

Faculty feature

**DR. DE'BROSKI
HERBERT**
Department of
Pathobiology



**PENN VET
HONORS & AWARDS
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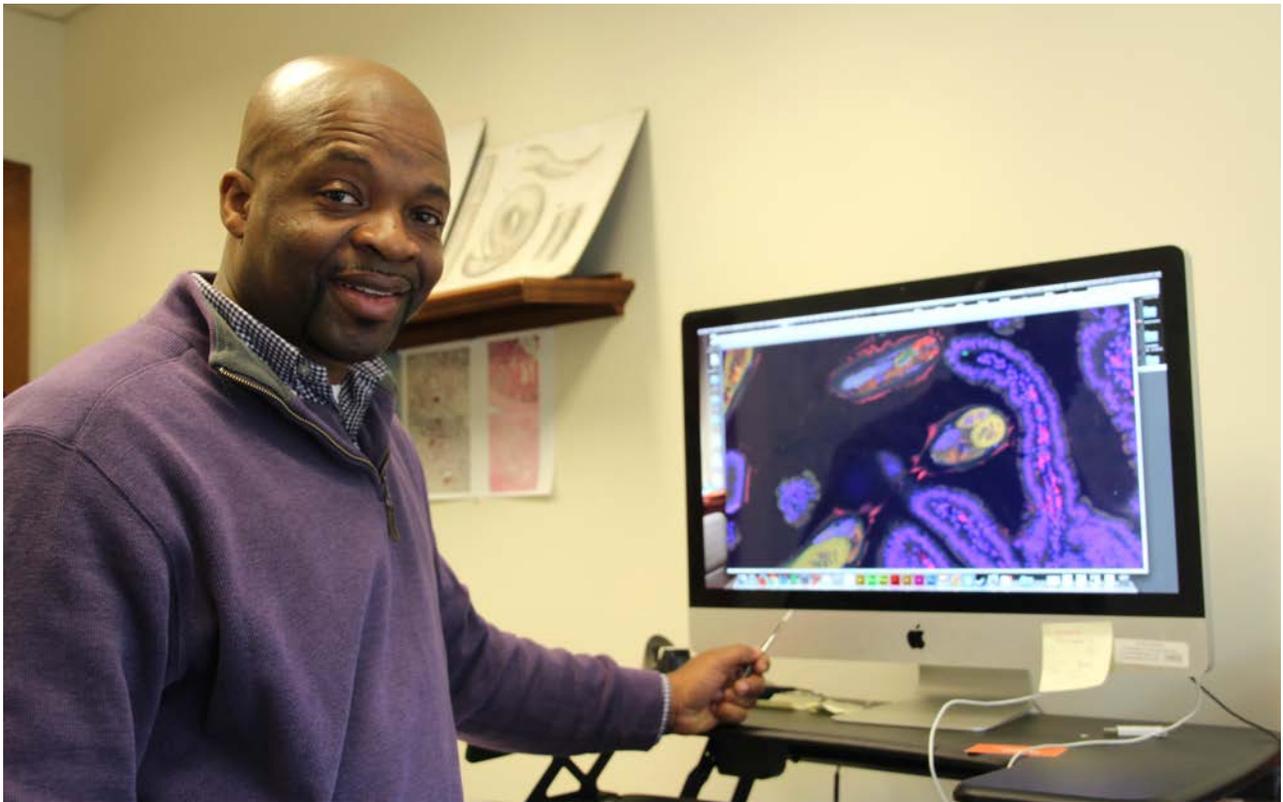


**STUDENTS MEET A
MENTOR NIGHT
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OLIVER GARDEN
New Chair in Clinical
Studies PHL PAGE 6

NEWSLETTER



Parasitic infections and chronic inflammatory disorders

Dr. De'Broski R. Herbert is an associate professor of infectious immunology in the Department of Pathobiology. Dr. Herbert received a B.S. in Microbiology from Xavier University of Louisiana in 1994. As an undergraduate Minority Access to Research Careers (MARC) scholar, he was provided the opportunity to conduct several summers of research at the University of California San Francisco (UCSF),

De'Broski Herbert is an associate professor in the Department of Pathobiology

where he worked on melanoma antigen-specific CD8⁺T cell responses and *Babesia microti* cysteine proteases. He received a Ph.D. in Immunology from Thomas Jefferson University in late 2000, where his research focused on the role of interleukin 5 and eosinophils in immunity against *Strongyloides stercoralis*. To fulfill a life-long dream, his post-doctoral work was done in South Africa at the University of Cape Town. During this time (2001-2005) he identified a fundamental role for alternative macrophage activation in host protection against *Schistosoma mansoni*. Dr. Herbert became a research instructor in 2006 at the University of Cincinnati and was promoted to tenure track assistant professor within the Immunobiology Department of the Cincinnati Children's Hospital in 2009. He was recruited to UCSF in the Department of Medicine in 2012 and following promotion to Associate Professor in 2016 was recruited to PennVet. Dr. Herbert's research interests are centered on the role of cytokines that control host immunity and tissue repair at mucosal sites in the context of gastrointestinal (GI) parasite infection.

The mucosal interface: Trefoil factor proteins regulate immunity and repair—

Parasitic helminth infections and chronic inflammatory disorders pose major challenges to worldwide health. Although infection-induced immune responses are critical for pathogen clearance, prolonged or uncontrolled immune responses can lead to excessive inflammation and tissue damage. Therefore, understanding the immunological mechanisms that underlie successful pathogen clearance as well as those that help resolve inflammation and prevent tissue damage are fundamental goals for successful therapeutic interventions that combat infectious and inflammatory diseases. While Type 2 cytokines (interleukins 4,5, 9 and 13, 25 and 33) are well-established drivers of host immunity against helminth infection, these cytokines fail to direct regeneration of damaged epithelial surfaces. The overarching theme for research in the Herbert laboratory is to characterize the potential immunoregulatory functions of endogenous repair molecules functioning at mucosal

Publications



Zhang K, Yin XF, Yang YQ, Li HL, Xu YN, Chen LY, Liu XJ, Yuan SJ, Fang XL, Xiao J, Wu S, Xu H, Chu L, Katlinski KV, Katlinskaya YV, Guo RB, Wei GW, Wang DC, Liu X, Fuchs SY. (2016) A potent in vivo anti-tumor efficacy of novel recombinant type I interferon. *Clin Cancer Res. clincanres.1386.2016*. [Epub ahead of print]



Bale T and Epperson CN (2017) Sex as a Biological Variable: Who, What, When, Why, and How (Review) *Neuropsychopharmacology* Volume 42, Issue 2, pp 386-396



Mason NJ, Gnanandarajah JS, Engiles JB, Gray F, Laughlin D, Gaurnier-Hausser A, Wallecha A, Huebner M, Paterson Y. (2016) Immunotherapy with a HER2-targeting *Listeria* induces HER2-specific immunity and demonstrates potential therapeutic effects in a Phase I trial in Canine Osteosarcoma. *Clin Cancer Res* 22 (17): 4380-90

barrier sites (skin, lung, and intestine) and to harness their effects therapeutically to prevent infection- and inflammation-induced tissue damage. Specifically, Dr. Herbert’s laboratory is intently focused on elucidating how Trefoil factor (TFF) proteins, which are enigmatic mucosal-cytokines, regulate the balance between inflammation and repair.

TFFs (TFF₁, TFF₂, TFF₃) are small, secreted motogenic proteins (6-18 kDa) that promote rapid movement of epithelia over denuded basement membrane[1] and mice deficient for *Tff1*, *Tff2*, or *Tff3* possess constitutive defects in GI barrier function[2-4]. Previous work from the Herbert lab demonstrated a critical role for TFF2 in driving IL-33 production for the initiation of Type 2 responses in the context of hookworm infection and allergic disease[5]. His group also demonstrated that TFF2 regulated both macrophage and dendritic cell function to attenuate Type 1 inflammation directed against the GI protozoa[3]. Currently, his group is involved in TFF receptor identification, as it remains unclear whether bona-fide receptors exist for any of the Trefoils. Notably, his group has identified a putative TFF₃ receptor candidate and has produced several gene-deficient mouse lines for *in vivo* study. In addition, the Herbert lab has developed both TFF₂ and TFF₃ long-acting agonists for collaborative studies focused on promotion of wound healing and the amelioration of chronic inflammation.

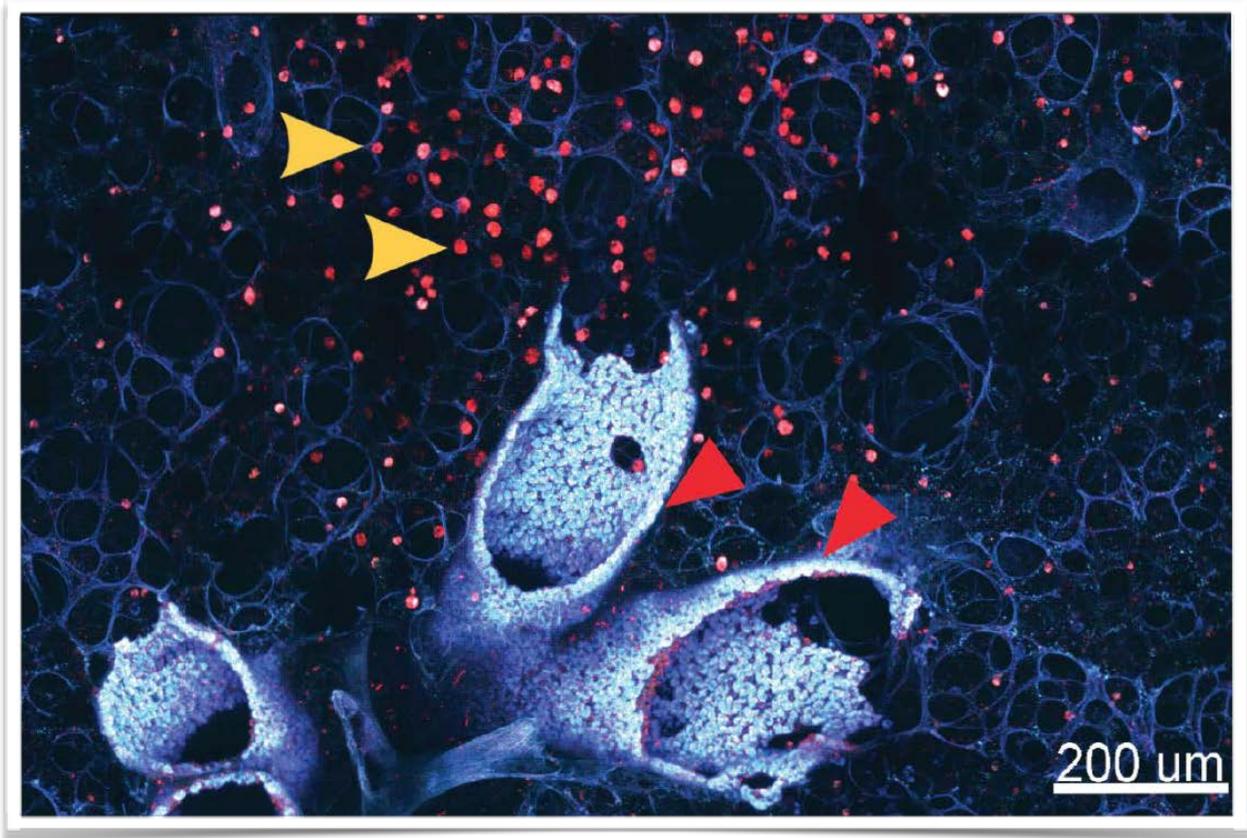


Figure 1 Representative confocal image shows Td-Tomato fluorescence within alveolar macrophages (yellow arrows) of a TFF2-Td-tomato reporter mouse at 4 days following infection with the hookworm *Nippostrongylus brasiliensis*. Red arrows point to small airway epithelia.

Honors & Awards



Phillip Scott

Ten professors from the University of Pennsylvania have been named **Fellows of the American Association for the Advancement of Science**. They are among a class of 391 members honored for their scientifically or socially distinguished efforts to advance science or its applications. Election as a Fellow of AAAS, the world’s largest scientific society, is an honor bestowed upon AAAS members by their peers. One of the ten named, **Phillip Scott, PhD**, is a professor of microbiology and immunology, Department of Pathobiology and vice dean for research and academic resources. He was honored for distinguished contributions to the field of microbiology, particularly for immunologic research that provides a foundation for developing new vaccines and immunotherapies for cutaneous leishmaniasis.

The **Penn Fellows Program** provides leadership development to select Penn faculty in mid-career. Begun in 2009, it includes opportunities to build alliances across the university, meet distinguished academic leaders, think strategically about university governance, and consult with Penn’s senior administrators. **Carolina López, PhD**, Department of Pathobiology, has been honored as a Penn Fellow starting in 2017. Dr. López has a new paper in *Vaccine* (Sun Y, and **López CB**. (2016) The innate immune response to RSV: Advances in our understanding of critical viral and host factors. *Vaccine* doi.org/10.1016/j.vaccine.2016.09.030.



Carolina López



Dan Ory of Washington University St. Louis with Charles Vite

Charles Vite, DVM, PhD, Department of Clinical Studies PHL, received an award from Global Genes, the RARE Champion of Hope for Collaborations in Science and Technology in Huntington Beach CA—the 5th annual tribute to champions of hope. **Global Genes** is a leading rare genetic disease advocacy organization. The award was for collaborative research involving Dr. Vite with Drs. Dan Ory, Steve Walkley, and Cristin Davidson on developing therapies for a lysosomal storage disease, and several family foundations for Niemann-Pick-C disease.

Continued from page 3

Regenerative macrophages: an enigmatic myeloid subset

While some macrophage subsets can prevent tissue damage by secreting Wingless-Int (Wnt) glycoproteins, a family of regenerative molecules that control epithelial cell proliferation, differentiation, and polarity[6], others produce epidermal growth factor (EGF), which in some instances, drives neoplastic growth. Thus, it is critical to identify the signals that control macrophage-specific production of each of these epithelial proliferative factors in order to harness them for therapeutic purposes. The recent generation of TFF2 fluorescent reporter mice by Dr. Herbert's group has provided new insight into this issue by revealing that TFF2 can be induced within alveolar macrophages at the nidus of *Nippostrongylus brasiliensis* infection-induced injury (Figure 1). In a recently submitted manuscript, Dr. Herbert and colleagues demonstrated that TFF2 promotes production of non-canonical Wnt ligands by alveolar macrophages, thereby preventing emphysematous pathology and promoting the expansion of epithelial progenitor cells. This study highlights the important role of macrophage-epithelial cell cross-talk in the context of tissue repair and identifies TFFs as potential therapeutic agents that could promote epithelial regeneration at the mucosal interface.

Lung injury and repair

Lung disorders affect millions worldwide, including sufferers of asthma, allergic rhinitis, bronchitis, COPD, lung cancer, emphysema, and pulmonary fibrosis[8]. Persistent epithelial cell injury caused by smoking, allergens, pollutants, particulates, and pathogens predisposes the development of chronic lung pathology. In fact, lung diseases were the 5th leading cause of death in the United States in 2001 and are predicted to be the 3rd leading cause by 2020 [9]. Clearly, there is a great need for understanding how inflammation and repair are regulated within the pulmonary tract. *continued on page 8*

Students organize 3rd annual Meet a Mentor Night



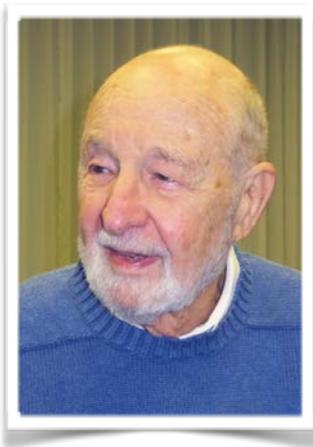
Emma Price, Emily Knebel, & Tanya Qiu



Students looking for a summer research experience were introduced to a broad range of opportunities at Penn. Students organized 20-minute rotating sessions with faculty members. Among the participating researchers at the fall event were: Carolina López, Oliver Garden, R. Duran-Struock, Rumela Chakrabarti, Montserrat Anguera, DeBroski Herbert, Narayan Avadhani, James Monslow, and Hansell Stedman.

Tracy Bale receives the Daniel H. Efron Research Award

Tracy Bale, PhD, professor of neuroscience in Penn Vet’s Department of Biomedical Sciences as been awarded the **Daniel H Efron Research Award** from the American College of Neuropsychopharmacology (ACNP). The award acknowledges outstanding basic research contributions to the field of neuropsychopharmacology. She was chosen for her role in deciphering the critical genes, circuits and epigenetic mechanisms that contribute to stress dysregulation as a risk factor in neurodevelopment and neuropsychiatric diseases. She used mouse models to investigate timing and sex specificity of early life events promoting disease susceptibility, the maturation of the brain during key development periods and the epigenetic mechanisms underlying enduring effects following stress exposure.



Robert R. Marshak, DVM’45, received the 2016 [Salmon Award](#) at Cornell on October 1, 2016. This is their highest honor for alumni of distinction. Dr. Marshak served as Dean of Penn’s School of Veterinary Medicine from 1973 to 1987, and continued to emphasize scientific excellence and professional integrity. He encouraged his faculty in both basic and clinical sciences to incorporate the latest findings into the curriculum. He was at the forefront of encouraging female student applicants to the School and hiring women as faculty. In 1990, Dr. Marshak was inducted into the prestigious National Academy of Medicine, one of very few veterinarians selected for that honor. His Penn students included former Cornell CVM Dean Michael Kotlikoff, VMD, who is now Provost for Cornell University. Dr. Kotlikoff said that "Bob Marshak was constantly on the lookout for students who he thought had promise to be the next generation of veterinary scientists, who could influence the profession."

Dr. Oliver Garden joins Penn Vet as chair of Clinical Studies-Philadelphia

—Oliver Garden, BSc, BVetMed, PhD has arrived at the University of Pennsylvania to assume his new role as chair of Penn Vet’s Department of Clinical Studies-PHL. Dr. Garden hails from the Royal Veterinary College, University of London, where he served as professor of comparative medicine and immunology and headed the Oncology Special Interest Group. He was also a clinician in the Queen Mother Hospital for Animals. Dr. Garden’s research focuses on regulatory T cells and myeloid-derived suppressor cells in dogs and mice, in both the healthy organism and in the context of autoimmune disease and cancer.



Funding Awards

(direct costs)

Montserrat Anguera
NIH/NIAID R21-A1124084-01A1 Expression of X-linked autoimmunity genes in B cells during female-biased autoimmunity
12/01/16- 11/30/18
\$275,000

Serge Y. Fuchs
NIH/NCI. R01-CA092900-15 Role of HOS in Cell transformation and Apoptosis
12/1/2016 —11/30/2021
\$1,068,750

Jorge Alvarez
Sub NIH R01 Regulation of Heme Oxygenase in HIV/HAND Pathogenesis
8/18/16-5/31/17 (5/31/21)
\$365,745

Charles Bradley
Int'l Society for Vet. Dermatopathology Discriminatory features of Wells-like syndrome and Sweets syndrome in dogs: A clinicopathological and immunohistochemical study
7/1/2016-6/30/17 \$4,976

Bruce Freedman
NIH R01 R56-A1125415 Calcium regulation of NF-kB
9/3/16-8/31/17 \$363,143

Chris Hunter
Sub to Univ of Colorado Molecular and cellular basis of Combined Adjuvant-Elicited Cellular Immunity
7/7/2016-6/30/17 \$799,969

Oriol Sunyer
Sub to USGS (Dept of Ag G16AC00332) Immune Reagent Network for Aquacultured species
9/1/16-5/31/19 \$92,281

Paula Henthorn
Scottish Deerhound Club of America. Next Step with Cystinuria research in Scottish Deerhounds
11/1/16-12/31/17 \$12,269

Anna Kraus-Gelzer
I4C Innovations incorporated feasibility of ambulatory monitoring of dogs with heart disease using a wearable health and wellness monitoring collars
11/1/16-11/1/17 \$6531

Anna Kraus-Gelzer
I4C Innovations Incorporated Validation of a wearable health and wellness monitor for blood pressure and respiratory rate recording in normal dogs
9/26/16-9/26/17 \$38,290

Mark Rondeau
Royal Canin The role of the microbiome in resolution of canine chronic enteropathy
1/1/17-12/31/18 \$141,987

James Serpell
ASPCA: Project support for the C-BARQ
10/13/16-10/13/17 \$10,000

James Serpell
Simon Foundation Analysis and publication of AOIS findings
9/30/16-9/29/18 \$25,000

Dorothy Brown
Merck Animal Health Study Evaluating Clinical Efficacy & Safety of MK-0674 in Dogs with Stifle Osteoarthritis Secondary to CCL Rupture & TPLO Surgery
10/1/16-10/1/18 \$273,997



In the news.....

Science Newsline, Medicine highlighted an article by Igor Brodsky

identifying a new mechanism for antibacterial immunity entitled "Activity of Uncleaved Caspase-8 Controls Anti-bacterial



Immune Defense and TLR-Induced Cytokine Production Independent of Cell Death". The study was coauthored by Penn Vet's Naomi H. Philip, Alexandra DeLaney, Lance W. Peterson, Melanie Sandos-Marrero, Jennifer T. Grier, Yan Sun, Meghan A. Wynosky-Dolfi, Erin E. Zwack, Baofeng Hu, Carolina López and Daniel Beiting; Jorge Henao-Mejia of Penn's Perelman School of Medicine; Tayla M. Olsen and Andrew Oberst of the University of Washington; Anthony Rongvaux of the Fred Hutchinson Cancer Research Center; and Scott D. Pope of the Yale University School of Medicine. *PLoS Pathog.* 2016 Oct 13;12 (10): e1005910.

Congratulations to Zhengxia Dou, professor of agricultural systems, for having her paper, "Closing yield gaps in China by empowering smallholder farmers," published in Nature.

Zhang W, Cao G, Li X, Zhang H, Wang C, Liu Q, Chen X, Cui Z, Shen J, Jiang R, Mi G, Miao Y, Zhang F, Dou Z. (2016) Closing yield gaps in China by empowering smallholder farmers. *Nature* 537: 671-674.



Dr. Herbert continued from page 5

Dr. Herbert and colleagues are investigating the cellular and molecular mechanisms that control production of Wnt, Trefoil, and EGF family proteins from distinct myeloid subsets within the lung for regeneration post-injury. Dr. Herbert envisions that identification of specific regenerative factors may lead to improved diagnostic indicators and/or novel therapeutic options for a spectrum of diseases affecting mucosal sites in both the clinical and veterinary realms.

Dr. Herbert's research is funded by the NIH/NIGMS (R01GM083204), NIAID (R01AI095289, U01AI125940) and the Burroughs Wellcome Fund. His laboratory is located in Old Vet 372 and his office in 369E.

References

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4. McBerry, C., et al., Trefoil factor 2 negatively regulates type 1 immunity against *Toxoplasma gondii*. *J Immunol*, 2012. 189(6): p. 3078-84.
5. Tomasetto, C. and M.C. Rio, Pleiotropic effects of Trefoil Factor 1 deficiency. *Cell Mol Life Sci*, 2005. 62(24): p. 2916-20.
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7. Clevers, H. and R. Nusse, Wnt/beta-catenin signaling and disease. *Cell*, 2012. 149(6): p. 1192-205.
8. Hogan, B.L., et al., Repair and regeneration of the respiratory system: complexity, plasticity, and mechanisms of lung stem cell function. *Cell Stem Cell*, 2014. 15(2): p. 123-38.
9. Minino, A.M., et al., Deaths: final data for 2008. *Natl Vital Stat Rep*, 2011. 59(10): p. 1-126.



The Penn Vet Research Newsletter is distributed Quarterly. Suggestions, requests, comments and story ideas may be directed to resnews@vet.upenn.edu

Phillip Scott, PhD, Office of the Vice Dean for Research and Academic Resources

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