

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Levine, Jonathan M.

eRA COMMONS USER NAME (credential, e.g., agency login): LEVINEJ

POSITION TITLE: Professor, Helen McWhorter Chair, and Head of Department of Small Animal Clinical Sciences

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	B.S.	05/1995	Biology
Cornell University, Ithaca, NY	D.V.M.	05/2001	Veterinary Medicine
Colorado State University, Fort Collins, CO		07/2002	Internship, Medicine
University of Missouri, Columbia, MO	Diplomate ACVIM (Neurology)	01/2005	Residency, Neurology

A. Personal Statement

I am a veterinarian with expertise in canine naturally occurring neurological diseases and the use of these model systems in translational research. Our laboratory has worked to define inflammatory events, validate outcome measures (eg, magnetic resonance imaging, gait analysis), and develop high-impact canine-based clinical trials in pet dogs with glioma and spinal cord injury. Many of our completed and on-going studies are multi-institutional collaborations with major medical centers to investigate therapies or basic biology which have significant human healthcare or societal impact. Our current research portfolio includes studies examining tumor-mediated immunosuppression and re-directing host immune response in dogs with naturally occurring glioma (collaboration with Amy Heimberger, MD Anderson), kinematic/kinetic facets of recovery from spinal cord injury (collaboration with Gina Bertocci, University of Louisville), neuroprotective therapies (collaboration with Linda Noble, UCSF Medical School), and identification of anatomic/genetic determinants of olfaction in dogs (collaboration, Bob Wayne UCLA). Based on our track record working with Dr. Heimberger on immunotherapies for dogs with glioma and investigators at other institutions on translational projects with high impact, I know we are well positioned to complete the proposed work.

B. Positions and Honors**Positions and Employment**

Clinical Assistant Professor	Texas A&M University, College Station, TX	2005-2006
Assistant Professor	Texas A&M University, College Station, TX	2006-2012
Associate Professor	Texas A&M University, College Station, TX	2012-2015
Helen McWhorter Chair	Texas A&M University, College Station, TX	2014-present
Professor	Texas A&M University, College Station, TX	2015-present
Department Head	Texas A&M University, College Station, TX	2015-present

Honors

2009 Texas Veterinary Medical Association Faculty Research Award

C. Contribution to Science (from a total of 87 publications)

1. We have worked to define the early inflammatory events following spinal cord injury in dogs. In particular, we have identified MMP-9, IL-8, MCP-1, and acute phase proteins as critical modulators of injury severity/recovery. We have also shown MBP release in the CSF is predictive of failure to recover in this model system.

- a. Anderson KM, Welsh CJ, Young C, Levine GJ, Kerwin SC, Boudreau CE, Reyes I, Mondragon A, Griffin JF IV, Cohen ND, **Levine JM**. Acute phase proteins in cerebrospinal fluid from dogs with naturally occurring spinal cord injury. *J Neurotrauma* 2015; 32: 1658-1665.
- b. Taylor AR, Welsh J, Young C, Spoor E, Kerwin SC, Griffin JF, Levine GJ, Cohen ND, **Levine JM**. Cerebrospinal fluid inflammatory cytokines and chemokines in naturally-occurring canine spinal cord injury. *J Neurotrauma* 2014; 31:1561-1569.
- c. Levine GJ, Cook JR, Kerwin SC, Mankin J, Griffin JF, Fosgate GT, **Levine JM**. Relationships between cerebrospinal fluid characteristics, injury severity, and functional outcome in dogs with and without intervertebral disk herniation. *Vet Clin Pathol* 2014; 43: 437-446.
- d. **Levine JM**, Ruaux CG, Bergman RL, Coates JR, Steiner JM, Williams DA. Matrix metalloproteinase-9 activity in the cerebrospinal fluid and serum of dogs with acute spinal cord trauma from intervertebral disk disease. *Am J Vet Res*, 2006; 67: 283-287.

2. We have defined new techniques for imaging the canine spinal cord using MRI and methodologies for quantifying abnormalities. Additionally, our group has identified relationships between abnormal MRI signal and severity of injury/recovery in dogs.

- a. Li P, Yu X, Griffin J, **Levine JM**, Ji J. High-resolution MRI of spinal cords by compressive sensing parallel imaging. *Conf Proc IEEE Eng Med Biol Soc* 2015; 4266-4269.
- b. Griffin JF, Davis MC, Ji JX, Cohen ND, Young BD, **Levine JM**. Quantitative magnetic resonance imaging in a naturally-occurring canine model of spinal cord injury. *Spinal Cord* 2015; 53:278-284.
- c. Griffin JF, Cohen ND, Young BD, Eichelberger BM, Padua A, Purdy D, **Levine JM**. Thoracic and lumbar spinal cord diffusion tensor imaging in dogs. *J Magn Reson Imaging* 2013; 37:632-641.
- d. **Levine JM**, Fosgate GT, Chen AV, Rushing R, Nghiem PP, Platt SR, Bagley RS, Kent M, Hicks DG, Young BD, Schatzberg SJ. Magnetic resonance imaging findings associated with neurologic impairment in dogs with acute thoracic and lumbar intervertebral disk herniation. *J Vet Intern Med* 2009;23:1220-1226.

3. Our group has developed techniques to perform canine-based therapeutic trials in dogs with glioma and spinal cord injury to generate high quality pre-clinical data to inform human clinical trials. Many strategies we have worked with involve modulation of immune responses.

- a. Yaghi NK, Wei J, Hashimoto Y, Kong LY, Gabrusiewicz K, Nduom EK, Huang N, Zhou S, **Levine JM**, Fajt VR, Levine GJ, Porter BF, Marcusson EG, Tachikawa K, Chivukula P, Webb DC, Payne JE, Heimberger AB. Immune modulatory nanoparticle therapeutics for intracerebral glioma. *Cancer Res* (In Revision 2016).
- b. **Levine JM**, Cohen ND, Heller M, Fajt VR, Levine GJ, Kerwin SC, Trivedi A, Fandel TM, Werb Z, Modestino A, Noble-Haeusslein LJ. Efficacy of a metalloproteinase inhibitor in spinal cord injured dogs. *PLOS ONE* 2014; 9: e96408.
- c. **Levine JM**, Levine GJ, Porter BP, Topp K, Noble-Haeusslein LJ. Naturally occurring disk herniation in dogs: an opportunity for pre-clinical spinal cord injury research. *J Neurotrauma* 2011; 28:675-688.
- d. Baltzer WI, McMichael MA, Hosgood G, Kerwin SC, **Levine JM**, Steiner JM, Ruaux CG. Randomized, blinded, placebo-controlled clinical trial of N-acetylcysteine in dogs with spinal cord trauma from acute intervertebral disc disease. *Spine* 2008; 33: 1397-1402.

4. We have worked extensively to characterize the natural history and biology of canine gliomas. Our group has defined the MRI appearance of these tumors, validated minimally invasive brain biopsy techniques, and generated basic data concerning mechanisms of oncogenesis in dogs.

- a. LeBlanc AK, Mazcko C, Brown DB, Koehler JW, Miller AD, Miller CR, Bentley RT, Packer RA, Breen M, Boudreau CE, **Levine JM**, Simpson MR, Halsey C, Kisseberth W, Rossmeisl JH, Dickinson PJ, Fan T, Corps K, Aldape K, Puduvalli V, Gilber MR. Creation of an NCI comparative brain tumor consortium:

informing the translation of new knowledge from canine to human brain tumor patients. (Accepted, *Neuro Oncol*, January 2016)

- b. Xu S, Wei J, Kong LY, Ling XY, Nduom E, Gabrusieicz K, Doucette T, Yang Y, Yaghi NK, Fajt V, **Levine JM**, Qiao W, Li XG, Lang FF, Rao G, Fuller GN, Calin GA, Heimberger AB. Effect of miR-142-3p on the M2 macrophage and therapeutic efficacy against murine glioblastoma. *J Natl Cancer Inst* 2014; 106 (Epub Ahead of Print PMID: 24974128).
- c. Lin Y, Chen Y, Wang Y, Yang J, Zhu V, Cui X, Yan W, Jiang T, Fletcher SA, **Levine JM**, Kim DH, Zhu JJ, Li M. ZIP4 is a novel molecular marker for glioma. *Neuro Oncol* 2013; 15: 1008-1015.
- d. Taylor AR, Cohen ND, Fletcher S, Griffin JF, **Levine JM**. Application and machine accuracy of a new frameless CT-guided stereotactic brain biopsy system in dogs. *Vet Radiol Ultrasound* 2013; 54: 332-342.
- e. Young BD, **Levine JM**, Porter BF, Chen-Allen AV, Rossmesl JH, Platt SR, Kent M, Schatzberg SJ. Magnetic resonance imaging features of intracranial astrocytomas and oligodendrogliomas in dogs. *Vet Radiol Ultrasound* 2011; 52: 132-141.
- f. Stoica G, Lungu G, Martini-Stoica H, Waghela S, **Levine JM**, Smith III, R. Identification of cancer stem cells in dog glioblastoma. *Vet Pathol* 2009;46:391-406.

Complete List of Published Work in My

Bibliography: <http://www.scopus.com/authid/detail.url?authorId=25122824100>

D. Research Support

Ongoing Research Support:

NSF	Wayne (PI)	\$250,000	1/1/15-1/1/18
-----	------------	-----------	---------------

Collaborative research: The genetic and anatomical determinants of olfaction in dogs
Role: Co-PI

AKC-CHF	Bertocci (PI)	\$12,740	1/1/15-6/1/16
---------	---------------	----------	---------------

Development of a neuromusculoskeletal computer simulation gait model to characterize functional recovery in dogs with intervertebral disk herniation
Role: Co-PI

AKC-CHF	G.Levine (PI)	\$12,740	1/1/15-6/1/16
---------	---------------	----------	---------------

Describing the kinetic and kinematic recovery of Dachshunds with spinal cord injury
Role: Co-PI

Rapamycin Holdings	Levine (PI)	\$30,000	6/1/14-6/1/17
--------------------	-------------	----------	---------------

Phase I canine SCI study using eRapamycin
Role: PI

MD Anderson Cancer Center	Levine (PI)	\$177,000	1/15/14-6/1/17
---------------------------	-------------	-----------	----------------

miR-124 delivery in dogs with glioma
Role: PI (Sub-award, Rose Foundation)

Completed Research Support (Last 5 years):

DOD SC100140	Noble (PI)	\$916,931	10/1/11-10/1/15
--------------	------------	-----------	-----------------

Matrix metalloproteinases as a therapeutic target to improve neurological recovery after spinal cord injury
Role: Co-PI

UT Houston Health Science Center	Levine (PI)	\$39,950	3/1/11-3/1/13
----------------------------------	-------------	----------	---------------

Development of a canine brain tumor tissue bank
Role: PI

Dana Foundation	Cooper (PI)	\$200,000	1/1/10-1/1/13
T-cell therapy for diffuse interstitial pontine glioma.			
Role: Co-PI			
Mission Connect Foundation	Levine/Grill (PI)	\$7,837	2/1/11-2/1/12
Histomorphometric comparison of spinal cord injury pathology in the dog and rat as a phase I in establishing a small animal/large animal pipeline model.			
Role: PI			
American Kennel Club 1099	Schatzberg (PI)	\$67,612	09/11/08-09/11/10
Degenerate PCR for detection of viral, bacterial, and rickettsial genera in pugs and maltese dogs with necrotizing and granulomatous meningoencephalitis.			
Role: Co-I			
American Kennel Club 01180-A	Levine (PI)	\$12,000	06/8/08-12/31/09
The Prognostic Value of Various Cerebrospinal Fluid Biomarkers in Dogs with Acute Thoracolumbar Disk Herniation			
Role: PI			
R01 NS039278 (supplement)	Nobel (PI)	\$56,000	5/1/07-5/1/09
Matrix metalloproteinase and spinal cord injury			
Role: Co-I			