

### BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Alicia L. Bertone		POSITION TITLE Professor, Diplomate American College of Veterinary Surgeons, Diplomate American College of Veterinary Sports Medicine and Rehabilitation	
eRA COMMONS USER NAME (credential, e.g., agency login) Bertone04			
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)	MM/YY	FIELD OF STUDY
Cornell University	B.Sc.	1977	Ag & Life Sciences
Cornell University	D.V.M.	1982	Veterinary Medicine
Colorado State University	M.Sc.	1986	Surgery, Joint Pathology
Colorado State University	Ph.D.	1987	Biomedical Sciences
Center for Molecular Orthopedics, Harvard University	Fellowship	2002	Gene Therapy

#### A. Personal Statement

Dr Bertone is the Director of the Comparative Orthopedic Research Laboratories that serves the College of Veterinary Medicine and College of Medicine programs in the Dept of Orthopedics, the Sports Medicine Center at The Ohio State University. The focus of the laboratory's research has been the progressive translation of basic science in the area of molecular engineering, cell therapy, and orthobiologic therapies, preclinical models of regenerative orthopedics, and equine orthopedic research. Dr Bertone has had an interest in cell therapy for the musculoskeletal system and designed and patented the first commercial-grade equine microarray (equine GeneChip). Dr Bertone directs a robust, highly productive, and interactive graduate training program that has consistently produced translational scientists that are leaders in the field. Her students are well trained in comparative and translational science in orthopedics, engineered stem cell therapy, and preclinical models of bone and joint disorders. Dr Bertone has published over 170 peer reviewed original scientific papers, 325 abstracts and 175 proceedings and is one of the most well funded researchers in the College of Veterinary Medicine. Dr Bertone is still a practicing veterinary surgeon on a limited basis.

#### B. Positions and Honors

##### Positions and Employment

10/1987-10/1989 – Veterinary Surgeon, Assistant Professor, Dept of Clinical Sciences, School of Veterinary Medicine, Louisiana State University  
 10/1989-present – Veterinary Surgeon, Assistant, Associate, Professor, Dept of Veterinary Clinical Sciences, The Ohio State University  
 1/2000-present – Professor, Dept Orthopedics, College of Medicine, The Ohio State University  
 1/2001-present – Investigator, Davis Heart and Lung Research Institute, The Ohio State University  
 12/2001 -Trueman Family Endowed Chair, Director Comparative Orthopedic Research Laboratories, College of Veterinary Medicine, The Ohio State University.  
 10/2007 – 2010 – Assistant Director of Basic Science & Industry Research, The Ohio State University Sports Medicine Center  
 2/2013- Comparative Medicine (CM) Special Emphasis Panel (SEP), NCATS (National Center for Advancing Translational Sciences, NIH.  
 5/2014- Special Emphasis Panel NIH/NCATS Loan Repayment Program (LRP-Clinical Research and LRP – Pediatric Research).  
 9/2015- Panelist NIH/CRS IMST-80 K01 and T35 Mentored Training in Comparative Medicine  
 10/2015- Reviewer NIH/NCATS CTSA X02, Oct 26, 2015

### **Patents**

1998 U.S. Patent Number 5799660 (Bertone AL – Sole Inventor); 2005 PCT International Application File #18525/04130; 2012 International patent application 2011PCT/US/2010/056702 (Bertone AL – Sole Inventor)

### **Honors (Selected)**

Distinguished Alumni Speaker Cornell University Centennial Conf  
Invited Speaker World Veterinary Congress, Japan  
National Gamma Award in recognition to distinguished service to the veterinary profession;  
Pfizer Research Award  
Charles C. Capen Teaching Excellence Award for Graduate Education

### **Commercialization**

Equine Microarray (Gene Chip), OSU as Service Provider Nationally for Processing, Ohio Third Frontier Commercialization Proposals 2009, 2010 for a Cell Commercialization facility at OSU. Holds 2 patents, one expired and one on use of xenogeneic cells.

### **C. Selected Peer-reviewed Publications (Selected from >175 peer-reviewed publications)**

1. Mari Kaido, Allison H. Kilborne, Joy L. Sizemore, Natalie A. Reisbig, Turi K. Aarnes, **Alicia L. Bertone**. Effect of repetition within trials and frequency of trial sessions on quantitative parameters of vertical peak force in horses with naturally occurring lameness. Accepted, Am J Vet, Res, 2015.
2. Lauren N. Mundy, BS; Akikazu Ishihara, BVSc, PhD; Maxey L. Wellman, DVM, PhD; **Alicia L. Bertone, DVM, PhD**. Characterization of gravitational filtration to enrich selective equine bone marrow elements. Am J Vet Res 2015; 76(6):561-9.
3. Juan E. Santiago-Torres, Rebecca Lovasz, **Alicia L. Bertone**. Fetal vs Adult mesenchymal stem cells achieve greater gene expression, but less osteoinduction. World J Stem Cells, 2015 January 26;7(1):223-234.
4. Santangelo KS, Kaeding AC, Baker SA, **Bertone AL**. Quantitative Gait Analysis Detects Significant Differences in Movement Between Osteoarthritic and Nonosteoarthritic Guinea Pig Strains Before and After Treatment with Flunixin Meglumine. Arthritis, 2014; 2014:503519
5. Ishihara A, Weisbrode SE, **Bertone AL**. Autologous implantation of BMP2-expressing dermal fibroblasts to improve bone mineral density and architecture in rabbit long bones. J Orthop Res, 2014
6. Ishihara A, Ohmine K, Weisbrode SE, **Bertone AL**. Effect of Intra-Medullar and Intra-Venous Infusions of Mesenchymal Stem Cells on Cell Engraftment by *In-Vivo* Cell Tracking and Osteoconductivity in Rabbit Long Bones. Orthop Muscular Syst 2014; Nov 3(3)
7. **Alicia L. Bertone, DVM, PhD, DACVS**; Akikazu Ishihara, BVSc, PhD; Lisa J. Zekas, DVM, DACVR; et al.. Evaluation of a single, intra-articular injection of autologous protein solution (APS) for treatment of osteoarthritis in horses. Am J Vet Res 75(2):141-51, 2014.
8. Hayam Hussein, Akikazu Ishishara, Maria Menendez, **Alicia Bertone**. Pharmacokinetics and bone resorption evaluation of a novel Cathepsin K inhibitor (VEL-0230) in healthy adult horses. J Vet Pharmacol Ther 2014 Dec;37(6):556-64.
9. Fahie MA, Ortolano GA, Guercia V, Schaffer JA, Johnston G, Au J, Hettlich BA, Phillips T, Allen MJ, **Bertone AL**. A randomized controlled trial of the efficacy of autologous platelet therapy for the treatment of Osteoarthritis in dogs. J Am Vet Med Assoc 243:1291-7, 2013.
10. Ng VY, Jump SS, Santangelo KS, Russell DR, **Bertone AL**. Genetic engineering of juvenile human chondrocytes improves scaffold free mosaic neocartilage grafts. Clin Orthop Rel Res, Epub ahead of Print, Sept 25, 2012; Clin Orthop Relat Res (2013) 471:26–38. PMC3528904
11. K.S. Santangelo, G.J. Nuovo, **A.L. Bertone**. In vivo reduction or blockade of interleukin-1b in primary osteoarthritis influences expression of mediators implicated in pathogenesis. Osteoarthritis Cartilage 20:1610-1618, 2012. PMC3478416
12. Seth S. Jump, David S. Smith, David C. Flanigan, **Alicia L. Bertone**. Immunoresponse to allogeneic synovial or xenogeneic mesenchymal stromal cells in a co-culture model. Open J Cell Biol. 2012;2(1):1-9. Published on line, doi:10.4236/ojcb.2012 (<http://www.scirp.org/journal/ojcb>), 2012.

13. John H. Pigott, Akikazu Ishihara, Maxey L. Wellman, Duncan S. Russell, **Alicia L Bertone**. Investigation of the immune response to autologous, allogeneic, and xenogeneic mesenchymal stem cells after intra-articular injection in horses. *Vet.Immunol. Immunopathol.* 26(6):453-60, 2013.
14. Akikazu Ishihara and **Alicia L Bertone**. Cell-mediated and direct gene therapy for bone regeneration. *Expert Opin Biol Ther.* 2012 Apr; 12 (4):411-23;
15. Akikazu Ishihara, Jeffrey S. Bartlett, **Alicia L. Bertone**: Inflammation and immune response of intra-articular serotype-2 adeno associated virus or adenovirus vectors in a large animal model. *Arthritis*, (2012) 2012:4375402 EPUB Jan 11. PMC3263587
16. K.S. Santangelo, **A.L. Bertone**. Effective reduction of the interleukin-1 $\beta$  transcript in osteoarthritis-prone guinea pig chondrocytes via short hairpin RNA mediated RNA interference influences gene expression of mediators implicated in disease pathogenesis. *Osteoarthritis Cartilage* (2011) 19(122):1445-57. PMC3256924
17. M. I. Menendez, D.J. Clark, M. Carlton, D.C. Flanigan, G. Jia, S. Sammet, S.E. Weisbrode, M.V. Knopp, **A.L. Bertone**. Direct Delayed Human Adenoviral BMP-2 or BMP-6 Gene Therapy for Bone and Cartilage Regeneration in a Pony Osteochondral Model. *Osteoarthritis Cartilage* 19 (2011) 1066-1075. PMID: 21683796
18. K.S. Santangelo, E.M. Pieczarka, G.J. Nuovo, S.E. Weisbrode, **A.L. Bertone**. Temporal expression and tissue distribution of interleukin-1 $\beta$  in two strains of guinea pigs with varying propensity for spontaneous knee osteoarthritis. *Osteoarthritis Cartilage* Apr;19(4):439-48, 2011. PMC3073778
19. Pigott J, Ishihara A, Wellman ML, Russell D, **Bertone AL**. Inflammatory effects of autologous, genetically modified autologous, allogeneic, and xenogeneic mesenchymal stem cells after intra-articular injection in horses, *Vet Comp Orthop & Traumatol*, 26:2013.
20. Robert T. Gorsline, Prasam Tangkawattana, John J. Lannutti, Mamoru Yamaguchi, Christopher C. Kaeding, **Alicia L. Bertone**. Accelerated chondrogenesis in nanofiber polymeric scaffolds embedded with BMP-2 genetically engineered chondrocytes. *J. Biomedical Science and Engineering*, 2010, 3, 908-916.
21. Sally E. Henderson BS, Kelly S. Santangelo DVM, and **Alicia L. Bertone** DVM, PhD. Roles of retinoic acid and a retinoic acid antagonist (LE135) in chondrogenesis of equine bone marrow derived mesenchymal stem cells and chondrocytes, *Am J Vet Res*, (2011) Jul;72(7):884-92.
22. Sarah S. Dougherty, Kelly S. Santangelo, **Alicia L. Bertone**. Evaluation of Accell™ or Lipofectamine™2000 to deliver small interfering RNA molecules to equine and guinea pig cartilage *in vitro*. *Am J Vet Res*, 72 (6):813-819, 2011. PMID: 21627528
23. Akikazu Ishihara, Lisa J Zekas, Steven E. Weisbrode, **Alicia L Bertone**. Comparative efficacy of dermal fibroblast-mediated and direct adenoviral bone morphogenetic protein-2 gene therapy for bone regeneration in an equine rib model. *Gene Therapy*, June 17 (6): 733-44, 2010. PMID: 20220786

## D. Research Support

### Ongoing Support

- 2016-17 Anacura. Synovial fluid cytokine analysis in stem cell treated OA joints using a novel articular fracture model in horses. (April 1 – March 31 2017) Role; PI
- 2015-16 ArthroDynamics. Effect of polyglycan treatment on lipopolysaccharide-challenged synovial cells in vitro. (Feb 20, 2015- Feb 19, 2016) Role: PI
- 2013-15 Elanco, Inc. Topical Application of Fentanyl for Musculoskeletal Pain Management in horses. (Oct 1, 2013- Sept 30, 2014) Role: PI
- 2013-15 Biomet Veterinary, Inc. Pilot Clinical Trial on the Use of Intra-articular Autologous Protein Solution to Improve Lameness in Dogs with Osteoarthritis. Sponsored Research Project. (April 1 2013- Sept 1 2014) Role: PI

2012-15 DSCD, LLC. Clinical Stem Cell Study for musculoskeletal conditions. The goal of this study is to characterize a novel cell source for markers of stemness, viability and differentiation capacity, complete a dose escalation study, initial safety study, and prospective clinical efficacy study for use in OA, tendonitis and desmitis. Role: PI

2012-2017 USEF. Discovery of biomarkers for neuromuscular blocking agents in horses. (\$250,000) (09/01/2012 – 08/31/17) The goal of this study is to evaluate biologic fluids (blood, urine and spinal fluid) for markers that signal effects of compounds used as calming agents in sport horses. Role: PI

2012-2015 Freestride Therapeutics, Inc. Bone Remodeling efficacy of VEL-0230 pharmaceutical in exercising horses. (\$184,084.00) (06/01/2012-05/31/13) The goal of this study is to determine the bone remodeling and osseous anti-inflammatory effects of this novel cathepsin K inhibitor. Role: PI

2012-2014 Freestride Therapeutics, Inc. Dosing Interval – Pharmacology Study of VEL-0230 pharmaceutical in exercising horses. (\$57, 581.00) (06/01/2012 – 05/31/13). The goal of this study is to determine the optimal interdosing interval of a cathepsin K activator using bone biomarkers. Role: PI

2012-2013 PALL Corp. Characterization and Performance of Stem Cells Isolated Using a Novel Filtration System. (\$66, 252.00) (04/15/12 – 04/14/13) The goal of this study is to characterize the cell populations of the concentrated bone marrow product obtained after using a filtration system. Role: PI

2011-2012 Biomet Biologics, Inc. Autologous Solution Derived From Whole Blood in Treatment of Horses with Osteoarthritis. (\$291,417) (03/31/11-03/30/12). The goal of this study was to complete a placebo controlled clinical trial to prove efficacy of this novel blood product in the treatment of pain of OA. Role: PI

### **Completed Research Support (selected)**

2010-2011 PALL Corp. Pilot study using filtered Platelet Concentration as therapy for OA in dogs. (\$35,000) (06/01/10-05/31/11)

2010-2011 Biomet Biologics, Inc. ASC Comparison of BMA Needle Designs. (\$79,479.00) (05/01/10-04/30/11)

2011-2013 Biomet Biologics, Inc. Autologous Blood Solution for intra-articular treatment of osteoarthritis. (\$268,500.00) (04/01/11 – 03/31/13)

3K08AR049201-05S1 Bertone (PI) National Institutes of Health/NIAMS Administrative Supplement. Gene Therapy for Cartilage Injury. 04/01/04-8/31/10.

Sponsored Research Agreement. Bertone (PI) Velcura, Inc. (Sponsor) Pharmacokinetics of a new bone remodeling drug for use in sport horses. (09/15/09-09/14/10)

Sponsored Research Agreement and Foundation Gift, Bertone (PI), 08/08-07/09  
Pfizer Animal Health – Equine Business Unit and United States Equestrian Federation. Pharmacokinetics of Intra-articular medications in Exercising Horses

Sponsored Research Agreement Bertone (PI) 4/1/08-3/31/09 Pluripotentiality and Chondrogenic Potency of a New Stem Cell.

Program Director/Principal Investigator (Last, First, Middle):

Osteogenesis Imperfecta Foundation Award, Bertone (Sponsor) Ishihara (recipient), 7/1/08-6/30/09. Cell-based BMP Therapy for OI.

F32 AR053805-01 Santangelo K (candidate) Bertone AL (sponsor), Ruth L. Kirshstein National Research Service Award, NIH/NIAMS. Knockdown of Interleukin-1 signaling in osteoarthritis.