

Navigating the two-way street of comparative oncology

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“Cancer, unlike politics and religion is not a topic of controversy. No one is for it.”



-S. Mooney, 1989, A Snowflake in My Hand



Comparative Oncology (Re-)Defined



The shortest route may not be the best



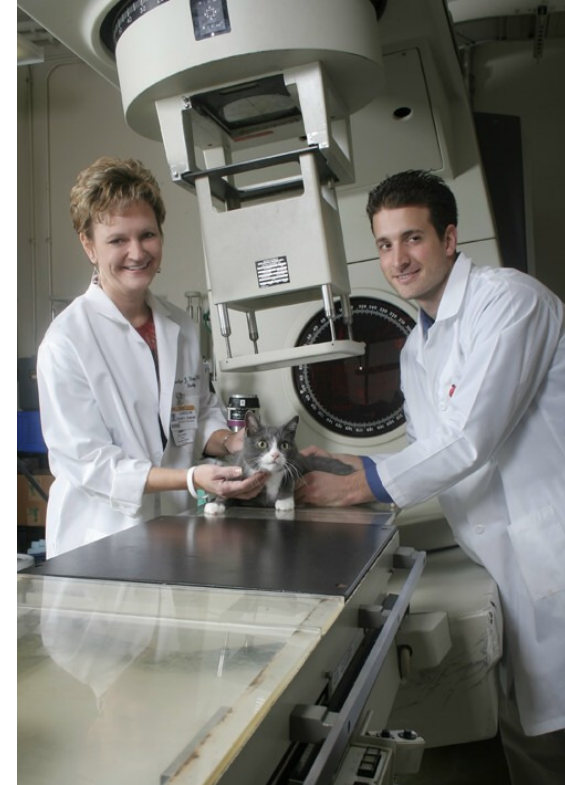
Limitations of rodent models



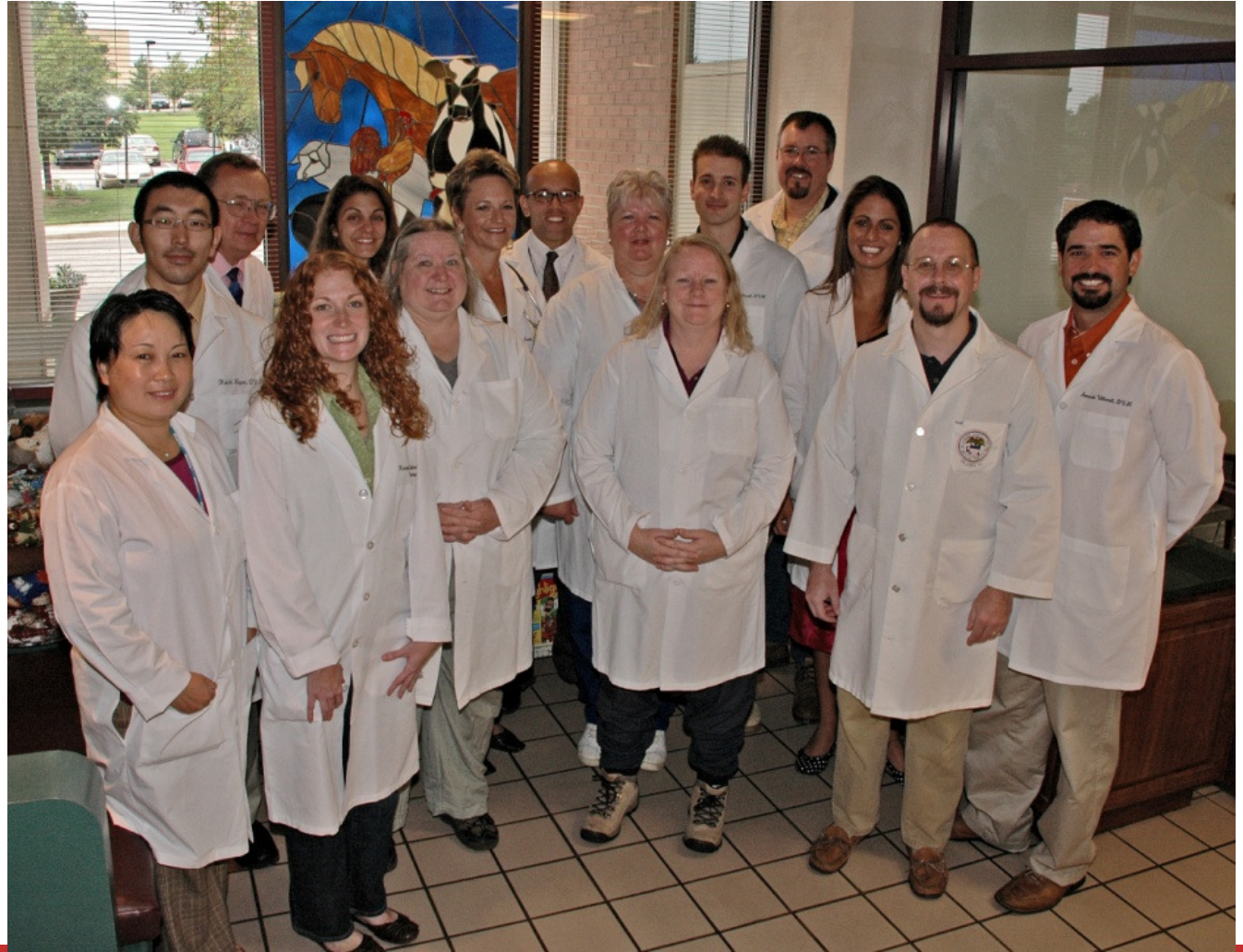
- Incompetent immune system
- Lack heterogeneity
- Rapid tumor progression
- Biosampling limitations



A different kind of lab



UMC VMTH Oncology





Advantages of companion animal models



- Standard of care may not exist
- Anatomical size and structural similarity allows refinement of surgical and other techniques
- Ability to assess outcome when treating minimal residual disease



Cancer in Domestic Animals



- Cancer is the leading cause of death in dogs
- Necropsy (autopsy) study of 2000 dogs*:
 - 23% of all dogs died of cancer
 - 45% of dogs ≥ 10 years died of cancer
- Improved methods of diagnosis
- Increased demand for care



*Bronson RT, AJVR 1982;43:2057-2059

Annual Incidence per 100,000



TUMOR TYPE	DOG	CAT	HUMAN
NH Lymphoma Leukemia	25.0	161	29.9
Lung	4.0	<1.0	28.0
Mammary	199	25.4	109
Oral	20.4	12.0	11.6
Connective Tissue	35.8	17.0	2.5

Annual Incidence per 100,000



TUMOR TYPE	DOG	CAT	HUMAN
Skin (non-melanoma)	90.4	34.7	5.2
Melanoma	25.0	<1.0	12.6
Bone	7.9	4.9	1.0
Stomach/Intestines	6.0	7.0	65.0
Liver and Biliary	7.2	5.0	5.4

Why are animal cancer models useful?



- Shared environment



Why are animal cancer models useful?



- Shorter life span



Why are animal cancer models useful?



- Controllable factors
 - lifestyle choices
 - diet
 - hormonal status
 - placebo effect



Why are animal cancer models useful?



- Outbred vs. inbred populations



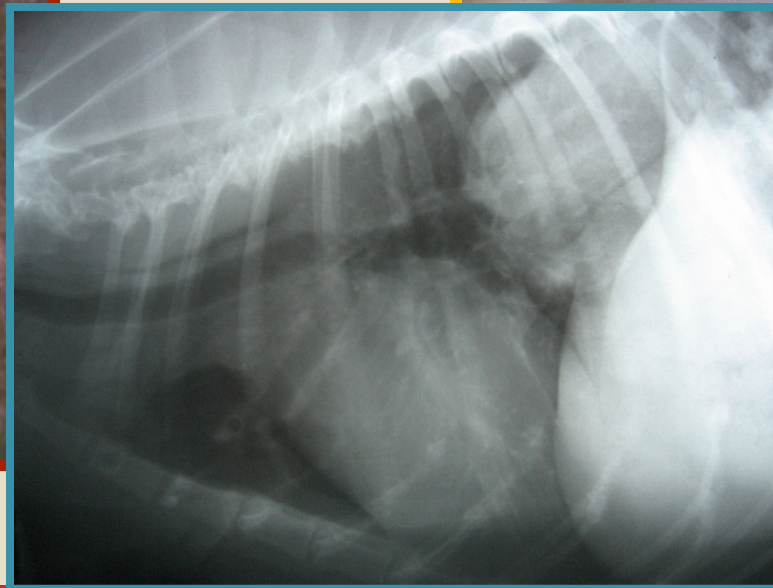
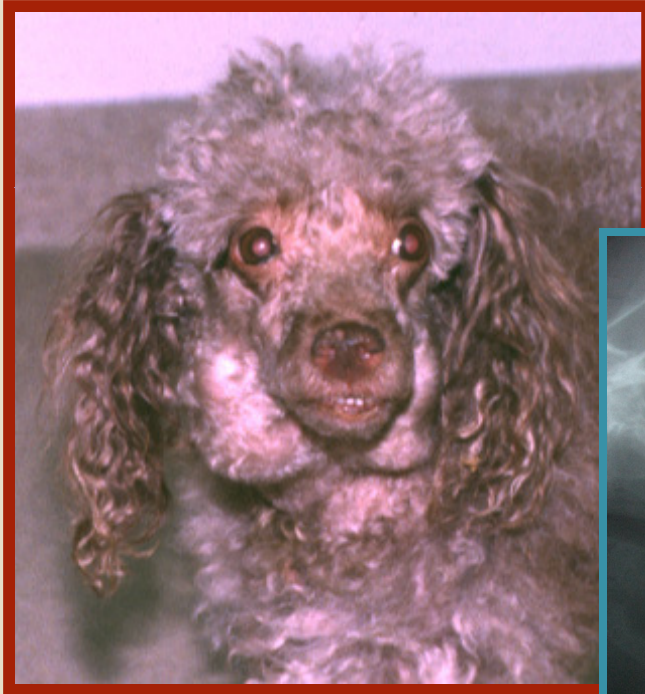
Why are animal cancer models useful?

- Genetics and pedigree may be known



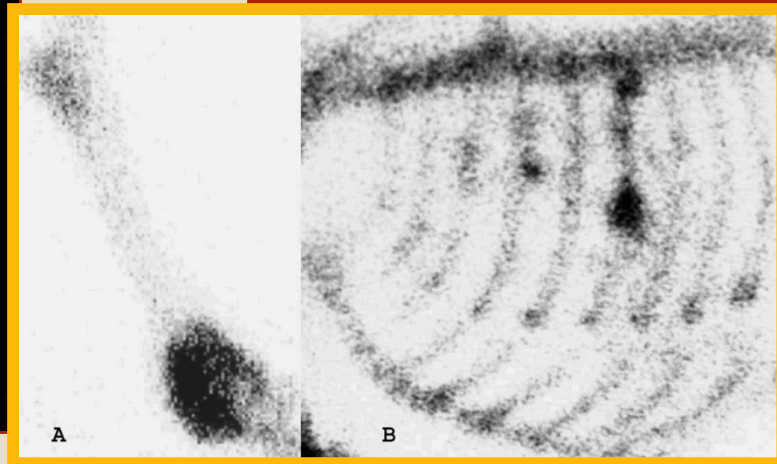
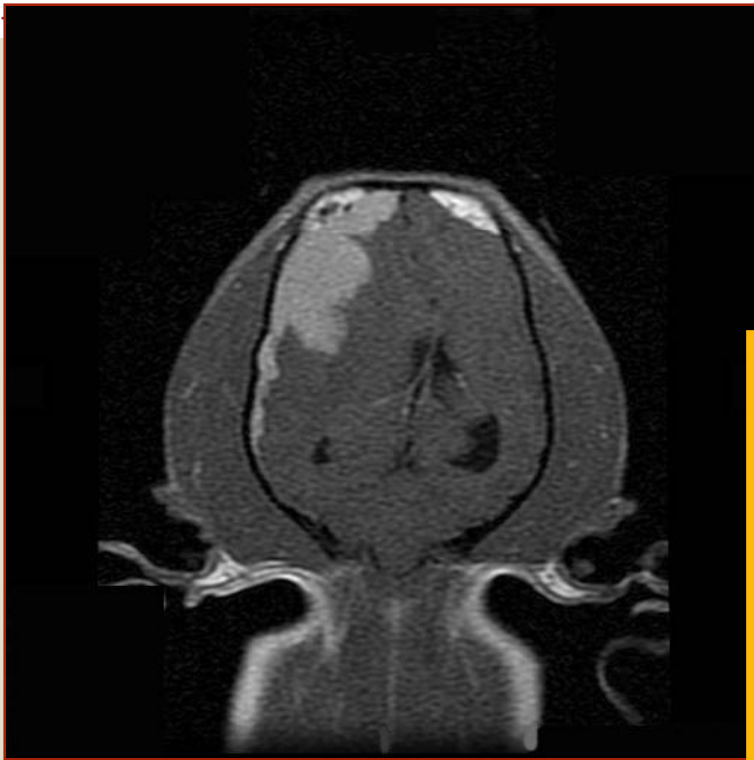
Why are animal cancer models useful?

- Spontaneously-arising tumors
 - Variables in natural state of disease



Why are animal cancer models useful?

- Similar diagnostic tools



Why are animal cancer models useful?



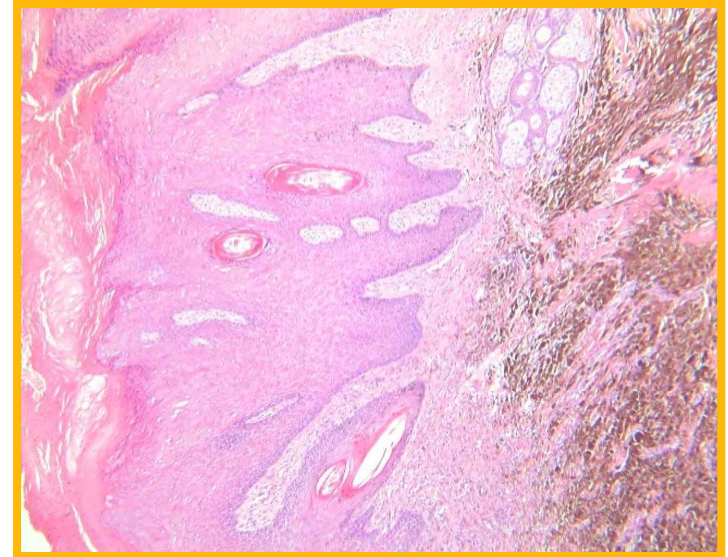
- Approvals are simplified



Why are animal cancer models useful?



- Necropsy more likely



Clinical Research Using Animal Tumor Models: A win-win



Funding Opportunities





AMERICAN KENNEL CLUB
CANINE HEALTH FOUNDATION



MORRIS ANIMAL FOUNDATION
Canine Cancer Campaign
Best Friends Helping Best Friends.

1 in 4
dogs die of cancer.

Together, we can cure this disease in the next ten to twenty years - the lifetime of a dog.

Photo by R. Scott Nolan

Fighting cancer in dogs

Morris Animal Foundation leads campaign to find cures

CHASE AWAY K9 CANCER
www.acvimfoundation.org

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Translational and Comparative Oncology- an Updated NCI Perspective



- **Comparative Oncology Trials Consortium**
 - ✦ translational research/clinical trial consortium under the NCI umbrella

- **Canine Comparative Oncology and Genomics Consortium**
 - ✦ biospecimen repository development

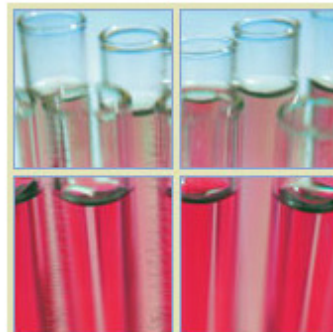
Comparative Oncology Program



FOR THE PUBLIC

Comparative Oncology describes the inclusion of naturally occurring cancer in animals in the study of cancer biology and treatment.

- [For the Public Home Page](#)
- [What is Comparative Oncology?](#)
- [Comparative Oncology Trials Consortium \(COTC\)](#)
- [Open Trials](#)
- [Disease Information](#)
- [News & Publications](#)
- [Contact COP](#)



FOR INDUSTRY

Integration of informative non-clinical models of cancer within clinical drug development

- [COTC](#)
- [Agreements](#)
- [Open Trials](#)
- [News & Publications](#)
- [Contact COP](#)



FOR SCIENTISTS

Companion animal malignancies as a Comparative Model for human disease.

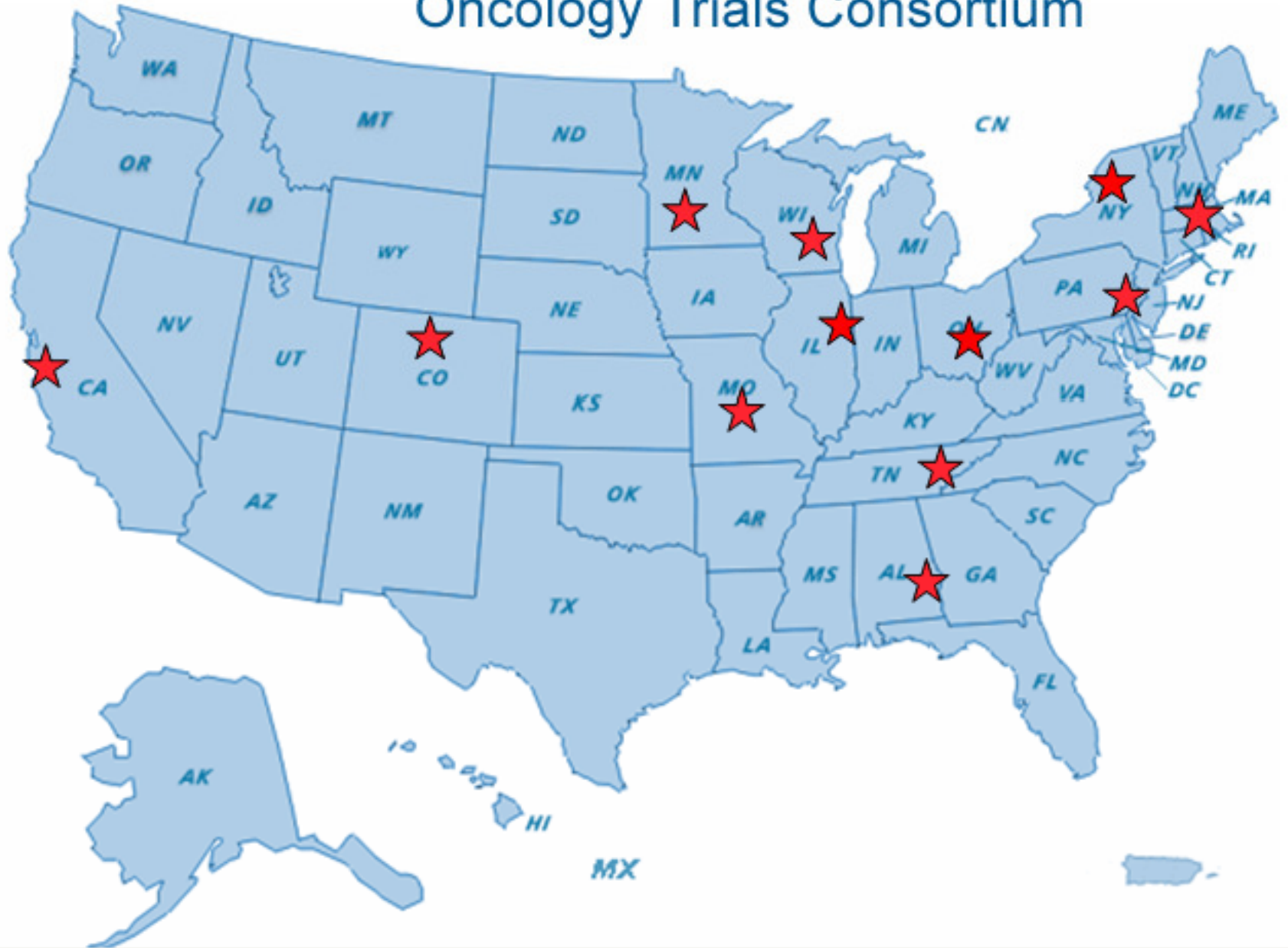
- [Biospecimen Repository](#)
- [Antibody Validation Project](#)
- [Microarray](#)
- [Tissue Microarrays](#)
- [Proteomics](#)
- [Canine Comparative Oncology Genomics Consortium \(CCOGC\)](#)
- [News & Publications](#)



FOR CONSORTIUM MEMBERS

- [Comparative Oncology Trials Consortium \(COTC\)](#)
- [Canine Comparative Oncology Trials Consortium \(CCOGC\)](#)

Members of the Comparative Oncology Trials Consortium



[PUBLIC](#)[INDUSTRY](#)[SCIENTISTS](#)[COTC MEMBERS - coming soon](#)

The Comparative Oncology Program

SCIENTISTS
SCIENTISTS

BIOSPECIMEN REPOSITORY

[COP Home](#)[Biospecimen
Repository](#)[Antibody Validation
Project](#)[Microarray](#)[Tissue Microarrays](#)[Proteomics](#)[CCOGC](#)[News & Publications](#)

The COP Biospecimen Repository will serve as a joint repository for two of the Comparative Oncology Program's initiatives, the Comparative Oncology Trial Consortium (COTC) and the Canine Comparative Oncology Genomics Consortium (CCOGC). All samples collected from the consortiums and other initiatives will be inventoried and linked to a central database so that patient characteristics, intervention, and follow-up data will be available to collaborators.

Contributing centers will have access to the Biospecimen Repository Database. The tissue bank will adhere to rigorous standards of practice for the procurement and transportation of paraffin-embedded and frozen tissues.

Tissue samples will include:

- tumor
- relevant and surrounding normal tissues
- serum
- plasma
- buffy coats



Clinical and biological information will be integrated into the Repository's database

Unique Tools



Veterinary Medical Database



- Most comprehensive veterinary database
- Began at Michigan State University in 1964
- Today 27 North American veterinary teaching hospitals are included
- PhD project at MU centered on “cleaning up” this database; now in searchable format without duplications



[VMDB Information](#)

[Data Summary](#)

[Search Request](#)

[Health Information Managers](#)

A Population Study of Neutering Status as a Risk Factor for Canine Prostate Cancer

Jeffrey N. Bryan,^{1*} Matthew R. Keeler,¹ Carolyn J. Henry,^{1,3} Margaret E. Bryan,²
Allen W. Hahn,¹ and Charles W. Caldwell⁴

Hindawi Publishing Corporation
Journal of Cancer Epidemiology
Volume 2009, Article ID 591753, 6 pages
doi:10.1155/2009/591753

Research Article

Hormonal and Sex Impact on the Epidemiology of Canine Lymphoma

**J. Armando Villamil,¹ Carolyn J. Henry,^{1,2} Allen W. Hahn,¹ Jeffrey N. Bryan,³ Jeff W. Tyler,^{1,4}
and Charles W. Caldwell⁵**

Partnerships with Industry



The Shared Goal: The Search for the Perfect Marker



Screening Test for Lymphoma



- PetScreen Ltd, Biocity, Nottingham UK
- Commercially available proteomic identification and profiling test for canine lymphoma
- Chance conversation at BSAVA meeting in 2007



Partnerships with Industry



- PetScreen North American lab now sited in Columbia, MO at the Life Sciences Business Incubator
- Synergy with Proteomics Core in MU Life Sciences Center
- Teaching, research, and service missions



Developmental Therapeutics



Clinical Trials –Successes in Vet Oncology



- **Canine Oral Melanoma Vaccine by Merial utilizing human tyrosinase**
 - USDA Approval in 2007; partnership between AMCNY and MMSKCC
- **Samarium-153-EDTMP for Canine Osteosarcoma**
 - radiopharmaceutical that targets bone lesions
 - developed at MU, tested in dogs, now marketed as Quadramet for people
- **Canine Mast Cell Tumors: can target c-kit with receptor tyrosine kinase inhibitors**
 - Palladia: Pfizer product approved by FDA in 2009
 - Masitinib: AB Science product approved in Europe

Clinical Trials –Ongoing



- Hormone-refractory prostate CA
 - Intratumoral gold nanoparticles delivery by EUS; minimally invasive surgery
- Muscle-invasive bladder CA
 - Chemotherapy , COX inhibitor, and Tavocept
 - EGCG infusion
- Feline Oral Squamous Cell Carcinoma
 - Retinoids and Interferon
- Primary and metastatic lung cancer
 - Inhalant chemotherapy -**J Aerosol Med and Pulmonary Drug Delivery, 2008;21(3):255.**
 - Evaluation of exhaled breath condensate
- Lymphoma
 - Molecular imaging of bcl-2 **J Nuclear Medicine Vol. 49 No. 3: 430**

Other Avenues of Investigation



- Additional epidemiologic investigations
 - Mesothelioma – 240 cases in dogs; sentinels?
 - Breast cancer – methylation changes; effect of diet
- Identification of genetic and epigenetic modifications
 - Familial adenomatous polyposis in dogs? Association with APC or MUTYH?
 - ATF-2 in Standard Poodles
 - Lymphoma
- In vivo modeling
 - Photoacoustic identification of melanoma micrometastases **J. Biomech. Eng. July 2009; 31 (7); 074519**
 - Effect of timing of post-surgical radiation on wound healing



THINKING OUTSIDE THE BOX

99% of the time, the solution is on the inside.

Parting Thoughts/Questions?

