Modeling Alveolar Capillary Dysplasia

To the Editor,

I read with great interest the article by Han et al. who studied lung morphology in developing endothelial NO synthase (eNOS)-deficient mice. The authors presented exciting data on defective peripheral lung vessel development, which was combined with impaired alveolar maturation. These data reflect very well the current thinking of lung development regulated by molecular cross-talk between mesenchymal and epithelial elements. One main point suggested by the authors was the resemblance of the eNOS-deficient mouse pulmonary phenotype to a “new” human clinical syndrome, alveolar capillary dysplasia (ACD). The authors observed thin-walled channels (veins) in close proximity to the pulmonary broncho-arterial units of the eNOS-deficient mouse lung (see Figure 4g in Han et al.), and, therefore, they proposed that the eNOS-deficient mouse be considered an animal model for ACD.

In my opinion, this proposal deserves careful rethinking. ACD, although uncommon, has been recognized for more than 2 decades. There is an ongoing debate regarding the exact pathomechanism, but it is clear that the main pathology primarily involves developing air-blood barriers. The characteristic pathologic findings are as follows: (1) decreased number of pulmonary capillaries per airway unit; (2) failure of fusion of individual capillaries with type I pneumocytes; and (3) central localization of capillaries in alveolar septae. Demonstration of decreased number of air-blood barriers or decreased numbers of type I pneumocytes is a much more reliable method in the assessment of ACD pathology than finding misaligned pulmonary veins, because they may or may not present in ACD and are, therefore, not considered essential in this disorder.

Given the experimental system of the authors, which clearly requires manipulation of main pulmonary arteries and airways, it is tempting to speculate that the presence of large, thin-walled channels on Figure 4g of their article may not be veins, but dilated lymphatics. In our pediatric pathology practice, dilated lymphatic channels within the pulmonary broncho-arterial units are commonly present in lung specimens of neonates requiring mechanical ventilation. Using a novel antibody, D2–40, with high specificity and modest sensitivity to lymphatic endothelium is a possible technique that could clarify this issue.

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