Stanford

Richard Bland

Professor (Research) of Pediatrics (Neonatology), Emeritus

Pediatrics - Neonatal and Developmental Medicine

CONTACT INFORMATION

- **Alternate Contact**

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Bio

ACADEMIC APPOINTMENTS

- Emeritus Faculty, Acad Council, Pediatrics - Neonatal and Developmental Medicine
- Member, Cardiovascular Institute

HONORS AND AWARDS

- Honorary Doctor of Medicine, University of Uppsala, Sweden (2004)
- Distinguished Alumnus Award, Boston University School of Medicine (1996)
- Established Investigator, American Heart Association (1979-1984)
- Ogden C Bruton Award, Uniformed Services (1972, 1973)

PROFESSIONAL EDUCATION

- BA, Yale University , Social Sciences (1962)
- MD, Boston University , Medicine (1966)

LINKS

- Rabinovitch/Bland Lab: http://med.stanford.edu/labs/rabinovitchbland/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our research program focuses on lung growth and development, and the adverse impact of prolonged mechanical ventilation on the incompletely formed lung, which in very premature infants often leads to a life-threatening condition that was first described as bronchopulmonary dysplasia (Northway WH Jr et al, Stanford University, New Engl J Med 276: 357-368, 1967). This form of neonatal chronic lung disease is the leading cause of long-term hospitalization and recurrent respiratory disorders seen in tiny infants who have been born at less than 28 weeks of gestation. Failed alveolar formation and excess, disordered lung elastin are prominent histological features of this disease, which in some ways resembles adult emphysema. We study the effects of mechanical ventilation, with either air or 40% O2, on genes and proteins that regulate lung growth and development in newborn mice, whose alveoli and pulmonary capillaries form mainly after birth at term gestation. As elastin

plays a crucial role in lung growth and development (elastin-null mice die soon after birth from cardiorespiratory failure related to defective alveolar and lung vascular formation), we are especially interested in studying the effects of prolonged mechanical ventilation (cyclic lung stretch) with O2-rich gas (which is often needed to sustain life of extremely premature infants) on genes that regulate elastin synthesis and assembly, which in turn can affect lung septation and angiogenesis. We currently study the effects of lengthy mechanical ventilation on lungs of mutant newborn mice that have defects in elastin assembly and associated abnormalities of lung structure. Because mechanical ventilation of the developing lung can induce the release of proteolytic enzymes that break down elastin, we recently began to study the effects of mechanical ventilation with O2-rich gas in a transgenic mouse that over-expresses elafin, a potent inhibitor of serine elastase activity. We think that these studies will pave the way for novel and effective strategies to treat or prevent neonatal chronic lung disease, and perhaps other respiratory disorders that exhibit similar pathological features in older children and adults.

Publications

PUBLICATIONS

- **Elafin Treatment Rescues EGFR-Klf4 Signaling and Lung Cell Survival in Ventilated Newborn Mice.** *American journal of respiratory cell and molecular biology*
  Alejandre Alcazar, M. A., Kaschwich, M., Ertsey, R., Preuss, S., Milla, C., Mujahid, S., Masumi, J., Khan, S., Mokres, L. M., Tian, L., Mohr, J., Hirani, D. V., Rabinovitch, et al
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- **Elafin Treatment Rescues EGFR-Klf4 Signaling and Lung Cell Survival in Ventilated Newborn Mice** *AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY*
  Alcazar, M., Kaschwich, M., Ertsey, R., Preuss, S., Milla, C., Mujahid, S., Masumi, J., Khan, S., Mokres, L. M., Tian, L., Mohr, J., Hirani, D., Rabinovitch, et al
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- **Elafin Reverses Pulmonary Hypertension via Caveolin-1-Dependent Bone Morphogenetic Protein Signaling** *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE*
  Nickel, N. P., Spiekerkoetter, E., Gu, M., Li, C. G., Li, H., Kaschwich, M., Diebold, I., Hennigs, J. K., Kim, K., Miyagawa, K., Wang, L., Cao, A., Sa, et al
  2015; 191 (11): 1273-1286

- **Lung matrix and vascular remodeling in mechanically ventilated elastin haploinsufficient newborn mice.** *American journal of physiology. Lung cellular and molecular physiology*
  Hilgendorff, A., Parai, K., Ertsey, R., Navarro, E., Jain, N., Carandang, F., Peterson, J., Mokres, L., Milla, C., Preuss, S., Alcazar, M. A., Khan, S., Masumi, et al
  2015; 308 (5): L464-78

- **Neonatal mice genetically modified to express the elastase inhibitor elafin are protected against the adverse effects of mechanical ventilation on lung growth** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Hilgendorff, A., Parai, K., Ertsey, R., Rey-Parra, G. J., Thebaud, B., Tamosiuniene, R., Jain, N., Navarro, E. F., Starcher, B. C., Nicolls, M. R., Rabinovitch, M., Bland, R. D.
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- **Inhibiting Lung Elastase Activity Enables Lung Growth in Mechanically Ventilated Newborn Mice** *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE*
  Hilgendorff, A., Parai, K., Ertsey, R., Jain, N., Navarro, E. F., Peterson, J. L., Tamosiuniene, R., Nicolls, M. R., Starcher, B. C., Rabinovitch, M., Bland, R. D.
  2011; 184 (5): 537-546

- **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

- **Mechanical ventilation uncouples synthesis and assembly of elastin and increases apoptosis in lungs of newborn mice** *Am J Physiol Lung Cell Mol Physiol*
  Bland, R., Ertsey R, Mokres LM, Xu L, Jacobson BE, Jiang S, Alvira CM, Rabinovitch M, Shinwell ES, Dixit A
  2008; 294 (1): L3-L14

- **Mechanical ventilation with 40% oxygen reduces pulmonary expression of genes that regulate lung development and impairs alveolar septation in newborn mice** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Bland, R. D., Mokres, L. M., Ertsey, R., Jacobson, B. E., Jiang, S., Rabinovitch, M., Xu, L., Shinwell, E. S., Zhang, F., Beasley, M. A.

2007; 293 (5): L1099-L1110

- **Dysregulation of pulmonary elastin synthesis and assembly in preterm lambs with chronic lung disease** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Bland, R. D., Xu, L., Ertsey, R., Rabinovitch, M., Albertine, K. H., Wynn, K. A., Kumar, V. H., Ryan, R. M., Swartz, D. D., Csiszar, K., Fong, K. S.
  2007; 292 (6): L1370-L1384

- **Neonatal chronic lung disease in the post-surfactant era - Lessons learned from authentic animal models** *International Symposium on Recent Advances in Neonatal Medicine*
  Bland, R. D.
  KARGER.2005: 181–91

- **Inhaled nitric oxide effects on lung structure and function in chronically ventilated preterm lambs** *Am J Respir Crit Care Med*
  Bland RD, Albertine KH, Carlton DP, MacRitchie AN
  2005; 172 (7): 899-906

- **Pulmonary vascular dysfunction in preterm lambs with chronic lung disease** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Bland, R. D., Ling, C. Y., Albertine, K. H., Carlton, D. P., MacRitchie, A. J., Day, R. W., Dahl, M. J.
  2003; 285 (1): L76-L85

- **Reduced endothelial nitric oxide synthase in lungs of chronically ventilated preterm lambs** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
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- **Chronic lung injury in preterm lambs - Disordered respiratory tract development** *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE*
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- **Chronic lung injury in preterm lambs: Disordered pulmonary elastin deposition** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Pierce, R. A., Albertine, K. H., Starcher, B. C., Bohnsack, J. F., Carlton, D. P., Bland, R. D.
  1997; 272 (3): L452-L460

- **Severe Pulmonary Arterial Hypertension is Characterized by Increased Neutrophil Elastase and Relative Elafin Deficiency.** *Chest*
  Sweatt, A. J., Miyagawa, K., Rhodes, C. J., Taylor, S., Del Rosario, P. A., Hsi, A., Haddad, F., Spiekerkoetter, E., Bental-Roof, M., Bland, R. D., Swietlik, E. M., Gräf, S., Wilkins, et al
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- **Lung matrix and vascular remodeling in mechanically ventilated elastin haploinsufficient newborn mice.** *American journal of physiology. Lung cellular and molecular physiology*
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- **Elafin Preserves A Novel Egf Receptor-Kruppel-Like Factor 4 (EGFR-Klf4) Axis And Attenuates Apoptosis In Lungs Of Mechanically Ventilated Newborn Mice**
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- **Gunnar Sedin OBITUARY** *ACTA PAEDIATRICA*
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- **Tgf beta Blockade Preserves Vascular Endothelial Growth Factor (VEGF) Signaling And Enables Alveolar Formation In Mechanically Ventilated Newborn Mice**
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AMER THORACIC SOC.2014

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- **Chronic lung disease in preterm lambs: effect of daily vitamin A treatment on alveolarization** *AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY*
  Albertine, K. H., Dahl, M. J., Gonzales, L. W., Wang, Z., Metcalfe, D., Hyde, D. M., Plopper, C. G., Starcher, B. C., Carlton, D. P., Bland, R. D.
  2010; 299 (1): L59-L72

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- **ADVERSE EFFECTS OF MECHANICAL VENTILATION (MV) ARE BLUNTED IN TRANSGENIC NEWBORN MICE THAT OVER-EXPRESS THE SERINE ELASTASE INHIBITOR ELAFIN**
  Hilgendorff, A., Parai, K., Ertsey, R., Mokres, L., Rey-Parra, J., Thebaud, B., Jain, N., Navarro, E., RABINOVITCH, M., Bland, R.
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- **VENTILATION WITH EITHER AIR OR 40%-O-2 INDUCES APOPTOSIS AND CAUSES FAILURE OF ALVEOLAR SEPTATION AND PULMONARY ANGIOGENESIS IN NEWBORN MICE**
  Hilgendorff, A., Parai, K., Mokres, L., Ertsey, R., Alvira, C., Bland, R.
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- **Mechanical Ventilation (MV) for 24 Hours Disrupts VEGF Signaling, Induces Apoptosis and Inhibits Formation of Alveoli and Lung Blood Vessels in Newborn Mice.**
  Hilgendorff, A., Parai, K., Mokres, L., Ertsey, R., Alvira, C., Bland, R., Wall Cardiopulm Ctr
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- **Chronic minocycline-induced autoimmunity in children** *JOURNAL OF PEDIATRICS*
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- **Mechanical ventilation (MV) of newborn mice for 24 h leads to reduced VEGF receptor-2 (VEGFR2) and tenascin-C (TNC) proteins, enlarged airspaces and increased lung elastin (Eln)** *Experimental Biology 2006 Annual Meeting*
  Bland, R., Jacobson, B., Ertsey, R., Mokres, L., Jiang, S., Xu, L. W., Dixit, A.
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- **Altered expression of key growth factors (TGF alpha, TGF beta 1, PDGF-A) and flawed formation of alveoli and elastin (Eln) in lungs of preterm (PT) lambs with chronic lung disease (CLD)** *Experimental Biology 2006 Annual Meeting*
  Xu, L. W., RABINOVITCH, M., Bland, R.
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- **Neonatal chronic lung disease in the post-surfactant era.** *Biology of the neonate*
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  2005; 88 (3): 181-91

- **Increased expression of genes associated with elastin synthesis and assembly in lungs of mechanically ventilated preterm lambs compared to term lambs** *Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences*
  Bland, R. D., Xu, L. W., RABINOVITCH, M., Kumar, V., Ryan, R. M., Wynn, K.
  FEDERATION AMER SOC EXP BIOL.2005: A1603–A1603

- **Mechanical ventilation of newborn mice: impact on genes that regulate lung development**
  Jacobson, B., Ertsey, R., Bland, R.

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- **Effects of mechanical ventilation on genes that regulate lung development in newborn mice.**
  Jacobson, B., Bland, R.
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- **Neonatal chronic lung disease (CLD) in terms vs. preterm lambs: Differing paradigms of lung injury and repair** *Annual Meeting of the Pediatric-Academic-Societies*
  Bland, R., Xu, L., Kolansky, S., RABINOVITCH, M., Ryan, R., Kumar, V., Wynn, K., Swart, D., Albertine, K., Duhl, M., Williams, M.
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- **Impaired alveolar development and abnormal lung elastin in preterm lambs with chronic lung injury: Potential benefits of retinol treatment** *18th Annual International Workshop on Surfactant Replacement*
  Bland, R. D., Albertine, K. H., Pierce, R. A., Starcher, B. C., Carlton, D. P.
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- **Novel notions on newborn lung disease** *NATURE MEDICINE*
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- **Altered vascular development in preterm lambs with chronic lung injury** *Thomas L Petty 40th Annual Aspen Lung Conference on Biology and Pathobiology of the Lung Circulation*
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- **SURFACTANT TREATMENT AT BIRTH REDUCES LUNG VASCULAR INJURY AND EDEMA IN PRETERM LAMBS** *PEDIATRIC RESEARCH*
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