
Mesodermal Pten inactivation leads to alveolar capillary dysplasia-like phenotype.

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Public Summary:

Alveolar capillary dysplasia (ACD) is a congenital, lethal disorder of the pulmonary vasculature. Phosphatase and tensin homologue deleted from chromosome 10 (Pten) encodes a lipid phosphatase controlling key cellular functions, including stem/progenitor cell proliferation and differentiation; however, the role of PTEN in mesodermal lung cell lineage formation remains unexamined. To determine the role of mesodermal PTEN in the ontogeny of various mesenchymal cell lineages during lung development, we specifically deleted Pten in early embryonic lung mesenchyme in mice. Pups lacking Pten died at birth, with evidence of failure in blood oxygenation. Analysis at the cellular level showed defects in angioblast differentiation to endothelial cells and an accompanying accumulation of the angioblast cell population that was associated with disorganized capillary beds. We also found decreased expression of Forkhead box protein F1 (Foxf1), a gene associated with the ACD human phenotype. Analysis of human samples for ACD revealed a significant decrease in PTEN and increased activated protein kinase B (AKT). These studies demonstrate that mesodermal PTEN has a key role in controlling the amplification of angioblasts as well as their differentiation into endothelial cells, thereby directing the establishment of a functional gas exchange interface. Additionally, these mice could serve as a murine model of ACD.

Scientific Abstract:

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