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Biography:

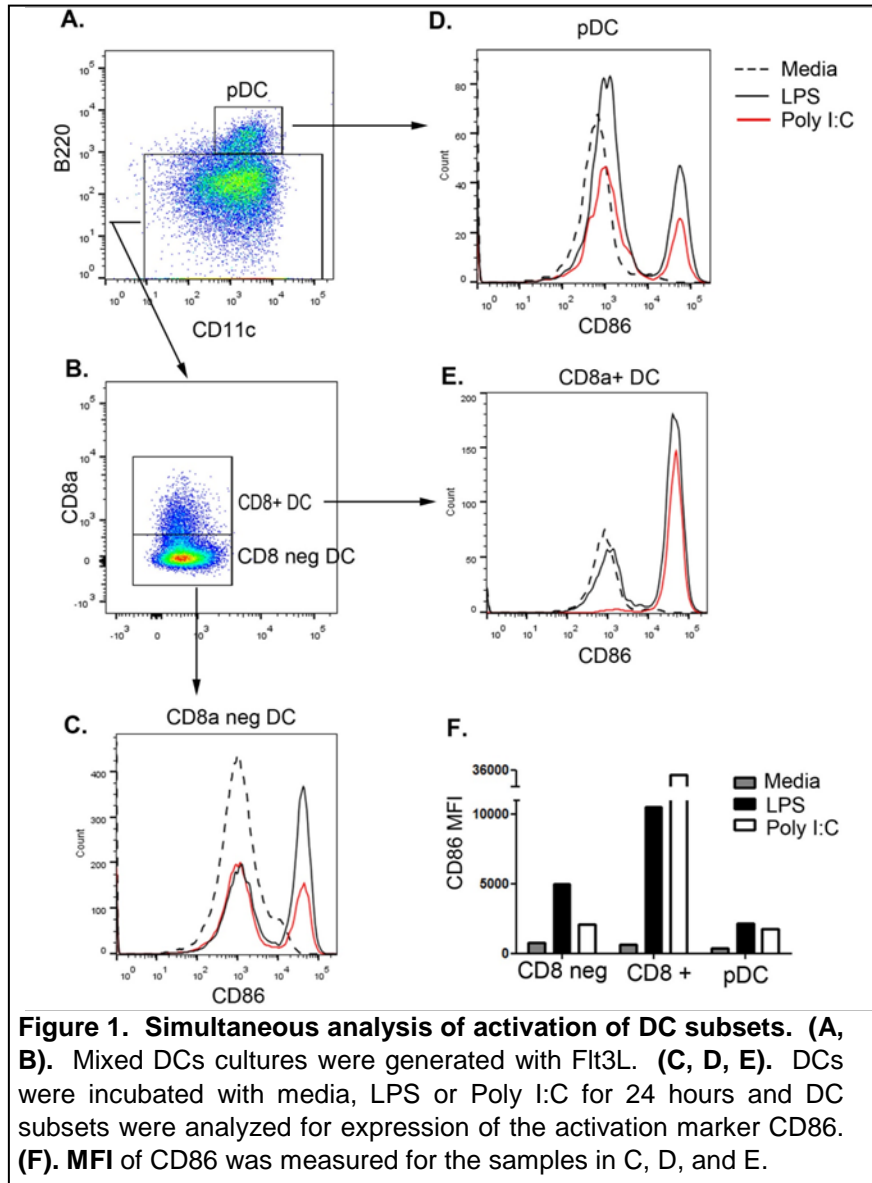
Steven B. Bradfute, Ph.D., is a Research Assistant Professor in the University of New Mexico Center for Global Health and Department of Internal Medicine. Dr. Bradfute received his Ph.D. in Immunology from Baylor College of Medicine (2005) and completed a postdoctoral fellowship at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), where he studied immune responses to hemorrhagic fever viruses (HFVs). HFVs are dangerous pathogens that include filoviruses (ebolaviruses and marburgviruses) and arenaviruses (such as Junín, Machupo, and Chapare viruses). HFVs can cause severe disease in humans, and there have been increases in HFV prevalence and geographical spread in recent years. As there are few treatments or vaccines available for many of these viruses, Dr. Bradfute is interested in basic immunology and vaccine development for HFVs. Current projects in the lab include modification of HFV immunogens for improved vaccines, development and testing of vaccines that generate cross-reactive immune responses against multiple HFVs, and determination of the mechanisms of immunity of efficacious HFV vaccines. He has existing collaborations with researchers at USAMRIID, the Los Alamos National Laboratory, and the National Institutes of Health.

Academic and research interests:

Dr. Bradfute has studied immunity to HFVs for over 10 years. His early work showed that the widespread lymphocyte apoptosis that occurs in lethal Ebola virus infection does not contribute to pathogenesis. At that time, it was accepted as fact that the massive lymphocyte apoptosis induced in lethal filovirus infection was the reason for a lack of adaptive immune responses. Together with Richard Hotchkiss at Washington University and Sina Bavari at USAMRIID, Dr. Bradfute defined the mechanistic pathways of lymphocyte apoptosis in Ebola virus infection, but more importantly, showed that inhibition of lymphocyte apoptosis did *not* result in protection from infection. Quite the opposite—transgenic animals that were protected from lymphocyte apoptosis not only died at the same time as wild-type animals, but also had higher levels of viremia and decreased CD8+ T cell responses (Bradfute et al., *Journal of Immunology* 184:327). During these studies, Dr. Bradfute found that contrary to dogma, there were activated CD8+ T cells generated in lethal Ebola virus infection, and that adoptive transfer of these cells from dying mice protected naïve mice from challenge (Bradfute et al., *Journal of Immunology* 180:4058). These findings were unexpected and altered approaches for vaccination and therapeutics. Dr. Bradfute has also found, through careful review of the literature and his own published work, that many of the Ebola virus vaccines that are protective in monkeys appear to utilize different immune cell subsets to generate protection, strongly suggesting that there is no

single mechanism of immunity in filovirus protection. These ideas have been expressed and defended in a number of reviews he has written (see *Human Vaccines* 7:701; *Viruses* 3:982).

Current work in Dr. Bradfute's lab focuses on improving experimental HFV vaccines by modification of HFV immunogens. By modifying the sequence or glycosylation of HFV glycoproteins used in vaccines, immunogenicity can be improved. Testing of HFV vaccine immunogenicity *in vitro* is conducted using a novel assay that determines activation of distinct dendritic cell subsets (Figure 1). *In vivo* vaccination in mice is also used to determine effects of modified HFV vaccines on antibody and T cell responses.



Key publications:

1. **Bradfute SB**, Anthony SM, Stuthman K, VanTongeren S, Wells J, Ayithan N, Tailor P, Bray M, Ozato K and Bavari S. Mechanisms of immunity in post-exposure vaccination against Ebola virus infection. *PLoS One* 2015 10(3):e0118434. PMID: 25785602
2. Ayithan N, **Bradfute SB**, Anthony SM, Stuthman K, VanTongeren S, Wells J, Tailor P, Bray M, Bavari S and Ozato K. Virus-like particles activate type I interferon pathways to facilitate post-exposure protection against Ebola virus infection. *PLoS One* 2015 10(2):e0118345. PMID: 25719445.
3. Ayithan N, **Bradfute SB**, Anthony SM, Bavari S, Bray M and Ozato K. Ebola virus- like particles stimulate type I interferons and proinflammatory cytokine expression through the toll-like receptor and interferon signaling pathways. *J Interferon Cytokine Res* 2014 34(2):79-89. PMID: 24102579.
4. **Bradfute SB**, Warfield KL, Bray M. Mouse models for filovirus infections. *Viruses* 2012 4(9):1477-1508 PMID: 23170168.
5. **Bradfute S**, Stuthman KS, Shurtleff AC and Bavari S. A STAT-1 knockout mouse model for Machupo virus pathogenesis infection. *Virology* 2011 8:300. PMID: 21672221
6. **Bradfute SB**, Dye JM Jr. and Bavari S. Filovirus vaccines. *Hum Vaccin* 2011 7:701-711. PMID:21519188.
7. **Bradfute SB** and Bavari S. Correlates of immunity to filovirus infection. *Viruses* 2011 3(7):982-1000. PMID: 21994766.
8. Konduru K, **Bradfute SB**, Jacques J, Manageeswaran M, Nakamura S, Wood SC, Bavari S and Kaplan GG. Ebola virus glycoprotein Fc fusion protein confers protection against lethal challenge in vaccinated mice. *Vaccine* 2011 29(16):2968-77. PMID: 21329775
9. **Bradfute SB**, Swanson PE, Smith MA, Watanabe E, McDunn JE, Hotchkiss RS and Bavari S. Mechanisms and consequences of Ebolavirus-induced lymphocyte apoptosis. *J Immunol* 2010 184(1):327-335. PMID: 20028660.
10. Panchal RG, **Bradfute SB**, Peyser BD, Warfield KL, Ruthel G, Lane D, Kenny TA, Anderson AO, Raschke WC and Bavari S. Reduced levels of protein tyrosine phosphatase CD45 protect mice from the lethal effects of Ebola virus infection. *Cell Host Microbe* 2009 6(2):162-173. PMID:19683682.
11. Warfield KL, **Bradfute SB**, Wells J, Lofts L, Cooper MT, Alves DA, Reed DK, Van Tongeren SA, Mech CA and Bavari S. Development and characterization of a mouse model for Marburg hemorrhagic fever. *J Virology* 2009 83(13):6404-6415. PMID: 19369350.
12. **Bradfute SB**, Warfield KL and Bavari S. Functional CD8+ T cell responses in lethal Ebola virus infection. *J of Immunol* 2008 180:4058-4066. PMID: 18322215
13. **Bradfute SB**, Braun DR, Shamblin JD, Geisbert JB, Paragas J, Garrison A, Hensley LE and Geisbert TW. Lymphocyte death in a mouse model of Ebola virus infection. *J Infect Dis* 2007 196:S296-304. PMID: 17940964

Book Chapters:

Bradfute SB, Bavari S, Jahrling PB, and Kuhn JH. (2013). Marburgviruses. In: *Viral Hemorrhagic Fevers*. (Singh S and Ruzek D, eds.). CRC Press Inc.

Shurtleff AC, **Bradfute SB**, Radoshitzky SR, Jahrling PB, Kuhn JH, and Bavari S. (2012). Arenaviruses: Hemorrhagic Fevers. In: *BSL3 and BSL4 Agents—Epidemiology, Microbiology, and Practical Guidelines* (Elschner MC, Cutler SJ, Weidmann M, and Butaye P, eds.). Wiley-VCH Verlag GmbH & Co. KGaA.