
BIOGRAPHICAL SKETCH

Provide the following information for the 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.**

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|---|---|---------|-----------------------------------|
| NAME James N. MacLeod | POSITION TITLE Professor of Veterinary Science | | |
| eRA COMMONS USER NAME | | | |
| EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i> | | | |
| INSTITUTION AND LOCATION | DEGREE <i>(if applicable)</i> | YEAR(s) | FIELD OF STUDY |
| University of Delaware | B.S. | 1980 | Animal Science |
| University of Pennsylvania | V.M.D. | 1984 | Veterinary Medicine |
| University of Pennsylvania | Ph.D. | 1990 | Pathology |
| University of Pennsylvania | Endocrine Fellowship | 1992 | Endocrinology Medical Genetics |

A. Personal Statement

My laboratory studies biological and biomedical aspects of the musculoskeletal system and equine sports medicine, with an emphasis on the growth and maturation of articular cartilage, development and progression of osteoarthritis, and the repair of articular lesions. For the past 15 years, we have used genomic (transcriptomic) analyses to study differential gene expression both in terms of quantitative changes at gene loci and qualitative differences in exon splicing patterns and transcript variants. The data have been used to study the cell biology of chondrocytes, annotate equine protein-coding gene structure, improve the horse reference genome, develop new computational methods for analyzing RNA-seq data, and collaborate on equine evolutionary experiments and genome-wide association studies (GWAS).

B. Positions and Honors.

Positions and Employment:

- 1988-1992 Research Fellow, University of Pennsylvania, School of Medicine and the Howard Hughes Medical Institute, Philadelphia, Pennsylvania.
- 1992-1999 Assistant Professor of Molecular Genetics, James A. Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University, Ithaca, New York.
- 1999-2003 Associate Professor of Molecular Genetics, James A. Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University, Ithaca, New York.
- 2003- Professor of Veterinary Science, John S. and Elizabeth A. Knight Chair, Maxwell H. Gluck Equine Research Center, University of Kentucky, Lexington, Kentucky.
- 2016- Director, Equine Sports Science Initiative, College of Agriculture, Food and Environment, University of Kentucky, Lexington, Kentucky.

Honors and Awards (selected):

- 1998 Pfizer Award for Research Excellence
- 2003 John S. and Elizabeth A. Knight Chair
- 2008 Dickson Professor of Equine Science and Management
- 2009 Prestigious Research Paper Award (co-recipient), College of Agriculture, Univ of Kentucky.
- 2012-2015 Morris Animal Foundation, Scientific Advisory Board

C. Contributions to Science

Articular Cartilage Repair – studies on the pathogenesis of osteoarthritis and cellular variables that limit the ability of structural lesions in articular cartilage to heal.

Mienaltowski MJ, Huang L, Frisbie DD, McIlwraith CW, Stromberg AJ, Bathke A, MacLeod JN. 2009. Transcriptional profiling differences for articular cartilage and repair tissue in equine joint surface lesions. *BMC Medical Genomics*, 14;2:60.

Mienaltowski, MJ, Huang, L, Bathke AC, Stromberg, AJ, MacLeod, JN 2010. Transcriptional comparisons between equine articular repair tissue, neonatal cartilage, cultured chondrocytes, and mesenchymal stromal cells. *Briefings in Functional Genomics*, 9:238.

Cosden RS, Lattermann C, Romine S, Gao J, Voss SR, MacLeod JN. 2011. Intrinsic repair of full-thickness articular cartilage defects in the axolotl salamander. *Osteoarthritis and Cartilage*, 19:200.

Cosden RS, Bickett MM, Lattermann C, MacLeod JN. 2012. Structural and functional analysis of intra-articular interzone tissue in axolotl salamanders. *Osteoarthritis and Cartilage*, 20:1347.

Equine Cervical Stenotic Myelopathy – studies on the skeletal pathology and clinical imaging of Cervical Stenotic Myelopathy (Wobbler Syndrome) in the horse.

Janes JG, Garrett, KS, McQuerry KJ, Pease AP, Williams NM, Reed SM, MacLeod JN. 2014. Comparison of MRI to standing cervical radiographs for evaluation of vertebral canal stenosis in equine cervical stenotic myelopathy. *Equine Veterinary Journal*, 46:681-686, doi: 10.1111/evj.12221.

Janes J, Garrett KS, McQuerry KJ, Waddell S, Voor M, Reed SM, Williams NM, MacLeod JN. 2015. Skeletal Pathology of the Cervical Articular Processes in Equine Cervical Stenotic Myelopathy. *Veterinary Pathology*, 52(5):919-927, doi: 10.1177/0300985815593127.

Equine reference genome and structural annotation of protein-coding genes – studies to generate and improve the equine reference genome.

Wade CM, Giulotto E, Sigurdsson S,...MacLeod JN,...Lander ES, Lindblad-Toh K. (58 co-authors total) 2009. Genome sequence, comparative analysis and population genetics of the domestic horse (*Equus caballus*). *Science*, 326:865.

Coleman SJ, Zeng Z, Wang K, Luo S, Khrebtukova I, Mienaltowski MJ, Schroth GP, Liu, J., MacLeod JN. 2010. Structural annotation of equine protein-coding genes determined by mRNA sequencing. *Animal Genetics*, 41 (Suppl. 2):121.

Coleman SJ, Zeng Z, Hestand MS, Liu, J., MacLeod JN. 2013. Analysis of unannotated equine transcripts identified by mRNA sequencing. *PLoS One*, 8: e70125. doi: 10.1371.

Hestand MS, Kalbfleisch TS, Coleman SJ, Zeng Z, Orlando L, MacLeod JN. 2015. Annotation of the protein-coding regions of the horse genome. *PLoS One*, 10(6):e0124375. doi: 10.1371/journal.pone.0124375.

Computational analyses of transcriptome data – development and assessment of computational and statistical methods to analyze transcriptome data, including both quantitative and qualitative analyses of differential gene expression.

Wang K, Singh D, Zeng Z, Coleman SJ, Huang Y, Savich GL, Xiaping H, Mieczkowski P, Grimm SA, Perou CM, MacLeod JN, Chiang DY, Prins JF, Liu J. 2010. MapSplice: accurate mapping of RNA-seq reads for splice junction discovery. *Nucleic Acids Research*, doi:10.1093/nar/gkq622.

Liu X, MacLeod JN, Liu J. iMapSplice: a lightweight and personalized RNA-seq alignment approach to improve transcriptome profiling. Submitted.

Zhang Y, Liu X, MacLeod JN, Liu J. DeepSplice: Deep Classification of Novel Splice Junctions Revealed by RNA-seq. Submitted.

Fibronectin, erythropoietin, growth hormone, and liver drug metabolism – older papers.

Randolph JF, Scarlett JM, Stokol T, MacLeod JN. Clinical efficacy and safety of recombinant canine erythropoietin in dogs with anemia of chronic renal failure and dogs with recombinant human erythropoietin-induced red cell aplasia. *Journal of Veterinary Internal Medicine*, 18:81-91, 2004.

Stewart MC, Saunders KM, Burton-Wurster N, MacLeod JN. Phenotypic stability of articular chondrocytes *in vitro*: the effects of culture models, BMP-2 and serum supplementation. *Journal of Bone and Mineral Research*, 15:116-174, 2000.

MacLeod, JN, Burton-Wurster N, Gu DN, Lust G. Fibronectin mRNA splice variant in articular cartilage lacks bases encoding the V, III-15, and I-10 proteins segments. *Journal of Biological Chemistry*, 271:18954-18960, 1996.

MacLeod JN, Lee AK, Liebhaber SA, Cooke NE. Developmental control and alternative splicing of the placentally expressed transcripts from the human growth hormone gene cluster. *Journal of Biological Chemistry* 267:14219-14226, 1992.

MacLeod JN, Pampori NA, Shapiro BH. Sex differences in the ultradian pattern of plasma growth hormone concentrations in mice. *Journal of Endocrinology* 131:395-399, 1991.

MacLeod JN, Shapiro BH. Growth hormone regulation of hepatic drug metabolizing enzymes in the mouse. *Biochemical Pharmacology* 38:1673-1677, 1989.

D. Research Support

Ongoing Research Support

Lourie Foundation (J. MacLeod, PI) 12/1/2010 – 11/30/2016
Cellular Mechanisms of Articular Cartilage, Tendon, and Ligament Repair. Major goals: Cell biology and restricted differentiation potential of tissue-specific progenitor cells. Role: PI.

National Institute of Health (1 R01 HG006272-01A1) (J. Liu and J. Prins, Co-PIs) 4/1/2012 – 3/31/2017
Unlocking transcript diversity via differential analyses of splice graphs. Major goal: Develop computational methods for differential analysis of mRNA alternative splicing events. Role: Co-I

Morris Animal Foundation, (T. Kalbfleisch, PI). 1/1/2015 – 12/31/2017
Improving the reference genome of the horse. Major goal: Generate a new version of the reference genome of the horse, correcting errors and omissions in the primary sequence, as well as improving both gene and variant annotation. Role: Co-I.

American College of Veterinary Surgeons. (J. MacLeod, PI) 4/1/2016 – 3/31/2017
Comparative chondrogenic potential of equine fetal progenitor cells and adult mesenchymal stem cells. Major goal: Comparing quantitative and qualitative aspects of the chondrogenic potential in different equine cell types. Role: PI.

Morris Animal Foundation, (J. MacLeod, PI). 6/1/2016 – 5/30/2019
Developmental Progenitor Cells of Articular Cartilage. Major goal: Cell biology and differentiation potential of interzone cells from developing diarthrodial joints. Role: PI.

Completed Research Support (last 3 years)

National Institute of Health (1 K18 DC014050-01) (T. McClintock, PI) 7/1/2014 – 6/30/2016
Odorant Receptor Expression and Sensitivity to Odorants. Major goal: Transcriptional profiling of olfactory neurons by mRNA sequencing. Role: Mentor.

Morris Animal Foundation, (J. MacLeod, PI). 1/1/2014 – 6/30/2016
Unique patterns of gene expression in articular chondrocytes: important insight for cell-based therapies for articular cartilage lesion repair. Major goal: Fellowship support for Dr. Emma Adam. Role: Mentor.
