NAME OF FELLOWSHIP APPLICANT	POSITION TITLE
Austin Basil Bigley	Research Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) abbigley	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Houston	B.S. (Magna cum laude)	05/2008	Biology
University of Houston	Ph.D.	08/2014	Exercise Immunology

A. Personal Statement

I am a research assistant professor working in the laboratory of Dr. Richard Simpson at the University of Houston. I joined Dr. Simpson's lab in 2009 and was funded my first two years as a teaching fellow and my last three years as a research assistant working on NASA grant NNX12AB48G. In September 2015, I won a NSBRI First Award Fellowship and I am currently PI on NSBRI Project #PF04307. I am interested in spaceflight immunology and cancer immunotherapy using NK-cells, especially how exercise, spaceflight, and Cytomegalovirus (CMV) infection modulate NK-cell activity against hematologic malignancies. My goal is to understand the mechanisms underlying the effects of exercise, spaceflight, and CMV infection on the phenotype, cytotoxicity, proliferative capacity, and persistence of NK-cells with an eye toward developing adjuvants for allogeneic adoptive transfer of NK-cells. Over the course of my academic career, I have acquired expertise in cell culture techniques, cytotoxicity assays, and flow cytometry methods that have led to multiple publications in prestigious peer-reviewed journals.

B. Positions and Honors

Positions and Employment

ACTIVITY/OCCUPATION	BEGINNING DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/COMPANY	SUPERVISOR/ EMPLOYER
Tissue Collection Specialist	08/08	05/10	Organ/tissue procurement	Lifegift	Mark W. Roth
X-ray Tech. / Billing coordinator	08/08	01/13	Clinic	Northshore Occ. Medical Clinic	Maximo Roth, M.D.
Teaching Fellow	08/09	08/11	Education	University of Houston	Richard Simpson, Ph.D.
Research Assistant	08/11	08/2014	Exercise Immunology	University of Houston	Richard Simpson, Ph.D.
Post-Doc	08/14	10/15	Space Immunology	University of Houston/ NASA	Richard Simpson, Ph.D.
NSBRI First Award Fellow	10/15	Present	Space Immunology	University of Houston/ NASA (NSBRI)	Richard Simpson, Ph.D.

Professional Memberships

2012- Member, Psychoneuroimmunology Research Society

2012- Member, American College of Sports Medicine

Honors

2010	NSF Graduate Research Fellowship Program Honorable Mention
2011	NSF Graduate Research Fellowship Program Honorable Mention
2011	College of Liberal Arts and Social Sciences Research Assistant Stipend Award for 2011-2012
2013	Invited to review manuscript for special issue of *Brain, Behavior & Immunity: Exercise Immunology in Health and Disease*
2014	Excellence in Research Award Finalist, M.D. Anderson Energy Balance and Cancer Research Retreat
2015	Invited to review manuscript for the *International Journal of Sport Nutrition*
2015	Invited to review manuscript for the *Exercise Immunology Review*
2015	National Space Biomedical Research Institute First Award Fellowship
2016	Abstract reviewer for the M.D. Anderson Energy Balance and Cancer Research Retreat
2016	Invited to review manuscript for *Medicine & Science in Sports & Exercise*
2016	Invited presentation at the University of Calgary, Human Performance Laboratory Seminar, Sports Medicine Centre, Calgary, AB, Canada.
2016	Invited to review manuscript for *Cellular Immunology*

C. Contribution to Science

1. I have published extensively on the redeployment of specific lymphocyte subsets with exercise and how this process is effected by aging and CMV. These publications showed how latent infection with a herpesvirus can have marked effects on the fight-or-flight response. For example, I showed for the first time that the exercise-induced mobilization of NK-cells, the most exercise-responsive lymphocyte subset, was markedly lower in CMV-seropositive individuals and that NK-cell inhibitory receptor expression was much lower in those with CMV. We also showed that CMV infection protects the old from contraction of CD8+ T-cells and is associated with a marked increase in the redeployment of highly-differentiated CD8+ T-cells, particularly in the old. In all of these studies, I did the flow cytometry analysis to identify specific lymphocyte subsets (i.e. NK-cells, T-cells, gammadelta T-cells, etc.) and subtypes based on differentiation status (i.e. expression of specific inhibitory/activating receptors and maturity markers). These studies opened the door to new studies investigating the effects of CMV and exercise on NK-cell function with an eye towards clinical application.

a. **Bigley, A.B.,** Lowder, T.W., Spielmann, G., Rector, J.L., Pircher, H., Woods, J.A., and Simpson, R.J. (2012). NK-cells have an impaired response to acute exercise and a lower expression of the inhibitory receptors KLRG1 and CD158a in humans with latent cytomegalovirus infection. *Brain Behav Immun* 26(1), 177-186.

b. Simpson, R.J., Lowder, T.W., Spielmann, G., **Bigley, A.B.,** LaVoy, E.C., and Kunz, H. (2012). Exercise and the aging immune system. *Ageing Res Rev* 11(3), 404-420.

c. **Bigley, A.B.,** Spielmann, G., LaVoy, E.C., and Simpson, R.J. (2013). Can exercise-related improvements in immunity influence cancer prevention and prognosis in the elderly? *Maturitas* 76(1), 51-56.

d. Pistillo, M., **Bigley, A.B.,** Spielmann, G., LaVoy, E.C., Morrison, M.R., Kunz, H., and Simpson, R.J. (2013). The effects of age and viral serology on gammadelta T-cell numbers and exercise responsiveness in humans. *Cell Immunol* 284(1-2), 91-97.

e. Lavoy, E.C., **Bigley, A.B.,** Spielmann, G., Rector, J.L., Morrison, M.R., O'Connor, D.P., and Simpson, R.J. (2014). CMV Amplifies T-cell Redeployment to Acute Exercise Independently of HSV-1 Serostatus. *Med Sci Sports Exerc* 46(2), 257-267.

f. Brown, F.F., **Bigley, A.B.,** Sherry, C., Neal, C.M., Witard, O.C., Simpson, R.J., and Galloway, S.D. (2014). Training status and sex influence on senescent T-lymphocyte redistribution in response to acute maximal exercise. *Brain Behav Immun* 39, 152-159.

g. Spielmann, G., Bollard, C.M., **Bigley, A.B.,** Hanley, P.J., Blaney, J.W., LaVoy, E.C., Pircher, H., and Simpson, R.J. (2014). The effects of age and latent cytomegalovirus infection on the redeployment of CD8+ T cell subsets in response to acute exercise in humans. *Brain Behav Immun* 39, 142-151.

h. **Bigley, A.B.,** Spielmann, G., Agha, N., and Simpson, R.J. (2015). The effects of age and latent cytomegalovirus infection on NK-cell phenotype and exercise responsiveness in man. *Oxid Med Cell Longev*, Article ID 979645.

i. Brown, F.F., **Bigley, A.B.,** Ross, J.C., LaVoy, E.C., Simpson, R.J., and Galloway, S.D. (2015). T-lymphocyte populations following a period of high volume training in female soccer players. *Physiol Behav* 152, 175-181.

j. Simpson, R.J., **Bigley, A.B.,** Spielmann, G., LaVoy, E.C.P., Kunz, H., and Bollard, C.M. (2016). Human cytomegalovirus infection and the immune response to exercise. *Exer Immunol Rev* 22, 8-26.

2. My more recent work has focused on how exercise and CMV affect NK-cell anti-tumor cytotoxicity. Previous studies had shown that NK-cells were highly mobilized by exercise and that killing of the HLA-deficient K562 cell line was transiently increased immediately post-exercise. This increase in cytotoxicity was due exclusively to an increase in NK-cell number post-exercise as there was no change in cytotoxicity per NK-cell. It was not known, however, how differentiation status effects the redeployment of NK-cells with exercise or how exercise affects NK-cell cytotoxicity against HLA-expressing tumor cell lines. I showed for the first time that acute aerobic exercise preferentially redeploys highly-differentiated NK-cells and that NK-cell cytotoxicity per cell is increased against HLA-expressing tumor cell lines during exercise recovery. Further, I was able to mechanistically link these changes in cytotoxicity to exercise-induced shifts in the proportion of NK-cells expressing activating and inhibitory receptors for specific HLA expressed by target cells. Given the importance of NK-cell receptor/HLA interactions to NK-cell cytotoxicity and the known perturbations in NK-cell inhibitory and activating receptor expression with CMV infection, I expanded on these findings by investigating the effect of latent CMV infection on NK-cell cytotoxicity against a variety of HLA-expressing tumor cell lines. I showed that CMV seropositivity was associated with a marked increase in NK-cell cytotoxicity against tumor cell lines expressing HLA-E, the natural ligand for NKG2C. This effect was proportionate to the magnitude of target cell HLA-E expression with the largest effect being seen in those target cells with the highest HLA-E expression. I also showed that NKG2C+ NK-cells are poorly exercise responsive and that accumulation of these cells was associated with a markedly blunted exercise-induced redeployment of NK-cells in those infected with CMV. In addition, I was able to show that the increase in NK-cell cytotoxicity against HLA-expressing tumor cell lines during exercise recovery was only seen in CMV-seronegative individuals. Collectively, these findings show that both exercise and CMV have cytotoxicity enhancing effects on NK-cells that can potentially be harnessed for clinical use.

a. **Bigley, A.B.,** Rezvani, K., Chew, C., Sekine, T., Pistillo, M., Crucian, B., Bollard, C.M., and Simpson, R.J. (2014). Acute exercise preferentially redeploys NK-cells with a highly-differentiated phenotype and augments cytotoxicity against lymphoma and multiple myeloma target cells. *Brain Behav Immun* 39, 160-171.

b. **Bigley, A.B.,** Rezvani, K., Pistillo, M., Reed, J., Agha, N., Kunz, H., O'Connor, D.P., Sekine, T., Bollard, C.M., and Simpson, R.J. (2015) Acute exercise preferentially redeploys NK-cells with a highly-differentiated phenotype and augments cytotoxicity against lymphoma and multiple myeloma target cells. Part II: Impact of latent cytomegalovirus infection and catecholamine sensitivity. *Brain Behav Immun* 49, 59-65.

c. **Bigley, A.B.** and Simpson, R.J. (2015). NK-cells and Exercise: Implications for cancer immunotherapy and survivorship. *Discov Med* 19(107), 433-445.

d. **Bigley, A.B.,** Spielmann, G., Agha, N., O'Connor, D.P., and Simpson, R.J. (2016). Dichotomous effects of latent CMV infection on the phenotype and functional properties of CD8+ T-cells and NK-cells. *Cell Immunol* 300, 26-32.

e. **Bigley, A.B.,** Rezvani, K., Shah, N., Sekine, T., Balneger, N., Pistillo, M., Agha, N., Kunz, H., Bollard, C.M., and Simpson, R.J. (2016). Latent CMV infection enhances anti-tumor cytotoxicity through accumulation of NKG2C+ NK-cells in healthy humans. *Clin Exp Immunol* 185, 239-251.

D. Research Support

Ongoing Research Support

NASA NNJ10ZSA003N Simpson (PI) 10/01/2011-9/30/2016

"Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity"

The goal of this flight definition study is to examine the effects of spaceflight on salivary and blood markers of innate immunity. Samples are being collected from astronauts before, during (on the international space station) and after a 24-week spaceflight mission. I am responsible for the determination of NK-cell phenotype and function before, during, and after spaceflight.

Role: **Co-Investigator**

NASA NNJ14ZSA001N-FLAGSHIP Simpson (PI) 9/01/2015-10/31/2017
"The impact of simulated microgravity and acute radiation exposure on cytomegalovirus reactivation and host immune evasion"
This project utilizes the rotating wall vessel cell culture analog to determine the impact of simulated microgravity and acute gamma ray exposure on CMV infectivity and reactivation and its ability to evade the host immune system.
Role: **Co-Investigator**

NSBRI Project #PF04307 10/01/2015-9/30/2016
"The Role of Microgravity and Stress-Related Humoral Factors in Dysregulated NK-Cell Function during Spaceflight"
This project will determine the impacts of simulated microgravity and stimulation with flight-derived serum on autologous NK-cells in order to provide insight into the mechanisms underpinning decreased NK-cell function during spaceflight.
Role: **Principal Investigator**

NASA Functional Immune Simpson (PI) 2/01/2016-1/30/2019
"The Impact of an ISS Mission on the Anti-viral and Functional Properties of NK-cells, T-cells, B-cells and Dendritic Cells"
This project will determine the impacts of spaceflight on NK-cell expansion/anti-viral cytotoxicity, viral-specific T-cell proliferation/cytokine release, and dendritic cell differentiation/antigen processing using cutting edge technology, such as the CyTOF and SPADE techniques.
Role: **Co-Investigator**

NIH R21 CA197527-01A1 Rezvani and Simpson (PI)
"CMV infection and NK-cell therapy for multiple myeloma 7/01/2016-6/30-2018
This project will determine the impact of CMV infection and NKG2C+/NKG2A- NK-cell expansion on rate of remission in multiple myeloma patients treated with autologous hematopoietic stem cell transplant. A secondary aim of this study is to preferentially expand NKG2C+/NKG2A- NK-cells *ex vivo* in order to target patient-derived multiple myeloma.
Role: **Co-investigator**