.

2) Figure 6b panel b. The labels on the x and y axis in the histogram are illegible even at high magnification and therefore font needs to be changed.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Page 3 line 20 “has no been tested” should be “has not been tested”

Page 5 line 10 “FASC” should be “FACS”

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.