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| **Dysregulated lymphatic vasculature accompanies impaired lung development in bronchopulmonary dysplasia** |
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| **Introduction/Aim:** Bronchopulmonary dysplasia (BPD) is a severe neonatal lung disease characterized by impaired lung maturation, disrupted microvasculature and inflammation. Whereas impaired pulmonary angiogenesis has been implicated in BPD, the role of the lymphatics, which coregulate fluid balance and leukocyte trafficking, is poorly understood.**Methods:** A neonatal hyperoxic BPD model was used to probe the effect of hyperoxia on pulmonary oedema and developmental impairment. The expression of several key developmental genes was assessed by real-time quantitative PCR, histopathology was used to assess lung structure, airspace size was quantitated by mean linear intercept, and immunofluorescence imaging was used to stain for blood and lymphatic vascular structures. VEGF-D-deficient mice were used to probe the role of VEGF-D in response to hyperoxia and the role of VEGF-D in pulmonary lymphangiogenesis.**Results:** The gene encoding the lymphatic transcription factor Prox1 was markedly upregulated alongside reduced levels of vascular endothelial growth factor-C (VEGF-C), a lymphangiogenic factor that is essential for lung lymphatic development. However, VEGF-D, a related factor thought to be redundant to VEGF-C, was markedly increased. VEGF-D-/- mice exposed to hyperoxia developed exacerbated fluid accumulation in airspaces and alveolar airspace enlargement, and further impaired respiratory function. Hyperoxia induced a disorganized lymphatic vasculature in VEGF-D-/- mice, with a significant increase in dilated small lymphatics associated with upregulation of inflammation. In normoxic conditions, adult VEGF-D-/- mice exhibited alveolar abnormalities resembling emphysema**Conclusion:** These data indicate that disordered growth of the lymphatic vasculature occurs in BPD and that precise regulation of VEGF-D expression is critical in this response as well as in normal lung development.**Grant Support:** This work was supported by NHMRC Project Grant 1141208**Keywords:** Bronchopulmonary dysplasia, neonatal lung disease, pulmonary oedema, lymphatic vasculature, inflammation.  **Grant Support:**  |