Stanford

Cristina M. Alvira

Associate Professor of Pediatrics (Critical Care) at the Stanford University Medical Center

Pediatrics - Critical Care

NIH Biosketch available Online

Curriculum Vitae available Online

CLINICAL OFFICES

- **Pediatric Intensive Care**

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  Palo Alto, CA 94304

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ACADEMIC CONTACT INFORMATION

- **Administrative Contact**

  Lisa Higdon - Administrative Associate

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Bio

BIO

Dr. Alvira completed her medical degree at Tufts University, and then came to Stanford University School of Medicine to complete both her pediatric residency and her clinical fellowship in pediatric critical care medicine. After fellowship, Dr. Alvira pursued postdoctoral fellowship training with Dr. Marlene Rabinovitch, a preeminent vascular biologist. Dr. Alvira was recruited to Stanford School of Medicine in the University Tenure Line in 2010, and currently runs an NIH-funded basic research program aimed at identifying novel mechanisms that direct lung growth and repair in infants and children. Dr. Alvira is currently a Stanford Child Health Research Institute John and Tashia Morgridge Faculty Scholar in Pediatric Translational Medicine.

CLINICAL FOCUS

- Intensive Care, Pediatric
- Pediatric Critical Care Medicine

ACADEMIC APPOINTMENTS

- Associate Professor - Med Center Line, Pediatrics - Critical Care
- Member, Cardiovascular Institute
- Member, Maternal & Child Health Research Institute (MCHRI)

ADMINISTRATIVE APPOINTMENTS

- Member, Society for Pediatric Research, (2012- present)
- Editorial Board, American Journal of Physiology-Lung, Cellular and Molecular Physiology, (2014- present)
- Assistant Fellowship Program Director (Research), Stanford University School of Medicine, (2015- present)

HONORS AND AWARDS

- Member, Alpha Omega Alpha National Honor Society (1998)
- Excellence in Clinical Medicine, Louis Weinstein Prize (1999)
- Travel Award, Western Society for Clinical Investigation (2004)

- Travel Award, Society for Pediatric Research (2004)
- Pediatric Clerkship Honor Roll for Teaching, Lucile Packard Children's Hospital at Stanford (2007)
- Fellow to Faculty Transition Grant, American Heart Association (2008-2013)
- Young Investigator Coaching Program, Society for Pediatric Research (2012)
- Outstanding Junior Investigator Award, American Journal of Physiology-Lung Molecular and Cellular Physiology (2013)
- Tashia and John Morgridge Faculty Scholar in Pediatric Translational Medicine, Stanford Child Health Research Institute (2015-2020)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Member, Society for Pediatric Research (2012 - present)
- Member, American Physiological Society (2016 - present)

PROFESSIONAL EDUCATION

- Medical Education: Tufts University School of Medicine (1999) MA
- Fellowship: Stanford University Pediatric Critical Care Fellowship (2005) CA
- Residency: Stanford University Pediatric Residency (2002) CA
- Internship: Stanford University Pediatric Residency (2000) CA
- Board Certification: Pediatric Critical Care Medicine, American Board of Pediatrics (2006)
- MD, Tufts University , Medicine (1999)
- BS, Tufts University , Biology (1995)

LINKS

- Alvira Lab Website: http://alviralab.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Secondary septation, the process that marks the alveolar phase of lung development,involves the coordinated activities of multiple different cell types within the lung. Secretion of extracellular matrix components, proliferation and migration of myofibroblasts and epithelial cells, and pulmonary capillary angiogenesis, have been identified as key players in this process. However, in contrast to the identification of multiple transcription factors controlling branching morphogenesis during the early stages of lung development, the regulators that control and coordinate the individual components of alveolarization remain unknown. The nuclear factor kappa-B (NFkB) family of transcription factors plays a key role in regulating cell survival, differentiation, and inflammation, however, a role in lung development has not been previously identified. A main focus of our work is to define a novel function for NFkB in regulating postnatal lung development using mouse models and primary cell lines.

Postnatal pulmonary angiogenesis is essential for alveolarization. We have recently demonstrated a high degree of constitutive NFkB signaling in primary pulmonary endothelial cells (PEC) isolated from neonatal mice as compared to those isolated from adult mice. Furthermore, inhibiting constitutive NFkB activity in the neonatal PEC with either pharmacologic inhibitors or RNA interference, blocked PEC survival, decreased proliferation, and impaired in vitro angiogenesis. In this project we are utilizing RNAi to block the individual components of the NFkB pathway, gene expression analysis, and endothelial specific conditional knock-out mice in order to identify novel NFkB mediated targets that are essential for postnatal pulmonary angiogenesis.

In a separate but related project, we are exploring pathways which help to preserve normal lung development in the setting of lung injury. Both local and systemic infections can injure the lung. Clinical and experimental evidence suggests that unique pathways may exist that serve to protect the immature lung from severe

inflammation, and potentially allow for a greater regeneration after injury. Using a murine model of acute respiratory distress syndrome induced by the administration of systemic lipopolysaccharide, we are exploring the molecular mechanisms that serve to protect the lung against injury, and identify how these mechanisms are distinct in immature and mature animals. We believe that the information learned from these studies will be clinically relevant to a broad number of pulmonary diseases including bronchopulmonary dysplasia, asthma, ARDS, and emphysema.

Publications

PUBLICATIONS

- **Aberrant Pulmonary Vascular Growth and Remodeling in Bronchopulmonary Dysplasia.** *Frontiers in medicine*
  Alvira, C. M.
  2016; 3: 21-?

- **The transient receptor potential vanilloid 4 channel modulates uterine tone during pregnancy** *SCIENCE TRANSLATIONAL MEDICINE*
  Ying, L., Becard, M., Lyell, D., Han, X., Shortliffe, L., Husted, C. I., Alvira, C. M., Cornfield, D. N.
  2015; 7 (319)

- **Activation of the nuclear factor-?B pathway during postnatal lung inflammation preserves alveolarization by suppressing macrophage inflammatory protein-2.** *American journal of physiology. Lung cellular and molecular physiology*
  Hou, Y., Liu, M., Husted, C., Chen, C., Thiagarajan, K., Johns, J. L., Rao, S. P., Alvira, C. M.
  2015; 309 (6): L593-604

- **Inhibiting NF-kappa B in the developing lung disrupts angiogenesis and alveolarization** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Iosef, C., Alastalo, T., Hou, Y., Chen, C., Adams, E. S., Lyu, S., Cornfield, D. N., Alvira, C. M.
  2012; 302 (10): L1023-L1036

- **Rho kinase modulates postnatal adaptation of the pulmonary circulation through separate effects on pulmonary artery endothelial and smooth muscle cells** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Alvira, C. M., Sukovich, D. J., Lyu, S., Cornfield, D. N.
  2010; 299 (6): L872-L878

- **Nuclear factor-kappa B activation in neonatal mouse lung protects against lipopolysaccharide-induced inflammation** *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE*
  Alvira, C. M., Abate, A., Yang, G., Dennery, P. a., Rabinovitch, M.
  2007; 175 (8): 805-815

- **beta1 Subunit of the Calcium-Sensitive Potassium Channel Modulates the Pulmonary Vascular Smooth Muscle Cell Response to Hypoxia.** *American journal of physiology. Lung cellular and molecular physiology*
  Barnes, E. A., Lee, L., Barnes, S. L., Brenner, R., Alvira, C. M., Cornfield, D. N.
  2018

- **Developmental Differences in Focal Adhesion Kinase Expression Modulate Pulmonary Endothelial Barrier Function in Response to Inflammation.** *American journal of physiology. Lung cellular and molecular physiology*
  Ying, L., Alvira, C. M., Cornfield, D. N.
  2018

- **TRPV4 Promotes Myometrial Inflammation and Contractility in Preterm Mice Exposed to Low Dose Lipopolysaccharide.**
  Rodriguez, Z., Ying, L., Cornfield, D. N., Alvira, C. M.
  SAGE PUBLICATIONS INC.2018: 190A

- **Distinct roles for I#B kinases alpha and beta in regulating pulmonary endothelial angiogenic function during late lung development** *Distinct roles for I#B kinases alpha and beta in regulating pulmonary endothelial angiogenic function during late lung development*
  Iosef, C., Liu, M., Ying, L., Rao, S., Concepcion, K., Chan, W., Oman, A., Alvira, C. M.
  2018: 1-13

- **Can We Understand the Pathobiology of Bronchopulmonary Dysplasia?** *JOURNAL OF PEDIATRICS*
  Alvira, C. M., Morty, R. E.
  2017; 190: 27–37

- **Long-term miR-29b suppression reduces aneurysm formation in a Marfan mouse model.** *Physiological reports*
  Okamura, H., Emrich, F., Trojan, J., Chiu, P., Dalal, A. R., Arakawa, M., Sato, T., Penov, K., Koyano, T., Pedroza, A., Connolly, A. J., Rabinovitch, M., Alvira, et al
  2017; 5 (8)

- **Developmental Expression of Transforming Growth Factor Beta-Induced Protein in the Alveolar Lung Promotes Nuclear Factor Kappa-B Dependent Pulmonary Endothelial Migration**
  Liu, M., Rao, S. P., Fu, S., Iosef, C., Umbach, G., Alvira, C. M.
  FEDERATION AMER SOC EXP BIOL.2017

- **Micro-RNA 203 Regulates Myometrial Smooth Muscle Cell Expression of the Transient Receptor Vanilloid 4 Channel**
  Ying, L., Barnes, E. A., Rodriguez, S., Alvira, C. M., Cornfield, D. N.
  FEDERATION AMER SOC EXP BIOL.2017

- **Absence of TNF-a enhances inflammatory response in the newborn lung undergoing mechanical ventilation.** *American journal of physiology. Lung cellular and molecular physiology*
  Ehrhardt, H., Pritzke, T., Oak, P., Kossert, M., Biebach, L., Förster, K., Koschlig, M., Alvira, C. M., Hilgendorff, A.
  2016; 310 (10): L909-18

- **Absence of TNF-alpha enhances inflammatory response in the newborn lung undergoing mechanical ventilation** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Ehrhardt, H., Pritzke, T., Oak, P., Kossert, M., Biebach, L., Foerster, K., Koschlig, M., Alvira, C. M., Hilgendorff, A.
  2016; 310 (10): L909-L918

- **A Role for the Transient Receptor Potential Vanilloid 4 Channel in Modulating Uterine Tone During Pregnancy**
  Ying, L., Alvira, C. M., Cornfield, D. N.
  FEDERATION AMER SOC EXP BIOL.2016

- **KCNMB1(-/-) Mice as a Model of Pulmonary Arterial Hypertension**
  Barnes, E., Chen, C., Barnes, S., Kim, F., Lee, L., Alvira, C., Cornfield, D.
  FEDERATION AMER SOC EXP BIOL.2016

- **KCNMB1(-/-) Mice as a Model of Pulmonary Arterial Hypertension**
  Barnes, E., Chen, C., Barnes, S., Kim, F., Lee, L., Alvira, C., Cornfield, D.
  FEDERATION AMER SOC EXP BIOL.2016

- **Loss of PPAR? in endothelial cells leads to impaired angiogenesis.** *Journal of cell science*
  Vattulainen-Collanus, S., Akinrinade, O., Li, M., Koskenvuo, M., Li, C. G., Rao, S. P., de Jesus Perez, V., Yuan, K., Sawada, H., Koskenvuo, J. W., Alvira, C., Rabinovitch, M., Alastalo, et al
  2016; 129 (4): 693-705

- **Loss of PPAR gamma in endothelial cells leads to impaired angiogenesis** *JOURNAL OF CELL SCIENCE*
  Vattulainen-Collanus, S., Akinrinade, O., Li, M., Koskenvuo, M., Li, C. G., Rao, S. P., Perez, V. D., Yuan, K., Sawada, H., Koskenvuo, J. W., Alvira, C., Rabinovitch, M., Alastalo, et al
  2016; 129 (4): 693-705

- **Activation of the nuclear factor-?B pathway during postnatal lung inflammation preserves alveolarization by suppressing macrophage inflammatory protein-2.** *American journal of physiology. Lung cellular and molecular physiology*
  Hou, Y., Liu, M., Husted, C., Chen, C., Thiagarajan, K., Johns, J. L., Rao, S. P., Alvira, C. M.
  2015; 309 (6): L593-604

- **HIF-1 alpha Expression is Decreased and Contractility is Enhanced in PASMC from PAH Patients**
  Barnes, E., Chen, C., Alvira, C., Cornfield, D.
  FEDERATION AMER SOC EXP BIOL.2015

- **Differential Focal Adhesion Kinase (FAK) Expression Accounts for the Developmental Regulation of Pulmonary Artery Endothelial Cell(PAEC) Barrier Function**
  Ying, L., Barnes, E., Alvira, C., Cornfield, D.
  FEDERATION AMER SOC EXP BIOL.2015

- **Pulmonary artery smooth muscle cell endothelin-1 expression modulates the pulmonary vascular response to chronic hypoxia.** *American journal of physiology. Lung cellular and molecular physiology*
  Kim, F. Y., Barnes, E. A., Ying, L., Chen, C., Lee, L., Alvira, C. M., Cornfield, D. N.
  2015; 308 (4): L368-77

- **Pulmonary artery smooth muscle cell endothelin-1 expression modulates the pulmonary vascular response to chronic hypoxia** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Kim, F. Y., Barnes, E. A., Ying, L., Chen, C., Lee, L., Alvira, C. M., Cornfield, D. N.
  2015; 308 (4): L368-L377

- **Enhanced Caspase Activity Contributes to Aortic Wall Remodeling and Early Aneurysm Development in a Murine Model of Marfan Syndrome** *ARTERIOSCLEROSIS THROMBOSIS AND VASCULAR BIOLOGY*
  Emrich, F. C., Okamura, H., Dalal, A. R., Penov, K., Merk, D. R., Raaz, U., Hennigs, J. K., Chin, J. T., Miller, M. O., Pedroza, A. J., Craig, J. K., Koyano, T. K., Blankenberg, et al
  2015; 35 (1): 146-154

- **Disrupted lung development and bronchopulmonary dysplasia: opportunities for lung repair and regeneration.** *Current opinion in pediatrics*
  Baker, C. D., Alvira, C. M.
  2014; 26 (3): 306-314

- **Nuclear factor-kappa-B signaling in lung development and disease: One pathway, numerous functions.** *Birth defects research. Part A, Clinical and molecular teratology*
  Alvira, C. M.
  2014; 100 (3): 202-216

- **Chronic Lung Disease in the Preterm Infant Lessons Learned from Animal Models** *AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY*
  Hilgendorff, A., Reiss, I., Ehrhardt, H., Eickelberg, O., Alvira, C. M.
  2014; 50 (2): 233-245

- **Haemophagocytic lymphohistiocytosis associated with coccidiomycosis.** *BMJ case reports*
  Ramsi, M., Alvira, C., Purohit, P., Cornfield, D.
  2014; 2014

- **Peroxisome Proliferator-Activated Receptor Gamma-Deficiency in Endothelial Cells Leads to Impaired Angiogenesis**
  Vattulainen, S., Koskenvuo, M. M., Li, C., Li, M., Perez, V., Alvira, C., Sawada, H., Koskenvuo, J. W., Rabinovitch, M., Alastalo, T.
  LIPPINCOTT WILLIAMS & WILKINS.2013

- **Apoptosis Participates in Early Aneurysm Development via ECM Remodeling in Marfan Syndrome**
  Emrich, F. C., Okamura, H., Dalal, A. R., Merk, D. R., Raaz, U., Hennigs, J. K., Chin, J. T., Miller, M. O., Blankenberg, F. G., Connolly, A. J., Alvira, C. M., Mohr, F. W., Robbins, et al
  LIPPINCOTT WILLIAMS & WILKINS.2013

- **Hypoxia-inducible factor-1a in pulmonary artery smooth muscle cells lowers vascular tone by decreasing myosin light chain phosphorylation.** *Circulation research*
  Kim, Y., Barnes, E. A., Alvira, C. M., Ying, L., Reddy, S., Cornfield, D. N.
  2013; 112 (9): 1230-1233

- **Hypoxia-inducible factor-1a in pulmonary artery smooth muscle cells lowers vascular tone by decreasing Myosin light chain phosphorylation.** *Circulation research*
  Kim, Y., Barnes, E. A., Alvira, C. M., Ying, L., Reddy, S., Cornfield, D. N.
  2013; 112 (9): 1230-1233

- **Voltage-Dependent Anion Channel-2 Interaction with Nitric Oxide Synthase Enhances Pulmonary Artery Endothelial Cell Nitric Oxide Production** *AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY*
  Alvira, C. M., Umesh, A., Husted, C., Ying, L., Hou, Y., Lyu, S., Nowak, J., Cornfield, D. N.
  2012; 47 (5): 669-678

- **Hypoxia-inducible factor-1 alpha regulates KCNMB1 expression in human pulmonary artery smooth muscle cells** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Ahn, Y., Kim, Y., Adams, E., Lyu, S., Alvira, C. M., Cornfield, D. N.

2012; 302 (3): L352-L359

- **miR-29b Participates in Early Aneurysm Development in Marfan Syndrome** *CIRCULATION RESEARCH*
  Merk, D. R., Chin, J. T., Dake, B. A., Maegdefessel, L., Miller, M. O., Kimura, N., Tsao, P. S., Iosef, C., Berry, G. J., Mohr, F. W., Spin, J. M., Alvira, C. M., Robbins, et al
  2012; 110 (2): 312-?

- **Neutrophil Elastase Is Produced by Pulmonary Artery Smooth Muscle Cells and Is Linked to Neointimal Lesions** *AMERICAN JOURNAL OF PATHOLOGY*
  Kim, Y., Haghighat, L., Spiekerkoetter, E., Sawada, H., Alvira, C. M., Wang, L., Acharya, S., Rodriguez-Colon, G., Orton, A., Zhao, M., Rabinovitch, M.
  2011; 179 (3): 1560-1572

- **Inhibition of Transforming Growth Factor beta Worsens Elastin Degradation in a Murine Model of Kawasaki Disease** *AMERICAN JOURNAL OF PATHOLOGY*
  Alvira, C. M., Guignabert, C., Kim, Y., Chen, C., Wang, L., Duong, T. T., Yeung, R. S., Li, D. Y., Rabinovitch, M.
  2011; 178 (3): 1210-1220

- **Prolonged mechanical ventilation with air induces apoptosis and causes failure of alveolar septation and angiogenesis in lungs of newborn mice** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Mokres, L. M., Parai, K., Hilgendorff, A., Ertsey, R., Alvira, C. M., Rabinovitch, M., Bland, R. D.
  2010; 298 (1): L23-L35

- **Tie2-mediated loss of peroxisome proliferator-activated receptor-gamma in mice causes PDGF receptor-beta-dependent pulmonary arterial muscularization** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Guignabert, C., Alvira, C. M., Alastalo, T., Sawada, H., Hansmann, G., Zhao, M., Wang, L., El-Bizri, N., Rabinovitch, M.
  2009; 297 (6): L1082-L1090

- **Increased expression of transient receptor vanilloid channels during pregnancy regulates uterine smooth muscle cell calcium entry and contraction**
  Becard, M., Lyu, S., Alvira, C., Adams, E., Umesh, A., Cornfield, D.
  MOSBY-ELSEVIER.2009: S251

- **Nuclear Factor Kappa B Mediates Postnatal Alveolarization by Promoting Pulmonary Angiogenesis via Vascular Endothelial Growth Factor Receptor-2 Regulation** *82nd National Conference and Exhibitions and Scientific Sessions of the American-Heart-Association*
  Alvira, C. M., Alastalo, T. P., Chen, C., Lyu, S., Ahn, Y., Cornfield, D. N.
  LIPPINCOTT WILLIAMS & WILKINS.2009: S1090–S1090

- **LC3-mediated fibronectin mRNA translation induces fibrosarcoma growth by increasing connective tissue growth factor** *JOURNAL OF CELL SCIENCE*
  Ying, L., Lau, A., Alvira, C. M., West, R., Cann, G. M., Zhou, B., Kinnear, C., Jan, E., Sarnow, P., van de Rijn, M., Rabinovitch, M.
  2009; 122 (9): 1441-1451

- **Tie2-Mediated Loss of Peroxisome Proliferator-Activated Receptor-gamma in Transgenic Mice Increases Platelet Derived Growth Factor-Receptor beta and Pulmonary Arterial Muscularization** *81st Annual Scientific Session of the American-Heart-Association*
  Guignabert, C., Alvira, C. M., Alastalo, T., Sawada, H., Perrez, V. D., Hansmann, G., Zhao, M., Wang, L., El-Bizri, N., Rabinovitch, M.
  LIPPINCOTT WILLIAMS & WILKINS.2008: S307–S307

- **Transforming Growth Factor Beta Inhibition Increases Matrix Metalloproteinase-9 Activity and Enhances Elastin Degradation in a Murine Model of Kawasaki Disease**
  Alvira, C. M., Kim, Y., Guignabert, C., Wang, L., Rabinovitch, M.
  LIPPINCOTT WILLIAMS & WILKINS.2008: S373

- **An antiproliferative BMP-2/PPAR gamma/apoE axis in human and murine SMCs and its role in pulmonary hypertension** *JOURNAL OF CLINICAL INVESTIGATION*
  Hansmann, G., de Jesus Perez, V. A., Alastalo, T., Alvira, C. M., Guignabert, C., Bekker, J. M., Schellong, S., Urashima, T., Wang, L., Morrell, N. W., Rabinovitch, M.
  2008; 118 (5): 1846-1857

- **Reactivation of gamma HV68 induces neointimal lesions in pulmonary arteries of S100A4/Mts1-overexpressing mice in association with degradation of elastin** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Spiekerkoetter, E., Alvira, C. M., Kim, Y., Bruneau, A., Pricola, K. L., Wang, L., Ambartsumian, N., Rabinovitch, M.
  2008; 294 (2): L276-L289

- **Mechanical ventilation uncouples synthesis and assembly of elastin and increases apoptosis in lungs of newborn mice. Prelude to defective alveolar septation during lung development?** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*

Bland, R. D., Ertsey, R., Mokres, L. M., Xu, L., Jacobson, B. E., Jiang, S., Alvira, C. M., Rabinovitch, M., Shinwell, E. S., Dixit, A.
2008; 294 (1): L3-L14