BIOGRAPHICAL SKETCH

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NAME: Petersen, Christine Anne

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POSITION TITLE: Professor, Immunoparasitology

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
Johns Hopkins University, Baltimore, MD	B.A.	05/1994	Biology
Cornell University, Ithaca, NY	D.V.M.	05/1998	Veterinary Medicine
Harvard University	Ph.D.	05/2005	Immun. and Infect. Dis.

A. Personal Statement

I have to date mentored eight PhD students and nine post-doctoral fellows/medical trainees all focused on immunoparasitology. The majority of my Ph.D-level trainees have been either immunology students (Boggiatto, Esch, Martinez, Fowler, currently MSTP Arumugam) or epidemiology PhD students (Toepp, Wilson, Hottel, Kontowicz, currently Mahachi). Of my PhD and post-doc mentees, three are Latinx (Boggiatto, Martinez, Pessoa), and two African-American (Wilson, Grinnage-Pulley) or African (Mahachi, Osanya). Diversity as broadly defined is critical to the way my group functions and is seen as a priority. We strive to provide an inclusive, supportive research environment. My mentoring of students includes weekly lab group meeting as well as individual meetings with students of all levels, which are longer based on longer time with the lab or in training. The rigor and excellence of my students work and my commitment to mentoring is reflected in the four Ballard Seashore dissertation awards for my students and four Provosts Research Excellence awards for their dissertations (Boggiatto, Esch, Toepp, Wilson, Kontowicz). I will continue to serve as a mentor for Immunology and epidemiology students, serve on thesis committees, and otherwise help however possible.

Over the past 10 years I have been the PI of six NIH-funded awards evaluating immune mechanisms for intervention in vector borne zoonotic disease; five focused on reservoir host targeted interventions for visceral leishmaniasis and one for Lyme disease. This has led to multiple publications, including 1-4 below, as well as sections C1, 2 and 5. I am the only non-European member of the internationally known group Leishvet, which provides guidance and education regarding control, treatment, and prevention of veterinary leishmaniosis. I am Scientific Program Director for the American Society for Tropical Medicine and Hygiene, and a standing member of the NIH Vaccines for Microbial Diseases study section. Since June 2013, I have been the Director of the Center for Emerging Infectious Diseases (CEID) housed within the Department of Epidemiology. The Center's focus is to bring together transdisciplinary research teams to lessen the burden of emerging zoonotic infectious diseases across health settings. For more than a decade my group has had ongoing NIH-funded studies of visceralizing *Leishmania* spp. in the US and as part of collaborative NIH TMRC funded studies in Brazil, India, and Ethiopia. I am Co-PI with Dr. Jacob Oleson of an R01 "*Epidemic modeling framework for complex, multi-species disease processes*", based on my laboratory's wet-lab discoveries of canine progressive leishmaniasis. This work is represented in (C2, C5). A sub-award from IDRI led to further trials of experimental vaccine immunogenicity ex vivo in cells from a hunting dog cohort, published in Vaccine in 2015 and a large CONSORT-guided vaccine field trial completed in spring of 2017, also published in Vaccine (4). Our active research group is focused on the long-term goal of protecting people and animals from zoonotic diseases through effective treatment, control and/or prevention using all hosts as intervention targets.

1. Toepp, A., Monteiro, G.R., Coutinho, J.F., Leal Lima, A., Mahachi, K., Larson, M., Wilson, G., Grinnage-Pulley, T., Bennett, C., Anderson, M., Anderson, B., Saucier, J., Buch, J., Chandrashekar, R., Brown,

G., Oleson, J., Jeronimo, S.M.B., **Petersen, C.,** (2019) Co-morbid infections induce progression of visceral leishmaniasis. Parasites and Vectors. doi.org/10.1186/s13071-019-3312. PMC6345068

2. Mou, Z., Li, J. Boussoffara, T., Ezzati, P., Hu, C., Yi, W., Liu, D., Khadem, F., Okwor, I., Jia, P.,Wang, J., Ndao, M., **Petersen, C**., Chen, J., Rafati, S., Louzir, H., Wilkins, J., Uzonna, J. (2015) "Combinatorial proteomics and cellular immunology identify conserved, immunodominant and cross species protective *Leishmania* antigen and the responding CD4+ T cells at clonal level." Sci. Trans. Med. Oct 21; 7(310):310ra167. doi: 10.1126/scitranslmed.aac5477. PMID: 26491077. *No US Federal funding used.*
3. Toepp, A., Larson, M., Wilson, G., Grinnage-Pulley, T., Leal-Lima, A., Bennett, C., Anderson, M., Fowler, H., Anderson, B., Jeffries, J., Beeman, G.M., Parrish, M., Hinman, J., Buch, J., Saucier, J., Gharpure, R., Cotter, C., **Petersen, C.**, (2018) "Randomized, controlled, double-blinded field trial to evaluate the efficacy of the Leish-Tec® vaccine as immunotherapy for canine leishmaniasis". Vaccine 36:6433-41. PMID: 30219369. *No US Federal funding used.*
4. Schaut RG, Lamb IM, Toepp AJ, Scott B, Mendes-Aguiar CO, Coutinho JF, Jeronimo SM, Wilson ME**,** Harty JT, Waldschmidt TJ, **Petersen CA.** (2016). Regulatory IgDhi B Cells Suppress T Cell Function via IL-10 and PD-L1 during Progressive Visceral Leishmaniasis. Journal of Immunology, Vol. 196: 4100-9. PMC4868652

B. Positions and Honors

Positions and Employment

1999-2004	Graduate Student, Dept. of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, MA
2004-2005	Affiliate Assistant Professor, Department of Vet. Path., College of Veterinary Medicine, Iowa State University, Ames, IA (title given to NIH K08 mentored training grant funded scientists)
2005-2012	Assistant Professor, Department of Vet. Path., College of Veterinary Medicine, Iowa State University, Ames, IA
2006-2013	Adjunct Assistant Professor, Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, IA
2012-2013	Associate Professor, Department of Vet. Path., College of Veterinary Medicine, Iowa State University, Ames, IA . With tenure.
2013-2020	Associate Professor, and Director of the Center for Emerging Infectious Diseases, Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, IA
2020-present	Professor, and Director of the Center for Emerging Infectious Diseases, Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, IA

Recent Awards and Honors

Scientific Program Chair, American Society for Tropical Medicine and Hygiene, 2020-2023.
Fellow, ASTMH.
President, American Council for Molecular, Cellular and Immunoparasitology. Nov. 2016-2018.
Inducted as member of Leishvet, the governing body that determines treatment and control guidelines for global veterinary Leishmaniosis. 2014- present.
Deputy Editor for PLoS Neglected Tropical Diseases, Editor, Infection and Immunity and guest editor for PLoS Pathogens.
Ad-hoc reviewer NIH NIAID Tropical Disease Research Centers P50, Sept. 2011, IHD study section, Feb. 2013, DVM-oriented T35/32 review Nov. 2014, Diagnostic Devices SBIR/STTR review, June, Nov. 2016, March 2017, VMD Oct. 2018, Feb. 2019, Clinical Research and Field Studies of Infectious Diseases (CRFS) Oct. 2019, special NIAID Tick-borne diseases panel Jan 2020.
Standing member of VMD 2020-2024.

Keynote speaker, Woods Hole Immunoparasitology meeting, April 2019.
Brazilian Society of Protozoology Annual Conference invited speaker, Caxambu, MG, Brazil, Oct. 2012.
Inaugural International Society for Companion Animal Infectious Diseases Symposium invited speaker, Toulouse, France, 2010.

Patents from work

Christine Petersen and Angela Toepp No US 62/630,053 filed Feb. 13, 2018
"Immunotherapy for canine leishmaniosis".

C. Contributions to Science

1. Immune alterations during progressive *L. infantum* infection expanded a large population of regulatory B cells, induced T cell exhaustion and led to clinical disease.

- U.S. and Brazilian infected with *L. infantum* have pronounced production of immunosuppressive IL-10 as disease progresses (Boggiatto *et al.* 2010, Esch et. al, 2013)**.** IL-10 production is produced by naïve-like, IgD^{hi} B regulatory cells and less so T regulatory cells (Schaut *et al.*, 2016).
- Concomitant with production of IL-10 and high levels of immunoglobulin, CD4+ T cells from U.S. hounds infected with *L. infantum* progressing to clinical VL have reduced ability to respond via T cell proliferation to any specific antigen. (Boggiatto *et al.* 2010), (Esch et al, 2013), (Vida et al, 2015).
- Effector responses by CD4+ T cells and to a lesser extent CD8+ T cells were significantly recovered after blockade of the inhibitory receptor ligand B7.H1. (Esch et al, 2013).
- Altered immunity and increased hypergammaglobulinemia leads to NLRP3 and autophagy-driven renal failure during clinical VL (Esch et al, 2015).

These findings identified that during progressive *L. infantum* infection there is robust production of IL-10 from B cells which can co-opt other B cells and T cells into a regulatory phenotype. The canine model for VL has similar tissue pathology and immune responses to human disease in endemic areas, including T cell exhaustion concomitant with progressive disease. This work substantiates that our cohorts of dogs are valid and useful model system for studying immunopathogenesis of visceral leishmaniasis, particularly given our ability to evaluate paired physical exams, repeated whole blood sampling across progression of disease and euthanasia with full tissue collection data. I served as the primary investigator for these studies.

2. Transmission of *Leishmania infantum* in dogs in non-endemic regions is primarily vertical, but retains ability for vector transmission.

My lab group determined and published the primary means of *Leishmania* transmission in U.S. dogs; vertical transmission, answering a question that had confounded multiple scientists and veterinarians for the last decade - how this disease is spreading focally in specific breeds without evidence of human infection or introduction into the U.S. canine population as a whole. This finding is significant to disease transmission throughout the 98 VL endemic countries, as focus on vector elimination alone will not eliminate VL. Without canine population control, mom-to-pup transmission will promote continued disease, with a calculated R_0 of 6. We also determined that despite the fact that transmission has been predominantly amastigote-based and transplacental, *L. infantum* has retained its ability to form infective metacyclic promastigotes once taken into *Lu. longipalpis* and infect other mammals.

- A very high percentage of pups born to a seropositive, *L. infantum*-infected bitch have disseminated parasites at birth. Twelve weeks after birth, at the time when the maternal immune response should have waned within the pups, there is decreased parasite dissemination. (Toepp *et al.* 2019)
- Despite evidence of parasite transmission while *in utero*, which can interfere with the ability to distinguish parasite antigen from self, T lymphocytes from pups both at birth and twelve weeks after birth are able to make self/non-self distinction as demonstrated by proliferation in response to parasite antigen. (Boggiatto *et al.* 2011)
- Parasites from vertically-infected dogs still actively infect *Lu. longipalpis*, become highly infectious metacyclic promastigotes and via sand flies infect additional mammals; these parasites maintained the ability for vector borne transmission. (Schaut *et al.,* 2015)
- Vertical transmission of *L. infantum* occurs in multiple vertebrate hosts, including people and dogs. This is also true of parasitic family-member, *Trypanosoma cruzi*. (Grinnage-Pulley *et al.,* 2016*)*

These findings determined a novel means of *L. infantum* transmission without vectors, which maintains infection within the population and does not lead to differential pathology as the neonatal immune system is able to identify parasite antigen as non-self. These parasites have not lost their ability for vector transmission.

3. Dendritic cells and macrophages have altered maturation and subsequent function after *L. amazonensis* infection both *in vitro* and *in vivo* induced through MAP kinase ERK activation and alteration of NADPH oxidase function.

- Amastigote infection of bone marrow derived dendritic cells (BMDC) and bone-marrow macrophages (BMM) leads to rapid and significant activation of MAP kinase ERK, not seen in BMDC infected with the benign/healing disease causing parasite *L. major*. (Mukbel *et al.*, 2008, Boggiatto *et al.*, 2009, 2014)

- *L. amazonensis*-mediated ERK activation leads to a less mature DC population both *in vitro* and *ex vivo*. This defective DC phenotype can be recovered both *in vitro* and *in vivo* by blocking activation of ERK (Boggiatto *et al*., 2009)

These findings are important as they identified a specific signaling pathway (ERK1/2 phosphorylation) and location (the late endosome) as the unique signal and site of activation by non-healing chronic *L. amazonensis* infection as compared to healing *L. major* infection, promoting parasite persistence and chronic disease within the host.

4. Pathogen-derived oligosaccharide cap sugars differentially alter the immune response, these and other adjuvants can effectively recover immune responsiveness during progressive VL.

- Creation of pathogen-derived cap sugars provides a model system to discover how sugars alter the immune response. Pathogen-derived cap sugars differentially alter production of the critical cell mediated immunity cytokine IL-12 (Song *et al.* 2010, Osanya *et al.*, 2011)
- Pathogen-derived cap sugars differentially alter production of other critical cell mediated immunity cytokines using toll-like receptor (TLR) 2 and mannose receptor *in vitro* and TLR2 *in vivo* (Osanya *et al.*, 2011)
- Use of an acid-labile linker and carbohydrates attached to this linker in a dendrimer array provided a pseudo-pathogen model system to assess carbohydrate release within the phagolysosome and effector interaction(s) of carbohydrates with T cells (Choudhury *et al.,* 2015)
- TLR agonist adjuvants, including those specific to glycolipids, or oligosaccharides themselves were able to recover T cell responsiveness from cells obtained from animals across the VL spectrum (Schaut *et al*., 2016), and improve lesion resolution in *L. major*-infected mice (Grinnage-Pulley et al., 2017).

With an invaluable team of collaborators, we have evaluated how structurally similar oligosaccharides with only one sugar difference can lead to very different innate immune responses, using different lectin-binding, leading to differences in clinical outcomes. Further studies used novel “pseudopathogen” particles to determine further how these sugars, provided in a multimeric display, are recognized by antigen presenting cells and promote effector functions in T cell subsets.

5. Exposure to domestic animals, whether dead-end or reservoir hosts, which are preferred vector blood meal sources, can greatly increase human vector exposure and subsequent likelihood of vector-borne infection. These interactions can be modeled, and effect of interventions predicted, using Bayesian statistical modeling.

- Caretakers of multiple hunting dogs had 5.89 greater risk of tick exposure than people out in tick environments without birds (Toepp *et al.* 2018)
- Exposure to tick borne diseases greatly increased the likelihood of clinical progression of leishmaniosis in dogs. (Toepp *et al*, 2018)
- Using serology exposures of different hosts and knowledge of vector patterns, a predictive model can be designed. (Ozanne *et al*, 2018, 2019)

With an invaluable team of collaborators, we have evaluated how dog exposure increased the risk of people working with dogs to find embedded ticks on their body. We found that after controlling for time spent outdoors and other variables, people working with large kennels of hunting dogs were at much higher risk of tick and therefore tick-borne disease exposure. We have used similar approaches to look at how coinfection with tick-borne diseases can alter another vector borne disease, Visceral Leishmaniasis. Collaboratively we have used data sets from these and other studies for compartmental Bayesian statistical modeling to predict changes in transmission over time with different means of transmission (vertical and vector) and how interventions may alter these vector borne disease exposures.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/christine a.petersen.1/bibliography/40335669/public/?sort=date&direction=ascending.