The American Boxer Charitable Foundation’s Impact on Canine Health

Peer Reviewed Scientific Publications and Presentations Resulting from Research Sponsored by the ABCF 1999-2013

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Total Grant Sponsorships:

$803,599.00
Oncology

Identification and Characterization of Genetic Mutations in Canine Mast Cell Tumors (0179)

Publications

AR-42, a novel HDAC inhibitor, exhibits biologic activity against malignant mast cell lines via down-regulation of constitutively activated Kit. Lin, Tzu-Yin; Fenger, Joelle; Murahari, Sridhar; et al. Blood. Volume: 115 Issue: 21 Pages: 4217-4225

Generation and characterization of novel canine malignant mast cell line CL1. Lin, Tzu-Yin; Thomas, Rachael; Tsai, Pei-Chien; et al. Veterinary Immunology and Immunopathology. Volume: 127 Issue: 1-2 Pages: 114-124 Published: JAN 15 2009

Characterization of Receptor Tyrosine Kinase Dysfunction in Malignant Histiocytosis (191)

Publications


Characterization and Modulation of Canine Mast Cell Derived Eicosanoids (0975)

Publications


Investigating the Role of STAT3 Activation in Canine Osteosarcoma (0976)

Publications


The novel curcumin analog FLLL32 decreases STAT3 DNA binding activity and expression, and induces apoptosis in osteosarcoma cell lines. Fossey, Stacey L.; Bear, Misty D.; Lin, Jiayuh; et al. BMC CANCER Volume: 11    Article Number: 112    Published: MAR 28 2011

Generation and Analysis of Canine Bone Marrow Derived Mast Cells (0678)

Publications


Significance of Tumor Suppressor Genes in Canine Cancer (1626)

Publications


Refereed Abstracts


Support from this CHF grant was acknowledged in the following presentations:

“The Role of Tumor Suppressor Genes in Melanoma: a Canine Model of Spontaneous Disease.” Presented for: the Department of Animal Science and the Comprehensive Cancer Center, University of Vermont, Feb. 8, 1999, Burlington, VT; the Committee of Comparative Medicine and Pathology, University of Chicago, April 29, 1999, Chicago, IL; the Center for Cancer Causation and Prevention, AMC Cancer Research Center, May 10, 1999, Denver, CO; Department of Pathology, Colorado State University, Oct. 8, 1999, Fort Collins, CO; and at Aspectos Moleculares de la Enfermedad con Tonos Tecnologicos (Molecular Aspects of Disease with Technological Overtones), October 21 - 22, 1999, Universidad Nacional de Asuncion, Asuncion, Paraguay.


“Use of the CellDyn 3500 to Predict Blast Cell Lineage in Peripheral Blood of Dogs and Cats with Leukemia or Leukemic Lymphoma.” Gordon Research Conference on Comparative Hematopoiesis, August 8 - 13, 1999, Tilton School, Tilton, NH.

“Genetics of Canine Cancer.” 1999 National Parent Club Health Conference, American Kennel Club, October 15 - 17, 1999, St. Louis, MO.

“Genes as Windows to Effective Treatment and Prevention of Canine Osteosarcoma.” BCOA National Meeting. May 25, 2000, Portland, OR.


Heritable and Sporadic Genetic Lesions in Canine Lymphoma and Osteosarcoma (2254)

Publications

Thomas, R., Bridge, W., Benke, K., Breen, M (2003). Isolation and chromosomal assignment of canine genomic BAC clones representing 25 cancer related canine genes. Cytogenetic and Genome Research 102, 249-253


Book Chapters


Abstracts and Scientific Presentations and Other Presentations That Included Data from This Work and Acknowledged the Support of CHF

M. Breen. Canine Myeloid Neoplasms and Cytogenetics. 56th Annual Meeting of the American College of Veterinary Pathologists, Dec 7th 2005. INVITED SPEAKER

J. F. Modiano. Canine Cancers to Model Disease Susceptibility and Outcomes. The Jaqua Foundation Symposium in Memory of Dr. Samuel Pollock at Michigan State University, November 16, 2005, East Lansing, MI, INVITED SPEAKER


Matthew Breen. The Canine Genome – Paws for thought. NCSU Biotechnology Center, NCSU, Nov. 2004. INVITED SPEAKER.


J. F. Modiano. (2003). Spontaneous Canine Models of Cancer for Development of Immunotherapy. Section of Medical Oncology, Department of Medicine Basic Science Conference, University of Colorado Health Sciences Center, January 28, 2003, Denver, CO. INVITED SPEAKER


Heritable and Sporadic Genetic Lesions in Canine Lymphoma (615A)

Publications


Refereed Abstracts


**Invited Research Seminars**

“Dogs, Cancer, and Evolution: a Contemporary Voyage of Discovery with the Beagle.” Invited Seminar for the “Comparative Models of Disease” Symposium sponsored by the American Association of Veterinary Immunologists at the 94th Annual Meeting of the American Association of Immunology, May 21, 2007, Miami, FL

“Hematopoetic Cancer - an Inevitable Inheritance of Mammalian Evolution.” Keynote Address, Meeting of the European Societies for Veterinary Oncology and Clinical Pathology and the European College of Veterinary Internal Medicine, September 13-15, 2007, Budapest, Hungary

“Heritable and Sporadic Factors in the Pathogenesis of Canine Leukemias.” State of the Art Lecture, Meeting of the European Societies for Veterinary Oncology and Clinical Pathology and the European College of Veterinary Internal Medicine, September 13-15, 2007, Budapest, Hungary

“ARF, SNF & Other Reasons Dogs Get Cancer.” University of Minnesota Cancer Center, Genetic Mechanisms of Cancer Program Seminar Series, September 27, 2007, Minneapolis, MN

“The Beagle Revisited - New Lessons about Cancer and Evolution.” Department of Laboratory Medicine and Pathology Grand Rounds, University of Minnesota School of Medicine, October 31, 2007, Minneapolis, MN

“Taking a Bite out of Cancer – How Dogs can Help Inform Cancer Biology and Treatment.” University of Minnesota Cancer Epidemiology Interest Group, January 18, 2008, Minneapolis, MN


“Cancer Genetics - the View down the Road to Effective Prevention and Treatment.” AKC Canine Health Foundation Breeders Symposium, October 14, 2006, Denver, CO
“Ten Years of Cancer Research for Canine Health in Partnership with the Rottweiler Health Foundation.”
Rottweiler National Specialty Health Seminar, May 24, 2008, Lake Elmo, MN

“The Comparative Oncology Program at the University of Minnesota.” University of Minnesota Adult Curiosity Camp – All Creatures Great and Small, July 17, 2008, St. Paul, MN

“Shared Pathogenesis of Human and Canine Tumors - an Inextricable Link between Cancer and Evolution.”
Genetic Epidemiology and Risk Assessment (GERA) & Hematologic Malignancies Programs, Mayo Clinic Cancer Center, October 24, 2008, Rochester, MN

Heritable and Sporadic Genetic Lesions in Canine Osteosarcoma (947b)

Publications and Scientific Presentations


Sarver AL, Thayanithy V, Scott MC, Cleaton AM, Hogendoorn PCW, Modiano JF, Subramanian S. (2013). MicroRNAs at 14q32 locus have prognostic significance in osteosarcoma. Orphanet J Rare Dis, 8(1), 7. PMID: 23311495

Lindblad-Toh K. (2013). Genome-wide analyses implicate 33 loci in heritable dog osteosarcoma, including regulatory variants near CDKN2A/B. Genome Biol, 14, R132. PMID: 24330828

**Refereed Abstracts**


Invited Research Seminars

“Comparative Assessment of the Prevalence, Etiology, and Natural History of Cancer in Dogs and Humans.”
Inaugural Skippy Frank Translational Medicine Meeting, Jan 15-17, 2009, Palo Alto, CA

“Going to the Dogs.” Developmental Origins of Cancer, a Minnesota Futures Symposium, February 29 – March 1, 2009, Minneapolis, MN

“Everything I wanted to Know about Cancer, I Learned from My Dog.” 40th Anniversary VMSTP Reunion, March 19-20, 2009, Philadelphia, PA

“Heritable Traits in Sporadic Cancers: How Old Dogs Teach People New Tricks.” Oregon State University College of Veterinary Medicine Guest Speaker Series, March 31, 2009, Corvallis, OR

“Uncovering Heritable Influences on Dog Cancer.” 27th Annu ACVIM Forum, June 2-6, 2009, Montreal, Quebec, Canada

“Taking a Bite out of Cancer –Dogs and Comparative Oncology Inform the Biology, Heritability and Treatment of Cancer.” Ontario Veterinary College Research Seminar Series, September 18, 2009, Guelph, Ontario, Canada


“Tracking a Killer – How Dogs can Help Find Cures for Cancer.” Department of Veterinary Clinical Sciences Grand Rounds, University of Minnesota College of Veterinary Medicine, September 24, 2009, St. Paul, MN

“From Research to Treatment - University of Minnesota Animal Cancer Care and Research Program: Leadership in the Battle Against Cancer.” Bearded Collie Club of America National Specialty Health Seminar, October 7, 2009, Minneapolis, MN

“University of Minnesota Animal Cancer Care and Research Program and Masonic Cancer Center Comparative Oncology.” Annual Meeting of the Van Sloun Foundation, University of Minnesota Arboretum, November 7, 2009, Chaska, MN

“Heritable Traits and Cancer.” Bernese Mountain Dog Club of the Greater Twin Cities Health Seminar, Stone Mountain Pet Lodge, Blaine, MN

“Everything You Want to Know about Cancer.” Keeshond National Specialty Health Seminar, Olympia Resort, May 27, 2010, Oconomowoc, WI
**Genetic Background and the Angiogenic Phenotype in Cancer (1131)**

**Publications**


Schappa JT, Frantz AM, Gorden BH, Dickerson, EB, Vallera DA, Modiano JF. (2013). Hemangiosarcoma and its cancer stem cell subpopulation are effectively killed by a toxin targeted through epidermal growth factor and urokinase receptors. Int J Cancer, 133(8), 1936-1944. PMID: 23553371


**Manuscripts Submitted**

**Graduate Thesis**


**Manuscripts in Preparation**

Frantz AM, Sarver AL, Gorden BH, Lewellen M, O’Brien TD, Modiano JF. Conserved transcriptional drivers of tumorigenicity identified through uniform culture of ontogenetically distinct cancers of the dog.

**Refereed Abstracts**


Frantz A, Sahli N, Dickerson E, O’Brien TD, Modiano JF. (2010). Ontogenetically distinct cancers of the dog form sphere cultures in a shared culture condition. Points of Pride Proceedings (Sept. 29, UMN CVM Research Symposium), St. Paul, MN


Schappa JT, Frantz A, Gorden B, Vallera DA, Modiano JF, Dickerson E. Sensitivity of canine hemangiosarcoma to a ligand targeted toxin containing epidermal growth factor and urokinase. Proceedings Masonic Cancer Center Research Symposium, Minneapolis, MN May 18, 2011
Frantz AM, Gorden BH, Dickerson EB, O’Brien TD, Modiano JF. Ontogenetically distinct cancers of the dog form sphere cultures in a shared culture condition. Points of Pride Proceedings (UMN CVM Research Symposium), St. Paul, MN Oct. 19, 2011 - This poster won First Prize in the Graduate Student Category


Frantz AM, Sarver AL, Dickerson EB, O’Brien TD, Modiano JF (2012). Cancer stem cells from three ontogenetically distinct canine tumors have shared patterns of gene expression. Proceedings of the 2nd World Veterinary Cancer Congress


Schappa JT, Frantz AM, Gorden BH, Dickerson EB, Vallera DA, Modiano JF. Hemangiosarcoma and its cancer stem cell sub-population are effectively killed by a toxin targeted through epidermal growth factor and urokinase receptors. Points of Pride Proceedings (UMN CVM Research Symposium), St. Paul, MN Oct. 10, 2012 - This poster won First Prize in the Post-Doctoral Fellows Category


Schappa JT, Frantz AM, Gorden BH, Dickerson EB, Vallera DA, Modiano JF (2012). Sensitivity of chemoresistant canine hemangiosarcoma and its cancer stem cell sub-population to a ligand-targeted toxin containing epidermal growth factor and urokinase. Proceedings of the First Meeting of the São Paulo Advanced School of Comparative Oncology

common to two malignancies in golden retrievers. Proceedings of the European Society of Veterinary Oncology


Presentations (Invited)

“Comparative Oncology Sarcoma Projects.” Sarcoma Program Retreat, Masonic Cancer Center, University of Minnesota, March 17, 2010, Minneapolis, MN


“Hemangiosarcoma – Who Art Thou?” Stem Cell Institute Research Conference, University of Minnesota, April 21, 2010, Minneapolis, MN

“Everything You Want to Know about Cancer.” Keeshond National Specialty Health Seminar, Olympia Resort, May 27, 2010, Oconomowoc, WI


“Molecular Approaches to Cancer: from the Lab to the Clinic and Back.” Leonberger National Specialty Health Seminar, April 14, 2011, Warwick, RI.
“Recent Progress in Molecular Genetics of Cancer and Challenges Ahead.” 2011 National Parent Club Health Conference, American Kennel Club, August 12 - 14, 2011, St. Louis, MO

“Molecular Genetic Tools in Cancer Diagnosis and Treatment: Recent Advances and Challenges Ahead.” 5th Tufts Canine & Feline Breeding and Genetics Conference, Sept. 16-17, 2011 Boston, MA

“Recent Advances in Canine Hemangiosarcoma.” Bouvier des Flandres National Specialty Health Seminar, October 5, 2011, St. Louis, MO.
“Cancer and Evolution: What is the Solution?” Keynote Address, University of Iowa Molecular and Cellular Biology Graduate Program Retreat, September 30, 2011, Iowa City, IA

“Recent Progress in Molecular Genetics of Cancer and Challenges Ahead.” AKC Canine Health Foundation Breeders Symposium, November 5, 2011, St. Paul, MN

“The Tumor Cell and its Microenvironment – Insights into Tumor Evolution and Tumor Heterogeneity.” Cancer Biology Fall Seminar Series at Cornell University, November 1, 2011, Ithaca, NY


“The Future is Now: Advances in Canine Cancer Care and Research.” Havanese National Specialty Health Seminar, July 10, 2012, Bloomington, MN

“From Bench to Cageside – An Update of Clinical Translation in Oncology at the U of M.” Comparative Oncology Seminar Series, University of Minnesota, September 13, 2012, St. Paul, MN

“The Animal Cancer Care and Research Program at the University of Minnesota and Advances in Our Understanding of Canine Hemangiosarcoma.” Portuguese Water Dog National Specialty Health Seminar, October 2, 2012, Lake Geneva, WI


“Persistence versus Stubbornness: How We Can Learn from Failure to Achieve Therapeutic Success in Cancer.” Annual Meeting of the American Animal Hospital Association, March 14-17, 2013, Phoenix, AZ
Gastrointestinal Disease

Mucosal Gene Expression Profiles in Canine Inflammatory Bowel Disease (0945)

Publications


Granulomatous Colitis In Boxer Dogs: Genetic Analysis of Disease and Functional Analysis of Bacterial Killing (1445)

Publications


Musculoskeletal Conditions and Disease

Phenotypic Characterization and Mapping Genes Associated with Canine Degenerative Myelopathy in the Boxer Dog (821)/Phenotypic Characterization of Peripheral Nerve Disease in Degenerative Myelopathy Dogs (1212)/Determination of Outcome Measures for Clinical Progression and Morphometric Studies of Spinal Cord Disease in Degenerative Myelopathy Dogs (1213)

Publications


One Medicine Impact

NIH Grant 5R21NS078242-02

PI / Project Leader: COATES, JOAN RIPLEY
Title: THERAPEUTIC DEVELOPMENT FOR AMYOTROPHIC LATERAL SCLEROSIS IN A CANINE MODEL
Awardee Organization: UNIVERSITY OF MISSOURI-COLUMBIA

Abstract Text:
DESCRIPTION (provided by applicant): Amyotrophic lateral sclerosis (ALS) is characterized by loss of motor neurons resulting in stiffness, slowing of movement, and severe muscle wasting and weakness. Patients die in 3-5 years secondary to failure of respiratory muscles. There are no effective therapies for ALS. The discovery of superoxide dismutase (SOD1) mutations as causative for a proportion of the inherited forms of ALS led to the generation of rodent SOD1 mutation models in the hope that these animal models would provide new therapeutics. Although the rodent ALS models have provided many advantages for the study of ALS and therapeutics, such animal models have failed to accurately predict therapeutic responses in ALS patients. However, clinical similarities between the inherited SOD1-related ALS and the more prevalent ALS with no SOD1 mutation, and recent findings of SOD1 aggregates in tissues of sporadic ALS patients, suggest that further study of SOD1 still is relevant to all ALS. Canine degenerative myelopathy (DM) is an inherited, progressive adult-onset neurodegenerative disease that has many similarities to human ALS and potentially serves as an important novel model for therapy development. Recently, we found that an E40K missense mutation in SOD1 underlies most cases of canine DM. Similarities between the canine and human nervous systems and homogeneity of the DM phenotype will facilitate translation of therapies into ALS patients. A promising therapeutic strategy using antisense oligonucleotides (ASOs) that target SOD1 mRNA to suppress SOD1 protein was recently demonstrated in a rodent ALS model. The SOD1 ASO decreased amounts of SOD1 in neurons and slowed disease progression. Studies of canine DM, with its spontaneous SOD1 mutation, may yield data more relevant to human ALS and help advance SOD1 ASO clinical trials in ALS patients. Guided by supportive preliminary data, studies will be conducted to achieve the following Specific Aims: 1) Evaluate the safety and pharmacokinetics of intrathecal delivery of a SOD1 ASO in normal dogs to develop an optimized protocol for therapy in DM. Acquisition of such data in normal dogs is critical for the development of this novel treatment approach before instituting a pilot study in privately owned DM-affected dogs. A study of ASO therapy in canine DM as a disease model for ALS is significant, because it should facilitate the translation of a therapeutic approach from laboratory to clinic. 2) Evaluate the safety and preliminary therapeutic effects of intrathecally administered SOD1 ASO in DM-affected dogs. If canine DM is to serve as an effective disease model by which to evaluate ALS therapies, we must demonstrate therapeutic efficacy through a comparative approach using objective measures of disease progression that are shared across species. MUNE is expected to serve as an ideal biomarker for therapeutic translation in DM-affected dogs because the technique is also performed in ALS patients. The proposed research is innovative because it focuses on a promising therapeutic approach in a naturally-occurring canine disease that is analogous to human ALS.
Reproductive Conditions and Disease

Whole Genome Association Analyses for Cryptorchidism in Dogs (1248)

Publication


Regenerative Medicine

Tissue Regeneration Using Canine Mesenchymal Stem Cells: Effects of Donor Characteristics and ex vivo Expansion on Cell Pluripotency (0971)

Publications


Isolation and Characterization of Canine Induced Pluripotential Stem Cells (iPS) (1272)

Publications

**Cardiology**

**Inheritance Patterns and Molecular Genetic Analysis of Doberman Pinschers and Boxer Dogs with Familial Dilated Cardiomyopathy (0021)**

**Publications**


**Evaluation of the Clinical Outcome of Asymptomatic Adult Boxers with Ventricular Arrythmias Over a Four-Year Period (0091)**

**Publications**


Evaluation of serum cardiac troponin I concentration in Boxers with arrhythmogenic right ventricular cardiomyopathy. Baumwart, Ryan D.; Orvalho, Joao; Meurs, Kathryn M. American Journal of Veterinary Research. Volume: 68 Issue: 5 Pages: 524-528 Published: MAY 2007

Assessment of plasma brain natriuretic peptide concentration in Boxers with arrhythmogenic right ventricular cardiomyopathy. Baumwart, RD; Meurs, KM. American Journal of Veterinary Research. Volume: 66 Issue: 12 Pages: 2086-2089 Published: DEC 2005

Arrhythmogenic right ventricular cardiomyopathy causing sudden cardiac death in boxer dogs. Basso, C; Fox, PR; Meurs, KM; et al. Conference: ESC Congress 2004 Location: Munich, GERMANY Date: AUG 28-SEP 01, 2004 Sponsor(s): ESC. European Heart Journal. Volume: 25 Supplement: 5 Pages: 111-111 Published: AUG-SEP 2004

Evaluation of spontaneous variability in the frequency of ventricular arrhythmias in Boxers with arrhythmogenic right ventricular cardiomyopathy. Spier, AW; Meurs, KM. Conference: 18th Annual Forum of
Molecular Analysis of Familial Ventricular Arrhythmias in the Boxer Dog (0156)

**Publications**


The Assessment of Ejection Murmurs in the Boxer Dog (0169)

**Publications**


A Molecular Evaluation of Two Forms of Canine Cardiomyopathy (0440)

**Publications**


An index of myocardial performance applied to the right ventricle of Boxers with arrhythmogenic right ventricular cardiomyopathy. Baumwart, Ryan D.; Meurs, Kathryn M. American Journal of Veterinary Research. Volume: 69 Issue: 8 Pages: 1029-1033 Published: AUG 2008

Identification of genetic modifiers that impact clinical expression of arrhythmogenic right ventricular cardiomyopathy in the Boxer dog (1753)

**Publications**

In progress
Publications Attributed To Alternate Funding Sources (Non-CHF)

Dr. Meurs would like to thank Boxer owners for their time, commitment and participation in the following studies:


A splice site mutation in a gene encoding for PDK4, a mitochondrial protein, is associated with the development of dilated cardiomyopathy in the Doberman pinscher. Meurs, Kathryn M.; Lahmers, Sunshine; Keene, Bruce W.; et al. Human Genetics. Volume: 131 Issue: 8 Pages: 1319-1325 Published: AUG 2012 (Funded by Ott Endowment)

Genome-wide association identifies a deletion in the 3' untranslated region of Striatin in a canine model of arrhythmogenic right ventricular cardiomyopathy. Meurs, Kathryn M.; Mauceli, Evan; Lahmers, Sunshine; et al. Human Genetics. Volume: 128 Issue: 3 Pages: 315-324 Published: SEP 2010 (Funded by Ott Endowment)


Desmosomal gene evaluation in Boxers with arrhythmogenic right ventricular cardiomyopathy. Meurs, Kathryn M.; Ederer, Martina M.; Stern, Joshua A. American Journal of Veterinary Research. Volume: 68 Issue: 12 Pages: 1338-1341 Published: DEC 2007 (Funded by Ott endowment)

Arrhythmogenic right ventricular cardiomyopathy in Boxer dogs is associated with Calstabin2 (FKBP12.6) deficiency. Oyama, MA; Reiken, S; Meurs, KM; et al. Journal of Veterinary Internal Medicine. Volume: 20 Issue: 3 Pages: 747-748 Published: MAY-JUN 2006

Clinical, echocardiographic, and electrocardiographic abnormalities in Boxers with cardiomyopathy and Journal of the American Veterinary Medical Association. Volume: 226 Issue: 7 Pages: 1102-1104 Published: APR 1 2005


Correlation of QT dispersion with indices used to evaluate the severity of familial ventricular arrhythmias in Boxers. Spier, AW; Meurs, KM; Muir, WW; et al. American Journal of Veterinary Research. Volume: 62 Issue: 9 Pages: 1481-1485 Published: SEP 2001 (Not funded)

Comparison of in-hospital versus 24-hour ambulatory electrocardiography for detection of ventricular premature complexes in mature Boxers. Meurs, KM; Spier, AW; Wright, NA; et al. Journal of the American Journal of Veterinary Medicine. Volume: 218 Issue: 2 Pages: 222-224 Published: JAN 15 2001 (Not funded)