BIOGRAPHICAL SKETCH

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NAME: Patricia R Taylor, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): PATTYT1024

POSITION TITLE: Assistant 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 Akron, Ohio	B.S.	2005	Microbiology
University of Akron, Ohio	M.S.	2007	Biology
Kent State University/NEOMED, Ohio	Ph.D.	2010	Biomedical Sciences
Case Western Reserve University, Ohio	Post-doctoral	2010-2014	Ocular Immunology

A. Personal Statement

The goal of my research is to identify the role of IL-17A the onset and progression of diabetic retinopathy, as well as identify potential therapeutics for non-proliferative diabetic retinopathy. Previously, in a murine model of diabetic retinopathy we found that diabetes-mediated IL-17A enhanced retinal inflammation, vascular leakage, and capillary degeneration. Ablation of IL-17A in transgenic mice delayed the onset of non-proliferative diabetic retinopathy. In our NEI R01 studies, we are now examining TRAF signaling pathways downstream of the IL-17 receptor in diabetic mice to identify potential therapeutic targets for non-proliferative diabetic retinopathy. In our VA Merit studies, we are examining the role of IL-17A in the onset and progression of diabetic retinopathy in human diabetics. Since this is one of the first targeted studies of IL-17A-dependent pathogenesis in proliferative diabetic retinopathy and diabetic macular edema, these novel discoveries should lead to potential therapeutics.

Ongoing projects that I would like to highlight include:

R01 EY030487
Taylor (PI)
04/01/20 – 03/31/25
Identification of immunomodulators for diabetic retinopathy therapeutics

VA Merit CX002204
Taylor (PI)
04/01/21 – 01/04/25
The role of IL-17A in the onset and progression of diabetic retinopathy in VA patients

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2010-2014 Post-doctoral Fellow, Department of Ophthalmology, Case Western Reserve Univ, Cleve, OH
2014-2016 Instructor, Department of Ophthalmology, Case Western Reserve Univ, Cleve, OH
2015- Research Health Scientist, VA Northeast Ohio Health Systems, Cleve, OH
2017- Assistant Professor, Department of Ophthalmology, Case Western Reserve Univ, Cleve, OH

Other Experience and Professional Memberships

2021- Director, VSRC Histology Core, Department of Ophthalmology, CWRU, Cleve, OH
2020- Ad-hoc Reviewer, NIH-NEI Brain Disorders and Clinical Neuroscience Study Section
2020- Editorial Board Member, International Journal of Immunology
2018- Voting Member, CWRU School of Medicine Faculty Council
2018- Director, CWRU Ophthalmology Research Seminars
2020- Interviewing Member, CWRU Medical School Admissions Committee
2020- Interviewing Member, CWRU MSTP Admissions Committee
2010- Member, FOCIS
2014- Member, ARVO
2018- Member, AAI

Honors

2018-2020 OLERF Lois Hagelberger Huebner Young Investigator Award
2020 Experimental Biology and Medicine Outstanding Reviewer Award
2017-2018 OLERF W.R. Bryan Diabetic Eye Disease Award
2013-2015 NIH LRP Extramural Clinical Research Award
2010 FOCIS Travel Award
2005 Magna cum Laude
2003-2004 McLaughlin Academic Scholarship
2004 Phi Sigma Alpha Scholastic Achievement
2003 Golden Key International Honor Society Award
2002 Mortar Board National College Senior Honor Society Award
2001 National Society of Collegiate Scholars Award
2001 Phi Theta Kappa Honor Society Award

C. Contributions to Science

My major contributions to science are in the field of cellular and ocular immunology, focusing on characterizing and immunomodulating innate immune cells. My neutrophil study published in Nature Immunology (2014) has been my highest impact work. In this paper, I characterized a novel subset of neutrophils that both produce and respond to IL-17, which makes this neutrophil the first autocrine IL-17 cell discovered. This IL-17 autocrine activity is important because it elicits increased production of reactive oxygen species and proteinases, which is very relevant to tissue damage in multiple infectious, autoimmune, and inflammatory diseases; including diabetic retinopathy.

1. Modulation of innate immune cells.

During my graduate studies, my research focused on identifying immune-mediated mechanisms that regulated the adaptive immune response against HSV-1 and HIV, using a ligand-epitope antigen presenting system. This included the identification of one of the first viral dendritic cell vaccines. During my pre-doctoral studies, my mentors and I successfully designed a method for modulating immunogenic responses by activating dendritic cells for immune interventions in multiple viral infections (Patent PCT/US2010/031054).

a. Rosenthal, K.S., **Taylor, P.R.,** Zimmerman, D.H. 2012. J-LEAPS Peptide and LEAPS-Dendritic Cell Vaccines. Microbial Biotechnology 5(2): 203-13 (2011). PMCID: PMC3815780.
b. **Taylor, P.R.**, Koski, G.K., Paustian, C.C., Bailey, E., Moore, F.B.G., Cohen, P.A., Zimmerman, D.H., Rosenthal, K.S. J-LEAPS Vaccines Initiate Murine Th1 Responses by Activating Dendritic Cells. Vaccine 28(34): 5533-42 (2010). PMID: 20600501.
c. **Taylor, P.R.**, Paustian, C.C., Koski, G.K., Zimmerman, D.H., Rosenthal, K.S. Maturation of dendritic cell precursors into IL12 producing DCs by J-LEAPS Immunogens. Cellular Immunology 262:1-5 (2010). PMCID: PMC4481128.
d. Zimmerman, D.H., **Taylor, P.**, Talor, E., Bendele, A., O'Neill, S., Rosenthal, K.S. CEL-2000 Therapeutic Vaccine Arrests Disease Progression in Collagen Type II Model for Rheumatoid Arthritis. International Immunopharmacology 10(4): 412-21 (2010). PMID: 20074669.

2. Characterization of IL-17 activation mechanisms in immune cells.

In my collaborative studies, I assisted in the mechanistic characterization of innate cell activation of IL-17

producing lymphocytes.

a. Deng, Z., Ma, S., Zhou, H., Zang, A., Fang, Y., Li, T., Shi, H., Liu, M., Du, M., **Taylor, P.R.,** Zhu, H.H., Chen, J., Meng, G., Li, F., Chen, C., Zhang, Y., Jia, X.M., Lin, X., Zhang, X., Pearlman, E., Li, A., Feng, G.S., Xiao, H. Tyrosine phosphatase SHP-2 mediates C-type lectin receptor-induced activation of the kinase Syk and anti-fungal TH17 responses. Nature Immunology 16: 642-652 (2015). PMCID: PMC4439382.
b. Paustian, C., **Taylor, P.,** Johnson, T., Xu, M., Rosenthal, K.S., Shu, S., Cohen, P.A., Czerniecki, B.J., Koski, G. Extracellular ATP and Toll-like Receptor Agonists Trigger Human Monocytes and Activation Program that Favors T helper 17 (2013). PLoS ONE 8(1): e54804. PMCID: PMC3561418.
c. Sun, Y., Karmakar, M., **Taylor, P.R.,** Rietsch, A., Pearlman, E. ExoS and ExoT ADP-ribosyltransferase activities mediate Pseudomonas aeruginosa keratitis by promoting neutrophil apoptosis and bacterial survival. Journal of Immunology 188(4): 1884-95 (2012). PMCID: PMC3273577.

3. <u>Discovery of a novel IL-17 producing neutrophil subset and it's role in multiple disease states.</u>

My post-doctoral project focused on the innate and adaptive immune response during cornea infections, which led to the discovery and characterization of a novel neutrophil population. I determined that this neutrophil population both produces and responds to IL-17, which is the first IL-17 autocrine cell discovered. As an instructor, I investigated the role of IL-17 producing neutrophils in autoimmune, inflammatory, and ocular disorders. My collaborators and I have determined that IL-17 producing neutrophils have a pathologic role in keratitis and cystic fibrosis.

a. **Taylor, P.R.**, Roy, S., Leal, S.M. Jr., Sun, Y., Howell, S.J., Cobb, B.A., Li, X., Pearlman, E.. Autocrine IL-17A / IL-17RC neutrophil activation in fungal infections is regulated by IL-6, IL-23, RORγ t and Dectin-2. Nature Immunology 2:143-151 (2014). PMCID: PMC3972892.
b. **Taylor, P.R.**, Leal, S.M. Jr., Sun, Y., Pearlman, E. Aspergillus and Fusarium corneal infections are regulated by Th17 cells and IL-17 producing neutrophils. Journal Immunology 192:3319-27 (2014). PMCID: PMC4020181.
c. Carrion, S.J., Abbondante, S., Clark, H.L., Marshall, M.E., Mouyna, I., Beauvais, A., Sun, Y., **Taylor, P.R.**, Leal, S.M. Jr., Armstrong, B., Carrera, W., Latge, J.P., Pearlman, E. Aspergillus fumigatus corneal infection is regulated by chitin synthases and by neutrophil-derived acidic mammalian chitinase. European Journal of Immunology. (2019). PMID: 30903663.
d. Hsu, D., **Taylor, P.**, Fletcher, D., van Heekeren, R., Eastman, J., van Heekeren, A., Davis, P., Chmiel, J., Pearlman, E., Bonfield, T. Interleukin-17 pathophysiology and therapeutic intervention in cystic fibrosis lung infection and inflammation. Infection and Immunity 84(9):2410-2421 (2017). PMCID: PMC4995906.
e. **Taylor, P.R.**, Bonfield, T.L., Chmiel, J.F., Pearlman, E. Neutrophils from F508del cystic fibrosis patients produce IL-17A and express IL-23-dependent IL-17RC. Journal Clinical Immunology 170:53-60 (2016). PMID: 2715536.
f. **Taylor, P.R.**, Roy, S., Meszaros, E.C., Sun, Y. Howell, S.J., Malemud, C.J., Pearlman, E. JAK/STAT regulation of Aspergillus fumigatus corneal infections and IL-6/23-stimulated neutrophil. IL-17, elastase, and MMP9 activity. Journal Leukocyte Biology 100(1): 213-222 (2016). PMCID: PMC4946614.
g. **Taylor, P.R.**, Pearlman, E. IL-17A production by neutrophils. Immunology Letters 169: 104-5 (2015). PMID: 26582721.

4. <u>Identification of the role of IL-17A and it's signaling cascade in diabetic retinopathy.</u>

Currently, I am investigating the role of IL-17 producing neutrophils and Th17 cells in diabetic retinopathy, as well as characterizing the activation mechanisms of IL-17-dependent retinal pathology. I have identified the cellular source of IL-17, discovered constitutive IL-17 receptor expression on multiple retinal cells, and have identified an IL-17A-IL-17R-mediated transcellular response that initiates retinal vascular pathology that leads to the onset of non-proliferative diabetic retinopathy. These discoveries are directly relevant to all of future proposals.

a. Lindstrom, S.I., Sigurdardottir, S., Zapadka, T.E., Tang, J., Liu, H., Taylor, B.E., Smith, D.G., Lee, C.A., DeAngelis, J., Kern, T.S., **Taylor, P.R.** Diabetes induces IL-17A-Act1-FADD-dependent retinal

endothelial cell death and capillary degeneration. Diabetes and its complications. (2019). PMCID: PMC6690768.

b. Sigurdardottitr, S., Zapadka, T.E., Lindstrom, S.I., Liu, H., Taylor, B.E., Lee, C.A., Kern, T.S., **Taylor, P.R.** Diabetes-mediated IL-17A enhances retinal inflammation, oxidative stress, and vascular permeability. Cellular Immunology. (2019). PMCID: PMC6599623.
c. Liu, H., Lessieur, E.M., Saadane, A., Lindstrom, S.I., **Taylor, P.R.,** Kern, T.S. Neutrophil elastase contributes to the pathological vascular permeability characteristic of diabetic retinopathy. Diabetologia. (2019). PMCID: PMC6866660.
d. Zapadka, T.E., Lindstrom, S.I., Taylor, B.E., Lee, C.A., Tang, J., Taylor, Z.R.R., Howell, S.J., **Taylor, P.R.** RORgammaT inhibitor-SR1001 halts retinal inflammation, capillary degeneration, and the progression of diabetic retinopathy. International Journal of Molecular Science. (2020). PMCID: PMC7279039.
e. Zapadka, T.E., Lindstrom, S.I., Batoki, J.C., Lee, C.A., Taylor, B.E., Howell, S.J., **Taylor, P.R.** Aryl hydrocarbon receptor agonist VAF347 impedes retinal pathogenesis in diabetic mice. International Journal of Molecular Science (2021). PMCID: PMC812242.
f. Howell, S.J., Lee, C.A., Batoki, J.C., Zapadka, T.E., Lindstrom, S.I., Taylor, B.E., **Taylor, P.R.** Retinal inflammation, oxidative stress, and vascular impairment is ablated in diabetic mice receiving XMD8-92 treatment. Frontiers in Pharmacology (2021). PMCID: PMC8385489.

https://www.ncbi.nlm.nih.gov/sites/myncbi/1fyYr5o1iY3kY/bibliography/51873000/public/?sort=date&direction=ascending