The American Boxer Club Charitable Foundation’s Impact on Canine Health

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Overview

• Financial contribution
• Highlights of the American Boxer Charitable Foundation’s contributions to medical progress
  • Degenerative Myelopathy
  • Cancer
    • Osteosarcoma
    • Hemangiosarcoma
    • Mast cell tumors
  • Heart Disease
• Overview of currently funded studies
Your Impact
• $803,599 on 47 grants
• Broad & significant “footprint” in canine health
  • Musculoskeletal Disease
  • Oncology
  • Cardiac disease
  • Gastrointestinal disease
• Impressive support of basic science
  • Long-term commitment
  • Deep understanding of research and medicine
Degenerative Myelopathy

- Progressive, fatal, adult-onset neurodegenerative disease
- 2006 funded grant 0821 (J. Coates) preliminary data from PWC that a genetic lesion present
- Landmark paper published in PNAS 2009 identifying SOD1
  - G to A transition, E40K missense mutation in the SOD1 gene
- SOD1:c.118A and SOD1:c.52T in 222 breeds
Degenerative Myelopathy as a Model for Amyotrophic Lateral Sclerosis (ALS)

• One Medicine Impact
• Similar to DM, ALS (Lou Gehrig's Disease) is a progressive neurodegenerative disease
• Dr. Coates received an NIH R21 grant (5R21NS078242-02): “Therapeutic development for ALS in a canine model” $223,938
  • “Characterization of Thoracic Motor and Sensory Neurons and Spinal Nerve Roots in Canine Degenerative Myelopathy, a Potential Disease Model of Amyotrophic Lateral Sclerosis”
Genes p53, Rb, p21 (waf-1), p16 (ink-4a), and PTEN
• Loss of function leads to metastasis
• Application to melanoma, osteosarcoma and hemangiosarcoma

1999 - Role in pathogenesis of canine disease was incompletely understood

2011 - Documented genomic instability in tumor suppressor genes and DNA copy number aberrations
• 2002 - Chromosome aberrations play an important role in the diagnosis, prognosis, and clinical management of human cancer – Dog?
  • Grant 119 brought molecular cytogenetic technology to the dog
  • Tumor-associated DNA copy number aberrations (CNAs), single copy deletions and amplifications, regional aneuploidy and whole chromosome aneuploidy

• 2013 – First documented treatment response using molecular cytogenetic techniques in a domestic animal with spontaneous cancer
  • “Cytogenetic remission” ushers in personalized medicine (Pmed) in the dog
Oncology: Osteosarcoma

• 2007: Goal of grants 0137 & 1317 to identify mutations and their functional consequence
• 2013: Genetic lesions upstream of CDKN2A/B
  • Functional consequence is altered regulation of cell cycle
  • Canine CDKN2A/B syntenic to the human 9p21 locus
  • Strong One Medicine Potential
• Enhanced understanding of molecular signaling responsible for angiogenesis
• 2005: Basic understanding of canine mast cells lacking
• Grants 179 & 678
  • Characterized mast cell function
  • Creation of mast cell tumor line (CL1)
  • Established mitotic index as a prognostic tool
• 2007: Targeted therapeutics were unavailable
  • Grant 975 - Modulation of mast cell-derived prostaglandins and leukotrienes impair mast cell function
  • NSAID Tepoxilan most effective
1997-2000
- Familial patterns of Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) recognized but genomics undefined
- Clinical outcomes of ventricular arrhythmias unclear

2010 Discovery of striatin mutation
- Not fully penetrant

2013 – Search for genetic modifiers continues
Restructuring of Scientific Program
Discovery continues….

- Conceptualize science as a “portfolio”
- Create natural division of science to build capacity in the science and create depth in research funding
  - RFPs that define specific Research Program Areas
  - Donors build capacity to fund in areas of importance to them

Portfolios:
- Dermatology
- Immunology
- Cardiology
- Oncology
Canine Cardiac Disease

- Mitral Valve Disease
- Cardiomyopathy
- Arrhythmia
- Pulmonary Hypertension

Early, Accurate Diagnosis

- Imaging & Biomarkers

Cutting Edge New Therapy

- Gene therapy

Genetic markers of disease

- Improved Therapy: Improved use of existing drugs

Directly through GWAS and indirectly through enhanced understanding mechanism of disease
Oncology

• Personalized Medicine (Pmed)
• Heritable risk factors (genetic and epigenetic)

- Cancer Stem Cells
- Cytogenetics
Gastrointestinal Disease Program Area

• **Grant 2002: Defining the Genetic Basis of Inflammatory Bowel Disease**
  - Principal Investigator: Dr. Karin Allenspach, DVM PhD
  - Institution: Royal Veterinary College, University of London
  - Total Grant Amount: $119,268.00

• **Grant 2050: Defining the Genetic Susceptibility to Granulomatous Colitis, a Severe Form of Inflammatory Bowel Disease**
  - Principal Investigator: Dr. Kenneth W. Simpson, BVMS, PhD
  - Institution: Cornell University
  - Total Grant Amount: $187,730.00
Grant 2057: Identification of the Genetic Cause of Corneal Ulcers (“Boxer Ulcers”)

- Principal Investigator: Dr. Keith W Montgomery, DVM
- Institution: North Carolina State University
- Total Grant Amount: $27,201.00
CCL Research

1762: Platelet Rich Plasma Treatment
1782: Computer Modeling of Surgery and Conformation
1856: Stem Cell Source for Treatment
1584: Creation of Conformation Score

Deepen our understanding of the cause and treatment of CCL disease

Today’s Breeder Magazine Issue 82 “Stabilizing the Stabilizer”
Continuing the Partnership Between ABCF and CHF
Current DAF Balance

$322,047.72
$150,000 sponsorship of the Cardiology Research Program Area

$50,000 sponsorship of Oncology Research Program Area

$27,000 sponsorship of Ophthalmology Research Program Area

$75,000 sponsorship of Gastrointestinal Disease Research Program Area

$302,000 total research sponsorships from Boxer Donor Advised Fund in 2014
• ABCF research sponsorships to date: $803,599

• Today’s request would move the ABCF total research sponsorships past the $1 million mark

• ABCF would be second largest all-time sponsor of research, less than $100,000 from the top spot
Why this unprecedented DAF transfer?

• Active CHF research includes multiple Boxer specific projects
  • Breed specific research must get the support of the breed’s parent club
  • It is more difficult to leverage sponsorships from other breeds when grants are Boxer specific
• The need to “refill the buckets” or build capacity in program areas, opening the door for renewed emphasis on cardiology, oncology, GI and other areas not included in 2014 RFPs
Why this unprecedented DAF transfer?

- Leadership
- Act as an example to other clubs with high DAF balances
  - The 10 largest Donor Advised Funds contain over $1.3 million
  - DAF sponsorship of $302,000 by the ABCF will be used to motivate and leverage other clubs
  - Unprecedented DAF transfers by most of these top 10 DAFs would increase CHFs ability to approve new research by building capacity in Research Program Areas
Why this unprecedented DAF transfer?

• Foster a new way of thinking about Donor Advised Funds
  • Place more value on funds allocated to research than on funds accumulated in DAF
  • Going forward, new donations to DAF are accompanied with instructions on what research program area to support
  • Keep DAF balances low

• Opportunities for Recognition
  • passing $1 million mark for sponsorship
  • largest single Donor Advised Fund transfer in CHF history
  • Newsletters, press releases, event recognition, banners
Thank you for your longstanding, tremendous support of CHF!