BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Doherty, Taylor Alan**

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, San Diego	B.S.	09/89-06/94	Biochemistry/Cell Bio
California State University, Fullerton	N/A	08/96-05/97	Postbacc/Pre-med
The Chicago Medical School/Rosalind Franklin	M.D.	07/98-06/02	Medicine
University of California, San Diego/La Jolla Institute	N/A	10/06-11/09	Post doctoral fellow allergy immunology

A. Personal Statement

My interest in asthma stems from caring for patients with asthma in inner city Chicago hospitals during medical school. Understanding the mechanisms underlying asthma pathogenesis inspired me to choose Allergy and Immunology as a specialty and has fueled my career as an independent physician scientist. My post-doctoral work at La Jolla Institute (LJI) in Dr. Michael Croft's laboratory led to a novel discovery revealing that TNF family member LIGHT contributes critically to airway remodeling and I first-authored a manuscript published in *Nature Medicine* in 2011. I was promoted to the faculty at UC San Diego as an assistant professor in 2009 and developed into a successful early-stage independent investigator after support from a NIH K08 award. Since becoming faculty in 2009, I have published 27 high quality original research manuscripts in journals that include *Nature Medicine*, *Journal of Experimental Medicine*, *Journal of Allergy and Clinical Immunology*, and *Journal of Immunology*. Our work over the past eight years has led to several novel discoveries including uncovering mechanisms of airway remodeling and Th2 cell responses in chronic asthma models, as well as identifying novel contributions of group 2 innate lymphoid cells (ILC2s) in human disease and mouse models of disease. Importantly, I am currently co-PI of a NIH U19 award and maintain R01 funding to investigate the roles and regulation of ILC2s in airway inflammation. I have expertise in studies of ILC2s, CD4 cells, and airway remodeling utilizing human samples and mouse models. For the current proposal, I am excited to There is no doubt that this work will have a significant impact in the field and potentially lead to future therapies for patients.

B. Positions and Honors

Positions and Employment

2002-2005 **Internal Medicine Resident**, University of California, San Diego Medical Center, Department of Medicine, San Diego, CA.

2005-2006 **Chief Medical Resident**, University of California, San Diego Medical Center, Department of Medicine, San Diego, CA.

2006-2008 **Allergy and Immunology Clinical Fellow**, University of California, San Diego Medical Center, Division of Rheumatology, Allergy and Immunology, San Diego, CA.

2006-2009 **Postdoctoral Research Fellow**, Croft Laboratory, Molecular Immunology, La Jolla Institute for Allergy and immunology, La Jolla, CA.

2009-2016 **Assistant Professor**, University of California, San Diego Medical Center, Division of Rheumatology, Allergy and Immunology, San Diego, CA.
2016-present **Associate Professor**, University of California, San Diego Medical Center, Division of Rheumatology, Allergy and Immunology, San Diego, CA.

Other experience and Professional Memberships

1999 Physicians for Social Responsibility, Chapter President
2006 Fellow-in-training member, American Academy of Allergy, Asthma & Immunology
2006 Fellow-in-training member, American College of Allergy, Asthma & Immunology
2007 Physician volunteer, American Lung Association SCAMP asthma camp
2009 Reviewer: *Immunology*
2009 Associate Faculty Member Contributor, Faculty of 1000
2009 Member, American Academy of Allergy, Asthma & Immunology
2011 Member, UCSD CTRI research grant review committee
2011 Member, AAAAI Cells and Mediators of Allergic Inflammation Committee
2011 Reviewer: *Journal of Allergy and Clinical Immunology*
2011 Member, American Association of Immunologists
2011 Member, Western Society of Allergy, Asthma and Immunology
2012 Advisory Board Member, Allergy Drug Discovery & Development Conference
2012 Problem-based learning instructor, UC San Diego School of Medicine
2013 Fellow, American Academy of Allergy, Asthma and Immunology (FAAAAI)
2014 Reviewer, *Journal of Immunology*
2013 UCSD CTRI education program advisory board member
2013 UCSD CTRI grant review committee member (KL2 awards and vouchers), ongoing
2013 Reviewer: *Molecular and Cellular Biology*
2014 Panelist, 2014 AAAAI meeting "Career Building for the Junior Investigator"
2014 Symposia speaker, 2014 AAAAI meeting "Type 2 Innate Lymphoid Cell Activation by CysLTs"
2015 Invited Bruton lecture speaker, 2015 AAAAI meeting "Innate Immune Mechanisms of Asthma and Implications for Treatment"
2015 Invited symposia speaker, 2015 AAAAI meeting "ILC2 Cells as Effectors of Lipid Mediators"
2015 Invited symposia speaker, 2015 AAAAI meeting "The Role of Cysteiny Leukotrienes and Prostaglandin D2 as Potent Inducers of ILC2 Activation"
2015 Problem Based Learning case author for MS2 class, UC San Diego Medical School
2015 Clinical Competency Committee member for UCSD Allergy and Immunology fellowship
2015 Reviewer: *Nature Communications and Mucosal Immunology*
2015 Invited speaker, 2015 International Eosinophil Society meeting "State of the art – ILC2s in Eosinophilic Inflammation"
2016 AAAAI Annual Meeting Basic Science Workshop Group Member
2016 AAAAI Annual Meeting Abstract Reviewer
2017 Reviewer: *Lancet Respirat. Medicine*

Honors

2001 Alpha Omega Alpha Honor Medical Society, Delta Chapter President
2002 Deans Award, The Chicago Medical School
2002 Board of Trustees Scholarship Award, The Chicago Medical School
2005 Boehringer Ingelheim Medical Resident Teaching Award

C. Contribution to Science

1) ILC2s in human allergic disease. The primary focus of our laboratory in recent years has been the role of group 2 innate lymphoid cells (ILC2s) in allergic diseases including asthma, allergic rhinitis, chronic rhinosinusitis with nasal polyposis, aspirin exacerbated respiratory disease (AERD) and eosinophilic esophagitis. Though T cells have been historically considered as primary orchestrators of the allergic response, the recent discovery of group 2 innate lymphoid cells has led to an important paradigm shift in

the field. Using samples from patients with allergic rhinitis, nasal polyposis, AERD and eosinophilic esophagitis, we have reported novel findings of increases in either blood or tissue ILC2s that correlate with disease activity. I was the primary investigator for (b) and (d) below and an equal co-investigator with Drs. Broide and Scott for (a) and Dr. Aceves for (c).

a) **Doherty TA**, Scott D, Walford HH, Khorram N, Lund S, Baum R, Chang J, Rosenthal P, Beppu A, Miller M, Broide DH. Allergen challenge in allergic rhinitis rapidly induces increased peripheral blood type 2 innate lymphoid cells that express CD84. *J Allergy Clin Immunol* (2014); 133(4):1203-5.
b) Walford HH, Lund S, Baum RE, White AA, Bergeron CM, Husseman J, Bethel KJ, Scott DR, Khorram N, Miller M, Broide DH, **Doherty TA.** Increased ILC2s in the eosinophilic nasal polyp endotype are associated with corticosteroid responsiveness. *Clin Immunol* (2014); 155(1):126-35.
c) **Doherty TA**, Baum R, Newbury RO, Yang T, Dohil R, Aquino M, Doshi A , Walford HH, Kurten RC, Broide DH and Aceves S. Group 2 innate lymphocytes (ILC2s) are enriched in active eosinophilic esophagitis. *J Allergy Clin Immunol* (2015) pii: S0091-6749(15)00862-3. doi: 10.1016/j.jaci.2015.05.048.
d) Eastman JJ, Cavagnero KJ, Deconde AS, Kim AS, Karta MR, Broide DH, Zuraw BL, White AA, Christiansen SC, **Doherty TA**. Group 2 innate lymphoid cells are recruited to the nasal mucosa in patients with aspirin exacerbated respiratory disease. *J Allergy Clin Immunol (2017);* Jul;140(1):101-108.

2) Mechanisms of ILC2 regulation in type 2 inflammation. To complement our human ILC2 studies, we have utilized in vitro functional assays and mouse models to determine novel mechanisms that regulate ILC2s. Initial reports identified that epithelial cytokines (IL-25, IL-33, TSLP) control ILC2 function. Our laboratory was a pioneer in the role of lipid mediator regulation of ILC2s which changed the paradigms of ILC2 biology as these mediators are produced by non-epithelial cells including eosinophils and mast cells during type 2 inflammation. Specifically, we have made several key discoveries in the field including the role of eicosnaoids found elevated in asthma (cysteinyl leukotrienes and prostaglandin D2) in the activation and chemotaxis of ILC2s. I was the primary investigator for (a), (b), and (d) below and a co-investigator with Drs. Broide and Chang for (c).

a) **Doherty TA**, Khorram N, Chang JE, Kim HK, Rosenthal P, Croft M, Broide DH. STAT6 regulates natural helper cell proliferation during lung inflammation initiated by *Alternaria*. *Am J Physiol Lung Cell Mol Physiol* (2012); 303(7):L577-88.
b) **Doherty TA**, Khorram N, Lund S, Mehta AK, Croft M, Broide DH. Lung type 2 innate lymphoid cells express cysteinyl leukotriene receptor 1, which regulates Th2 cytokine production. *J Allergy Clin Immunol* (2013);132(1):205-13.
c) Chang J, **Doherty TA**, Baum R, Broide DH. PGD2 regulates human type 2 innate lymphoid cell chemotaxis. *J Allergy Clin Immunol* (2014); 133(3):899-901.
d) Lund SJ, Portillo A, Baum R, Cavagnero K, Mehta A, Croft M, Broide DH, **Doherty TA**. Leukotriene C4 potentiates IL-33 induced ILC2 activation and lung inflammation. *J Immunol* (2017); Jun 30. pii: ji1601569. doi: 10.4049/jimmunol.1601569.

3) Mechanisms of airway remodeling in asthma. Airway remodeling includes subepithelial fibrosis and smooth muscle hypertrophy/hyperplasia that contributes to lung function decline and severity in asthma. My early work in the laboratories of Drs. Broide and Croft focused on novel pathways of airway remodeling. Using allergen challenge models, we found that NF-κB-regulated genes within the airway epithelium contribute to remodeling. Our further work showed that TNF family member LIGHT was critical to remodeling and thus represents a novel therapeutic target in asthma. More recently, we showed that the remodeling process begins during very early exposures to *Alternaria alternata*, a fungal allergen associated with severe asthma. I have also assisted with work to uncover the role of ORMDL3 (a gene strongly linked to asthma in GWAS studies) in remodeling. I performed nearly all experiments, analyzed all data and was primary author for (b) & (c). I performed the airway remodeling analysis that led to the conclusions in (a) and designed, performed, and analyzed the ORMDL3 flow cytometric data in (d).

a) Broide D, Lawrence T, **Doherty T**, Cho J, Miller M, McElwain K, McElwain S, Karin M. Allergen-induced peribronchial fibrosis and mucus production mediated by I kappa B kinase b-dependent genes in airway epithelium. *Proc Natl Acad Sci* (2005); 102:17723-17728.
b) **Doherty TA**, Soroosh P, Khorram N, Fukuyama S, Rosenthal P, Cho JY, Norris PS, Choi H, Scheu S, Pfeffer K, Zuraw BL, Ware CF, Broide DH, Croft M. The TNF family member LIGHT is a target for asthmatic airway remodeling. *Nature Medicine* (2011); 17:596-603.
c) **Doherty TA**, Khorram N, Sugimoto K, Sheppard D, Rosenthal P, Cho JY, Pham A, Miller M, Croft M, Broide DH. *Alternaria* induces STAT-6 dependent acute airway eosinophilia and epithelial FIZZ1 expression that promotes airway fibrosis and epithelial thickness. *J Immunol* (2012); 188:2622-9.
d) Miller M, Tam AB, Cho JY, **Doherty TA**, Pham A, Khorram N, Rosenthal P, Mueller JL, Hoffman HM, Suzukawa M, Niwa M, Broide DH. ORMDL3 is an inducible lung epithelial gene regulating metalloproteases, chemokines, OAS, and ATF6. *Proc Natl Acad Sci* (2012); 109:16648-16653.

4) CD4 T cell and adaptive immune responses in asthma. CD4+ Th2 cells that produce cytokines IL-4, IL-5, and IL-13 are known to orchestrate the adaptive immune response in asthma after allergen challenge. In contrast, regulatory T cells promote tolerance to allergens and prevent allergic inflammation. We have been interested in several aspects of CD4 T cell biology during airway allergen challenge responses in mice. First, we made the novel observation that CD4 cells contribute more to eosinophilic infiltration than airway remodeling during chronic allergen challenges. Second, we found that the TNFR family member HVEM regulates Th2 cell memory responses during allergic lung inflammation. Third, we found that lung macrophages are critical in the promotion of regulatory CD4+ T cells after allergen exposure. Finally, we have identified that Th2 cell recruitment to the lung is enhanced by innate challenges with *Alternaria* during an adaptive response to a completely different allergen. I performed all of the work for (a) and was principle investigator for (d). I participated in experimental design, data collection, and analysis for (b) & (c).

a) **Doherty T**, Soroosh P, Broide D, Croft M. CD4 cells are required for chronic eosinophilic inflammation but not airway remodeling. *Am J Physiol Lung Cell Mol Physiol* (2009); 296:L229-35.
b) Soroosh P, **Doherty TA**, So T, Mehta AK, Khorram N, Norris PS, Scheu S, Pfeffer K, Ware C, Croft M. Herpesvirus entry mediator (TNFRSF14) regulates the persistence of T helper memory cell populations. *J Exp Med* (2011); 208:797-809.
c) Soroosh P, **Doherty TA**, Duan W, Mehta AK, Choi H, Adams YF, Mikulski Z, Khorram N, Rosenthal P, Broide DH, Croft M. Lung Resident Tissue Macrophages Generate Foxp3+ Regulatory T cells and Promote Airway Tolerance. *J Exp Med* (2013); 210:775-788.
d) Kim HK, Kim H., Lund S., Baum R., Khorram N., Rosenthal P., **Doherty TA**. Innate Type-2 Response to *Alternaria* Extract Enhances Ryegrass-induced Lung Inflammation. *Int Arch Allergy Immunol* (2014); 163:92-105.

Complete list of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40791132/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support: **10/31/2014-10/30/2019**
NIH R01 Award (P.I. Doherty, T)
NIH AI114585
RBM3 regulation of type 2 innate lymphoid cells in allergic inflammation
The goals will be to investigate the role of the RNA binding protein RBM3 in control of type 2 innate lymphoid cells during lung inflammation.

NIH U19 Asthma and Allergic Diseases award (Project 3, PI, Doherty, T) **09/01/16 – 08/31/2021**
NIH AI070535-11
ALCAM/CD6 interactions in airway inflammation and remodeling
The goals will be to investigate the roles of CD6 and ALCAM in airway inflammation and remodeling.

Completed Research Support:

K08 Mentored Career Development Award (P.I. Doherty, T) **8/16/2010-7/31/2015**
NIH (1K08AI080938-01A1)
Mentor: David Broide, MB, ChB
OX40/OX40 ligand interactions in allergen-induced airway remodeling.
The goals are to investigate the role of OX40 and OX40 ligand in Th2-mediated airway remodeling.

ALA/AAAAI Allergic Respiratory Diseases Award **7/1/2012-6/30/2014**
American Lung Association & American Academy of Asthma, Allergy and Immunology
Lung natural helper cell (ILC2) regulation of innate allergen-induced inflammation.
The goals are to investigate the role of lung natural helper cells during innate allergen-induced airway inflammation.

AADCRC Junior Investigator Fund Opportunity Grant (P.I. Doherty, T) **4/2012-3/2013**
NIH
CysLT1R regulation of lung natural helper cell responses induced by *Alternaria.*
The goals are to investigate the role of CysLT1R on lung natural helper cells during innate allergen induced airway inflammation.

AAAAI bridge to K award (P.I. Doherty, T) **2/2010-8/2010**
OX40/OX40L interactions in chronic allergen-induced airway remodeling.
The goals are to investigate the control of airway inflammation and remodeling by TNF/TNFR members OX40 and OX40 ligand.

UCSD CTRI Junior Faculty Career Award (P.I. Doherty, T) **7/01/09-8/2010**
UCSD School of Medicine Grant
Mentor: David Broide, MB ChB
Targeting OX40/OX40L as a novel therapy for chronic asthma and remodeling.
The goals are to investigate human asthmatic TH2 responses mediated by OX40/OX40L and test therapeutic blockade in a mouse model of chronic asthma.