




## Edda Spiekerkoetter

Assistant Professor of Medicine (Pulmonary and Critical Care Medicine)

Medicine - Pulmonary & Critical Care Medicine

 Resume available Online

### CLINICAL OFFICES

- **Critical Care Medicine**

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Stanford, CA 94305

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### Bio

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### CLINICAL FOCUS

- Pulmonary Hypertension
- Vasoreactivity in pulmonary hypertension as a marker of vascular remodeling
- Biomarkers
- Clinical Trial, Phase II
- Pulmonary Disease

### ACADEMIC APPOINTMENTS

- Assistant Professor, Medicine - Pulmonary & Critical Care Medicine
- Member, Bio-X
- Member, Cardiovascular Institute

### HONORS AND AWARDS

- K08 Career development award, NIH (2011-2016)
- Postdoctoral Research Fellowship, Pulmonary Hypertension Association (2003-2005)
- Supplemental award of the Pulmonary Hypertension Association (PHA), Pulmonary Hypertension Association (2011 - 2016)
- Winner of Poster competition, Cardiovascular Institute Stanford (Sept 2012)
- Seed Grant - Small Molecule High Throughout Screen, Wall Center of Pulmonary Vascular Disease (2012)
- Seed Grant - Phase II Clinical Trial, SPARK and Spectrum Stanford (2012-2014)
- Seed Grant - Phase II Clinical Trial, Wall Center of Pulmonary Vascular Disease (2012-2014)
- Seed Grant- BMP signaling in the RV, Cardiovascular Institute Stanford (2013-2014)
- Helmholtz International Research Group Award, Helmholtz Zentrum Muenchen, Germany (2013-2016)
- Poster Award, Excellence Cluster Cardio-Pulmonary System (ECCPS) and Pulmonary Vascular Research Institute (PVRI) (Jan 2014)

- Manuscript Award, Cardiovascular Institute at Stanford (Feb 2014)
- Young Physician Scientist Award, American Society of Clinical Investigation (April 2015)

## **BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS**

- Pulmonary Circulation Program Committee, American Thoracic Society (2013 - present)
- Member at large, European Respiratory Society (2000 - present)
- Member at large, American Thoracic Society (1998 - present)

## **PROFESSIONAL EDUCATION**

- Fellowship: Stanford Medicine Pulmonary and Critical Care Fellowship (2009) CA
- Fellowship: Stanford University (2008) CA
- Fellowship: Lucile Packard Children's Hospital (2006) CA
- Residency: Medizinische Hochschule Hannover (2002) Germany
- Medical Education: University Hospital Freiburg (1995) Germany

## **PATENTS**

- Edda Spiekerkoetter. "United States Patent 61481317 Low-Dose FK506 for the treatment of Pulmonary Arterial Hypertension", Leland Stanford Junior University

## **LINKS**

- My Lab site: <http://med.stanford.edu/spiekerkoetterlab.html>

## **Research & Scholarship**

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### **CURRENT RESEARCH AND SCHOLARLY INTERESTS**

My research focuses on the importance of the Bone Morphogenetic Protein Receptor 2 (BMPR2) signaling pathway in pulmonary, pulmonary-vascular as well as cardiac disease.

In 2000 two independent groups discovered mutations in the BMPR2 pathway as the genetic basis for pulmonary arterial hypertension (PAH). Over the past years more mutations either directly involved in the BMPR2 pathway (Endoglin, ALK1, Smad9) or indirectly linked to the BMPR2 pathway (Caveolin-1) have been discovered, emphasizing the central role of BMPR2 signaling in familial PAH. It was subsequently found that reduced BMPR2 expression and signaling seems to be a feature of other sporadic or idiopathic forms of PAH.

Hypothesizing that increasing BMPR2 signaling might improve PAH, we have performed a High-Throughput Screen of FDA approved drugs to find BMPR2 activators and have identified the immuno-suppressive drug FK506 (Tacrolimus) as the main activator.

We have subsequently shown that FK506 could rescue endothelial dysfunction in PAH, and prevent and reverse PAH in rodent models of experimental PAH (Spiekerkoetter JCI 2013).

This discovery has led to the initiation of a phase II clinical trial to test the safety, tolerability and efficacy of low-dose FK506 in PAH at Stanford (<http://www.clinicaltrials.gov> NCT01647945)

My current research focuses on :

1. Novel ways how to modulate BMPR2 signaling (small molecule HTS screen, identifying novel modifier genes)

2. Evaluating the importance of BMP2 signaling in the development of Right Ventricular Hypertrophy (RVH) and failure, which is the leading cause of death in PAH (Collaboration with Dres Sushma Reddy and Daniel Bernstein, Pediatric Cardiology, Stanford).
3. Evaluating the importance of BMP2 signaling in vascular development in neonatal chronic lung disease (Collaboration with Dr. Anne Hilgendorff, Helmholtz Institute, Muenchen, Germany).

## CLINICAL TRIALS

- FK506 (Tacrolimus) in Pulmonary Arterial Hypertension, Recruiting

## Teaching

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### COURSES

#### 2017-18

- Applying Modern Techniques to Old Diseases: BIOS 269 (Win)

### STANFORD ADVISEES

#### Postdoctoral Faculty Sponsor

Mario Boehm

#### Postdoctoral Research Mentor

Mario Boehm

## Publications

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### PUBLICATIONS

- **RNA Sequencing Analysis Detection of a Novel Pathway of Endothelial Dysfunction in Pulmonary Arterial Hypertension** *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE*  
Rhodes, C. J., Im, H., Cao, A., Hennigs, J. K., Wang, L., Sa, S., Chen, P., Nickel, N. P., Miyagawa, K., Hopper, R. K., Tojais, N. F., Li, C. G., Gu, et al  
2015; 192 (3): 356-366
- **Low-Dose FK506 (Tacrolimus) in End-Stage Pulmonary Arterial Hypertension.** *American journal of respiratory and critical care medicine*  
Spiekerkoetter, E., Sung, Y. K., Sudheendra, D., Bill, M., Aldred, M. A., van de Veerdonk, M. C., Vonk Noordegraaf, A., Long-Boyle, J., Dash, R., Yang, P. C., Lawrie, A., Swift, A. J., Rabinovitch, et al  
2015; 192 (2): 254-257
- **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
- **Hedgehog Signaling Restrains Bladder Cancer Progression by Eliciting Stromal Production of Urothelial Differentiation Factors** *CANCER CELL*  
Shin, K., Lim, A., Zhao, C., Sahoo, D., Pan, Y., Spiekerkoetter, E., Liao, J. C., Beachy, P. A.  
2014; 26 (4): 521-533
- **Targeting the Wnt signaling pathways in pulmonary arterial hypertension.** *Drug discovery today*  
de Jesus Perez, V., Yuan, K., Alastalo, T., Spiekerkoetter, E., Rabinovitch, M.  
2014; 19 (8): 1270-1276
- **Current Clinical Management of Pulmonary Arterial Hypertension** *CIRCULATION RESEARCH*  
Zamanian, R. T., Kudelko, K. T., Sung, Y. K., Perez, V. D., Liu, J., Spiekerkoetter, E.  
2014; 115 (1): 131-147
- **Reduced BMP2 expression induces GM-CSF translation and macrophage recruitment in humans and mice to exacerbate pulmonary hypertension.** *journal of experimental medicine*  
Sawada, H., Saito, T., Nickel, N. P., Alastalo, T., Glotzbach, J. P., Chan, R., Haghighat, L., Fuchs, G., Januszzyk, M., Cao, A., Lai, Y., Perez, V. d., Kim, et al

2014; 211 (2): 263-280

- **FK506 activates BMPR2, rescues endothelial dysfunction, and reverses pulmonary hypertension.** *journal of clinical investigation*  
Spiekerkoetter, E., Tian, X., Cai, J., Hopper, R. K., Sudheendra, D., Li, C. G., El-Bizri, N., Sawada, H., Haghghat, R., Chan, R., Haghghat, L., de Jesus Perez, V., Wang, et al  
2013; 123 (8): 3600-3613
- **A case of recurrent pericardial constriction presenting with severe pulmonary hypertension.** *Pulmonary circulation*  
Brunner, N. W., Ramachandran, K., Kudelko, K. T., Sung, Y. K., Spiekerkoetter, E., Yang, P. C., Zamanian, R. T., Perez, V. d.  
2013; 3 (2): 436-439
- **Loss of adenomatous polyposis coli-a3 integrin interaction promotes endothelial apoptosis in mice and humans.** *Circulation research*  
de Jesus Perez, V. A., Yuan, K., Orcholski, M. E., Sawada, H., Zhao, M., Li, C. G., Tojais, N. F., Nickel, N., Rajagopalan, V., Spiekerkoetter, E., Wang, L., Dutta, R., Bernstein, et al  
2012; 111 (12): 1551-1564
- **Safety and efficacy of transition from systemic prostanoids to inhaled treprostinil in pulmonary arterial hypertension.** *American journal of cardiology*  
de Jesus Perez, V. A., Rosenzweig, E., Rubin, L. J., Poch, D., Bajwa, A., Park, M., Jain, M., Bourge, R. C., Kudelko, K., Spiekerkoetter, E., Liu, J., Hsi, A., Zamanian, et al  
2012; 110 (10): 1546-1550
- **Neutrophil Elastase Is Produced by Pulmonary Artery Smooth Muscle Cells and Is Linked to Neointimal Lesions** *AMERICAN JOURNAL OF PATHOLOGY*  
Kim, Y., Haghghat, 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
- **BMP promotes motility and represses growth of smooth muscle cells by activation of tandem Wnt pathways** *JOURNAL OF CELL BIOLOGY*  
Perez, V. A., Ali, Z., Alastalo, T., Ikeno, F., Sawada, H., Lai, Y., Kleisli, T., Spiekerkoetter, E., Qu, X., Rubinos, L. H., Ashley, E., Amieva, M., Dedhar, et al  
2011; 192 (1): 171-188
- **S100A4 and Bone Morphogenetic Protein-2 Codependently Induce Vascular Smooth Muscle Cell Migration via Phospho-Extracellular Signal-Regulated Kinase and Chloride Intracellular Channel 4** *CIRCULATION RESEARCH*  
Spiekerkoetter, E., Guignabert, C., Perez, V. D., Alastalo, T., Powers, J. M., Wang, L., Lawrie, A., Ambartsumian, N., Schmidt, A., Berryman, M., Ashley, R. H., Rabinovitch, M.  
2009; 105 (7): 639-U37
- **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
- **Experience with inhaled iloprost and bosentan in portopulmonary hypertension** *EUROPEAN RESPIRATORY JOURNAL*  
Hoepfer, M. M., Seyfarth, H. J., Hoefflken, G., Wirtz, H., Spiekerkoetter, E., Pletz, M. W., Welte, T., Halank, M.  
2007; 30 (6): 1096-1102
- **Mts1/S100A4 stimulates human pulmonary artery smooth muscle cell migration through multiple signaling pathways** *47th Annual Thomas L Petty Aspen Lung Conference*  
Spiekerkoetter, E., Lawrie, A., Merklinger, S., Ambartsumian, N., Lukanidin, D., Schmidt, A. A., Rabinovitch, M.  
AMER COLL CHEST PHYSICIANS.2005: 577S-577S
- **Goal-oriented treatment and combination therapy for pulmonary arterial hypertension** *EUROPEAN RESPIRATORY JOURNAL*  
Hoepfer, M. M., Markevych, I., Spiekerkoetter, E., Welte, T., Niedermeyer, J.  
2005; 26 (5): 858-863
- **Increased fibulin-5 and elastin in S100A4/Mts1 mice with pulmonary hypertension** *CIRCULATION RESEARCH*  
Merklinger, S. L., Wagner, R. A., Spiekerkoetter, E., Hinek, A., Knutsen, R. H., Kabir, M. G., Desai, K., Hacker, S., Wang, L. L., Cann, G. M., Ambartsumian, N. S., Lukanidin, E., Bernstein, et al  
2005; 97 (6): 596-604
- **Interdependent serotonin transporter and receptor pathways regulate S100A4/Mts1, a gene associated with pulmonary vascular disease** *CIRCULATION RESEARCH*  
Lawrie, A., Spiekerkoetter, E., Martinez, E. C., Ambartsumian, N., Sheward, W. J., MacLean, M. R., Harmar, A. J., Schmidt, A. M., Lukanidin, E., Rabinovitch, M.

2005; 97 (3): 227-235

- **Bosentan treatment in patients with primary pulmonary hypertension receiving nonparenteral prostanoids** *EUROPEAN RESPIRATORY JOURNAL*  
Hoepfer, M. M., Taha, N., Bekjarova, A., Gatzke, R., Spiekerkoetter, E.  
2003; 22 (2): 330-334
- **Effects of inhaled salbutamol in primary pulmonary hypertension** *EUROPEAN RESPIRATORY JOURNAL*  
Spiekerkoetter, E., Fabel, H., Hoepfer, M. M.  
2002; 20 (3): 524-528
- **Intravenous iloprost for treatment failure of aerosolised iloprost in pulmonary arterial hypertension** *EUROPEAN RESPIRATORY JOURNAL*  
Hoepfer, M. M., Spiekerkoetter, E., Westerkamp, V., Gatzke, R., Fabel, H.  
2002; 20 (2): 339-343
- **[Long-term treatment of primary pulmonary hypertension with inhaled iloprost].** *Pneumologie (Stuttgart, Germany)*  
Hoepfer, M. M., Schwarze, M., Ehlerding, S., Adler-Schuermeyer, A., Spiekerkoetter, E., Niedermeyer, J., Hamm, M., Fabel, H.  
2001; 55 (1): 38-43
- **Long-term treatment of primary pulmonary hypertension with aerosolized iloprost, a prostacyclin analogue.** *NEW ENGLAND JOURNAL OF MEDICINE*  
Hoepfer, M. M., Schwarze, M., Ehlerding, S., Adler-Schuermeyer, A., Spiekerkoetter, E., Niedermeyer, J., Hamm, M., Fabel, H.  
2000; 342 (25): 1866-1870
- **Prevalence of malignancies after lung transplantation** *International Congress on Immunosuppression*  
Spiekerkoetter, E., Krug, N., Hoepfer, M., Wiebe, K., Hamm, M., Harringer, W., Haverich, A., Fabel, H.  
ELSEVIER SCIENCE INC.1998: 1523-24