BIOGRAPHICAL SKETCH

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NAME: Weiss, Brian

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

POSITION TITLE: Research Scientist/Scholar

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Colorado, Boulder, Colorado	BS	05/1996	Environmental, Population and Organismic Biology
University of Queensland, Brisbane, Queensland	MS	05/1998	Entomology
University of Alberta, Edmonton, Alberta	PHD	06/2003	Physiology/Cell Biology
Yale School of Public Health, New Haven, CT	Other training	05/2005	Postdoctoral Associate, Epidemiology of Microbial Diseases
Yale School of Public Health, New Haven, CT	Postdoctoral Fellow	05/2008	Epidemiology of Microbial Diseases

A. Personal Statement

I am currently a Research Scientist in Serap Aksoy's lab, where I have worked with tsetse flies for 12 years. During this time my research has focused on deciphering the molecular mechanisms that underlie the relationship between tsetse flies and their associated microorganisms. The conceptual emphasis of my work more specifically focuses on 1) the association between tsetse's symbiotic bacteria and their role in host immunity and fecundity, and 2) tsetse immunity as it relates to the maintenance of symbiotic associations and defense against exogenous microbes (including pathogenic African trypanosomes).

B. Positions and Honors

Positions and Employment

1998 - 2002 Teaching Assistant - Zoology 241 - Animal Physiology and Homeostasis, University of Alberta, Department of Biological Sciences, Edmonton

1998 - 2003 Teaching Assistant - Zoology 250 - Invertebrate Zoology, University of Alberta, Department of Biological Sciences, Edmonton

2008 - Lecturer (course title 'Biology of Insect Disease Vectors), Yale School of Public Health, New Haven, CT

2008 - 2013 Associate Research Scientist/Scholar , Yale School of Public Health, New Haven, CT

2011 - 2011 Invited Consultant for a meeting on Enhancing Vector Refractoriness to Trypanosome Infection, United Nations, International Atomic Energy Association, Vienna

2013 - Research Scientist/Scholar, Yale School of Public Health, New Haven, CT

2016 - 2016 Invited Consultant for a meeting on Enhancing Vector Refractoriness to Trypanosome Infection, United Nations, International Atomic Energy Association, Lyon

Other Experience and Professional Memberships

Honors

1997	International Student Post-Secondary Studies Award, University of Queensland, Australia
1998	Graduate Studies and Research Scholarship, University of Alberta
2001	Graduate Students Association Teaching Assistantship Award, University of Alberta
2002	Departmental of Biological Sciences Excellence in Teaching Award, University of Alberta

C. Contribution to Science

1. Ticks reside in heavily populated suburban habitats and vector a more diverse complement of pathogens than do any other arthropod. Additionally, tick infestations can present an agricultural burden with economically devastating consequences. Novel control methods aimed at reducing tick population densities will alleviate the burden associated with these complications. These publications describe 1) physiological processes that mediate the hard tick 'commitment' to engorge, and 2) male tick-derived seminal proteins that stimulate female engorgement following mating. Information derived from these studies is of importance with regard to the development of anti-tick vaccines.

    a. Weiss BL, Reuben Kaufman W. The relationship between 'critical weight' and 20-hydroxyecdysone in the female ixodid tick, Amblyomma hebraeum. J Insect Physiol. 2001 Nov;47(11):1261-1267. PubMed PMID: 12770177.

    b. Weiss BL, Stepczynski JM, Wong P, Kaufman WR. Identification and characterization of genes differentially expressed in the testis/vas deferens of the fed male tick, Amblyomma hebraeum. Insect Biochem Mol Biol. 2002 Jul;32(7):785-93. PubMed PMID: 12044495.

    c. Weiss BL, Kaufman WR. Two feeding-induced proteins from the male gonad trigger engorgement of the female tick Amblyomma hebraeum. Proc Natl Acad Sci U S A. 2004 Apr 20;101(16):5874-9. PubMed PMID: 15069191; PubMed Central PMCID: PMC395891.

2. All animals house symbiotic bacteria within their gut that are of vital importance to the physiological homeostasis of their host. However, the molecular mechanisms that mediate host tolerance of beneficial/commensal organisms, versus intolerance of potentially harmful microbes, are poorly understood. These papers outline my use of the tsetse fly and it's associated symbionts (obligate *Wigglesworthia* and commensal *Sodalis*) as a model system to determine host and microbe adaptations that facilitate successful symbioses. Specifically, I have contributed significantly to the discovery of microbial adaptations that 1) facilitate tsetse host tolerance of symbiotic bacteria, and 2) promote tsetse's ability to utilize vertebrate blood as its sole source of nutrients.

    a. Michalkova V, Benoit JB, Weiss BL, Attardo GM, Aksoy S. Vitamin B6 generated by obligate symbionts is critical for maintaining proline homeostasis and fecundity in tsetse flies. Appl Environ Microbiol. 2014 Sep;80(18):5844-53. PubMed PMID: 25038091; PubMed Central PMCID: PMC4178588.

    b. Maltz MA, Weiss BL, O'Neill M, Wu Y, Aksoy S. OmpA-mediated biofilm formation is essential for the commensal bacterium Sodalis glossinidius to colonize the tsetse fly gut. Appl Environ Microbiol. 2012 Nov;78(21):7760-8. PubMed PMID: 22941073; PubMed Central PMCID: PMC3485708.

    c. Weiss BL, Wu Y, Schwank JJ, Tolwinski NS, Aksoy S. An insect symbiosis is influenced by bacterium-specific polymorphisms in outer-membrane protein A. Proc Natl Acad Sci U S A. 2008 Sep 30;105(39):15088-93. PubMed PMID: 18815366; PubMed Central PMCID: PMC2567497.

    d. Weiss BL, Mouchotte R, Rio RV, Wu YN, Wu Z, Heddi A, Aksoy S. Interspecific transfer of bacterial endosymbionts between tsetse fly species: infection establishment and effect on host fitness. Appl Environ Microbiol. 2006 Nov;72(11):7013-21. PubMed PMID: 16950907; PubMed Central PMCID: PMC1636136.

3. Symbiotic bacteria are intimately associated with the proper development and function of their host's immune system. We employ the tsetse fly, and it's two enteric microbes, as a model system for

studying the physiological mechanisms that underlie symbiont-mediated immune system development. The papers below indicate that tsetse must undergo larval development in the presence of it's endogenous microbes in order to present a functional immune system during adulthood. When these microbes are absent during larvagenesis, subsequent 'aposymbiotic' adults present 1) a severely compromised cellular immune system characterized by a conspicuously depleted population of hemocytes, and 2) a structurally compromised peritrophic matrix, which lines the flies gut and regulates pathogen infection establishment. This body of work broadens our knowledge of the factors that regulate trypanosome transmission in tsetse. Furthermore, the relative simplicity and cost-effectiveness of the tsetse model system makes it useful for deciphering the basic molecular mechanisms that underlie symbiont-mediated development and function of the animal immune system.

a. Benoit JB, Vigneron A, Broderick NA, Wu Y, Sun JS, Carlson JR, Aksoy S, Weiss BL. Symbiont-induced odorant binding proteins mediate insect host hematopoiesis. Elife. 2017 Jan 12;6PubMed PMID: 28079523; PubMed Central PMCID: PMC5231409.
b. Weiss BL, Savage AF, Griffith BC, Wu Y, Aksoy S. The peritrophic matrix mediates differential infection outcomes in the tsetse fly gut following challenge with commensal, pathogenic, and parasitic microbes. J Immunol. 2014 Jul 15;193(2):773-82. PubMed PMID: 24913976; PubMed Central PMCID: PMC4107339.
c. Weiss BL, Maltz M, Aksoy S. Obligate symbionts activate immune system development in the tsetse fly. J Immunol. 2012 Apr 1;188(7):3395-403. PubMed PMID: 22368278; PubMed Central PMCID: PMC3311772.
d. Weiss BL, Wang J, Aksoy S. Tsetse immune system maturation requires the presence of obligate symbionts in larvae. PLoS Biol. 2011 May;9(5):e1000619. PubMed PMID: 21655301; PubMed Central PMCID: PMC3104962.

4. Tsetse's commensal endosymbiont (*Sodalis* sp.) resides intra- and extracellularly within the fly's midgut. *Sodalis* is amenable to *in vitro* cultivation and genetic modification, making this bacterium a useful model for studying symbiont adaptation to iron and heme rich environments (tsetse feeds exclusively on vertebrate blood). These studies, which are the first of their kind in an insect endosymbiont, detail functional characterizations of *Sodalis'* iron and heme acquisition systems. Collectively this information increases our understanding of the basic biological mechanisms that underlie 1) bacterial adaptation to fluctuating environmental conditions, and 2) the maintenance of animal-bacterial symbioses, with specific emphasis on the tsetse-*Sodalis* system.

a. Smith CL, Weiss BL, Aksoy S, Runyen-Janecky LJ. Characterization of the achromobactin iron acquisition operon in Sodalis glossinidius. Appl Environ Microbiol. 2013 May;79(9):2872-81. PubMed PMID: 23435882; PubMed Central PMCID: PMC3623160.
b. Hrusa G, Farmer W, Weiss BL, Applebaum T, Roma JS, Szeto L, Aksoy S, Runyen-Janecky LJ. TonB-dependent heme iron acquisition in the tsetse fly symbiont Sodalis glossinidius. Appl Environ Microbiol. 2015 Apr;81(8):2900-9. PubMed PMID: 25681181; PubMed Central PMCID: PMC4375324.

5. Tsetse flies are the sole vectors of pathogenic African trypanosomes across sub-Saharan Africa. These parasites are the causative agents of human and animal African trypanosomiases (HAT and AAT, respectively), both of which are fatal if left untreated. Currently, no vaccines are available that prevent HAT or AAT, and control methods (trapping and pesticide application) are largely unsustainable. Acquiring a more complete understanding of the molecular mechanisms that underlie tsetse-trypanosome interactions will facilitate the development of novel disease control strategies. The work presented below provides insight into factors that mediate trypanosome colonization of tsetse's gut during crucial early infection processes.

a. Aksoy E, Vigneron A, Bing X, Zhao X, O'Neill M, Wu YN, Bangs JD, Weiss BL, Aksoy S. Mammalian African trypanosome VSG coat enhances tsetse's vector competence. Proc Natl

Acad Sci U S A. 2016 Jun 21;113(25):6961-6. PubMed PMID: 27185908; PubMed Central PMCID: PMC4922192.

b. Aksoy S, Weiss BL, Attardo GM. Trypanosome Transmission Dynamics in Tsetse. Curr Opin Insect Sci. 2014 Sep;3:43-49. PubMed PMID: 25580379; PubMed Central PMCID: PMC4286356.

c. Weiss BL, Wang J, Maltz MA, Wu Y, Aksoy S. Trypanosome infection establishment in the tsetse fly gut is influenced by microbiome-regulated host immune barriers. PLoS Pathog. 2013;9(4):e1003318. PubMed PMID: 23637607; PubMed Central PMCID: PMC3630092.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1RO1AI118789, NIH/NIAID Rio, Rita (PI) 06/01/15-05/31/19
Functional Differentiation of Tsetse Species Microbiota
The goal of this study is to increase our knowledge about tsetse species-specific microbiome integration, specifically as it relates to host metabolic physiology and vector competency.
Role: Co-Investigator

R15AI124105, NIH/NIAID Runyen-Janecky, Laura (PI) 08/01/16-07/31/19
Identifying and Characterizing Heme Tolerance Genes in the Tsetse Symbiont Sodalis glossinidius
The scientific goals of this project are to identify and characterize Sodalis heme tolerance genes, which encode proteins that protect the bacterium against toxicity from blood meal derived heme.
Role: Co-Investigator

Completed Research Support

5RO1AI051584, NIH/NIAID Aksoy, Serap (PI) 12/31/11-08/31/15
Molecular Aspects of Tsetse and Trypanosome Transmission
Study molecular basis of tsetse vector competence with a focus on the role of host immune pathways.
Role: Co-Investigator

R15AI094343-01A1, NIH/NIAID Laura Runyen-Janecky (PI) 08/01/12-07/31/15
Sodalis glossinidius Iron Acquisition
Acquiring a more complete understanding of the nature of the Sodalis-tsetse symbiosis will yield information to help control tsetse-borne disease. Furthermore, Sodalis is one of only a few intracellular insect symbionts to be cultured outside of the host. Thus, it may be useful as a model for studying the basic physiology of bacteria that present similar lifestyles.
Role: Co-Investigator

R21AI101456, NIH/NIAID Weiss, Brian (PI) 08/01/12-07/31/15
Symbiosis and Immunity in the Tsetse Fly
The goal of this study is to acquire a better understanding of the genetic mechanisms that underlie symbiont-induced immune system development in the tsetse fly.
Role: PI