ATS 2024 Highlights

Respiratory Structure and Function Early Career Professionals

Ke Cao, PhD

Post Doc Fellow
Division of Pulmonary, Critical Care and Sleep Medicine
College of Medicine
University of Cincinnati
caoke@ucmail.uc.edu

Get to know members of the RSF Assembly

Is your research clinical, basic science or translational?

Basic science.

Tell us about your research?

Currently, my research primarily focuses on lung development and pulmonary diseases, particularly the mechanisms by which mesenchymal progenitor/stem cells contribute to the pathogenesis of cystic lung diseases including congenital pulmonary airway malformation and Birt-Hogg-Dubé syndrome. Additionally, I am also studying lung injury and repair, such as pulmonary fibrosis.

Where do you see yourself in 5 years?

In five years, I hope to achieve significant breakthroughs in understanding the roles of mesenchymal stem cells in lung development and injury repair, as well as respiratory diseases. Hopefully, I will publish high impact papers, obtain my own research funding, and develop my independent academic career.

What do you find is the major benefit of RSF Assembly Membership?

The major benefit is taking advantage of the resources provided to learn and collaborate with peers.

ATS

Please follow us on LinkedIn and X @ATS_RSF

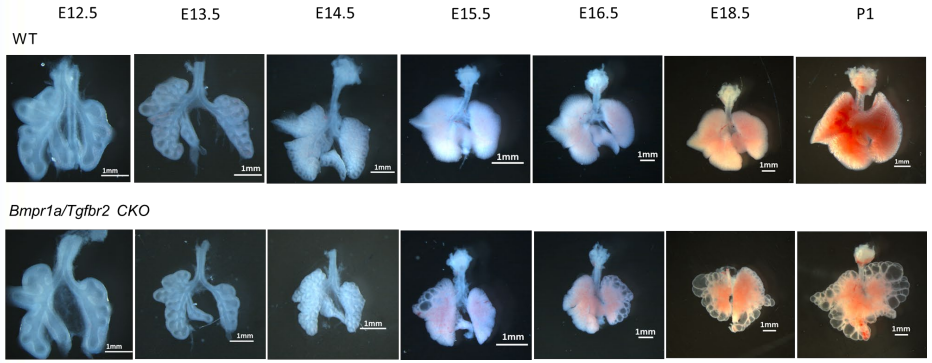
If you or someone you know would like to be featured as an ATS RSF ECP please email Carolyn Wang (carolyn.wang@hli.ubc.ca)

ATS 2024 Highlights

Respiratory Structure and Function Early Career Professionals

Ke Cao, PhD

Post Doc Fellow
Division of Pulmonary, Critical Care and Sleep Medicine,
College of Medicine
University of Cincinnati



Brightfield images of whole WT and Bmpr1a/Tgfbr2 CKO mouse lungs at different embryonic stages

Disruption Of Both BMP and TGF-β Signaling in Fetal Lung Mesenchyme Has Additive Effects on Developing Congenital Pulmonary Cysts

Objective: Congenital pulmonary cysts result from abnormal fetal lung development, particularly defective branching morphogenesis and saccular formation. Our previous studies find that mesenchymal BMP or TGF-β signaling is essential for normal fetal lung airway branching and abrogation of the related pathway results in congenital pulmonary cysts in mice. We also detected alterations of different Smad-independent pathways in the cystic lungs with mesenchymal deletion of BMP receptor versus TGF- β receptors. Our current study is to determine whether blockade of mesenchymal BMP and TGF-β signaling causes congenital lung cysts through different downstream pathways in vivo.

Methods: Lung mesenchyme-specific Bmpr1a and Tgfbr2 double knockout (DKO) mice were generated by crossing Tbx4-rtTA/TetO-Cre driver with floxed-Bmpr1a and floxed-Tgfbr2 mice. The gene deletions were induced by giving the dam doxycycline starting from embryonic day (E) 6.5. Lung tissues were harvested at various embryonic stages (including E12.5, E13.5, E14.5, W15.5, E16.5, E18.5, and P1) and examined by morphology and immunohistochemistry. The cystic lesions and the related molecular and cellular changes are compared between the Bmpr1a/Tgfbr2 DKO and the related single KO lungs.

Results: The Bmpr1a/Tgfbr2 DKO mice died at P1. Severe lung cysts with 100% of phenotypic penetrance were detected. Reduced epithelial branching and enlarged branching tips were observed as early as E13.5 in the Bmpr1a/Tgfbr2 DKO mice, which further developed into airway cysts at E15.5. In addition, tracheomalacia with defective cartilage ring formation was also detected. Immunofluorescent staining analysis revealed defective airway smooth muscle formation and subepithelial elastin production, as well as reduction of epithelial cells that express CC10 and β-tubulin IV in Bmpr1a/Tgfbr2 DKO lung at P1. Such phenotypic changes are more severe than those with the single knockout of either Bmpr1a or Tgfbr2.

Conclusion: Mesenchymal BMP and TGF-β signaling regulates fetal lung airway development through distinct downstream pathways. Abrogation of both pathways simultaneously has additive effects on developing congenital lung cystic lesions.

ATS

Please follow us on LinkedIn and X @ATS_RSF

If you or someone you know would like to be featured as an ATS RSF ECP please email Carolyn Wang (carolyn.wang@hli.ubc.ca)