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Angiogenesis and Lymphangiogenesis in Mouse Airways

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Changes in the blood and lymphatic vasculature contribute to many biological processes such development and pathological conditions including inflammation and cancer. Therefore, it is useful to have in vivo experimental preclinical models where blood vessels and lymphatics can be easily examined and subtle changes in them can be observed. The mouse trachea presents an ideal stage where these vascular actors can play very different roles depending on their developmental age, environment, and stimuli acting on them.

Tracheas of pathogen-free adult mice have a stereotyped two-dimensional network of blood vessels and lymphatics. Individual arterioles, capillary, venules and accompanying pericytes and smooth muscle cells can all be recognized (1). In newborn mice, the vascular network is much more primitive in appearance (2). It is rapidly remodeled over the first few postnatal days into the hierarchical adult network. The changes involve vascular regression followed by angiogenesis and are driven by changes in hypoxia and mechanical forces. Transgenic over-expression of VEGF-A in epithelial cells of the adult mouse trachea induces the rapid growth of blood vessels by angiogenic sprouting, but no lymphangiogenesis (3). The newly formed blood vessels also rapidly regress when the stimulus is turned off. In contrast, chronic inflammation as a result of airway bacterial infection with *Mycoplasma pulmonis* induces more complex responses from blood vessels and lymphatics, probably resulting from the concurrent influx of leukocytes and induction of multiple inflammatory genes (4, 5). An early change is vascular remodeling by lateral enlargement, whereby small capillaries gradually transform into venules capable of supporting leukocyte adhesion and plasma extravasation (4, 5). At later stages, small blood vessels grow by angiogenic sprouting. Lymphatics also grow by sprouting, driven by VEGFR-3 signaling (5). A surprising feature of the newly formed lymphatics is their persistence when the stimulus that originally induced them has been removed (5, 6). We conclude that the blood vessels and lymphatics of mouse trachea display an extraordinary plasticity of response and are an excellent system for studying vascular biology.

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