The National Academies of SCIENCES ENGINEERING MEDICINE

Poster Session for the National Academies Workshop on the Role of Companion Animals as Sentinels for Predicting Environmental Exposure Effects on Aging and Cancer Susceptibility in Humans

The poster session will have both virtual and in-person poster presentations.

VIRTUAL POSTER SESSION: during the workshop lunch breaks

- **12:15-1:30 pm ET on DECEMBER 1ST**
- **12:00-1:15 pm ET on DECEMBER 2ND**

Poster presenters will be available in Zoom breakout rooms for at least the first 30 minutes of the virtual poster session.

https://nasem.zoom.us/j/95073801945

IN-PERSON POSTER SESSION: during the workshop receptions

- **5:30-7 pm ET on DECEMBER 1ST**
- **5:00-6:30 pm ET on DECEMBER 2ND**

Poster presenters will be available at their posters for at least the first 30 minutes of the in-person poster session.

Poster recordings: https://bit.ly/3Dq9hca

Poster Title

A Systemic Multidisciplinary Approach to Study Aging in Retired Sled Dogs

Authors

Ekaterina Andrianova[1], Daria Fleyshman[1], Joseph Wakshlag[2], Heather Huson[2], John Loftus[2], Natasha Olby[3], Leonid Brodsky[4], Andrei Gudkov[1,5]

[1]Vaika, Inc., (Buffalo, NY) [2]Cornell University (Ithaca, NY); [3]North Carolina State University (Raleigh, NC); [4]University of Haifa (Israel); [5]Roswell Park Comprehensive Cancer Center (Buffalo, NY)

Presenting Authors

Ekaterina Andrianova and Andrei Gudkov

Abstract

Canines represent a valuable model for mammalian aging studies as large animals with short lifespans, allowing longitudinal analyses within a reasonable time frame. Moreover, they develop a spectrum of aging-related diseases resembling that of humans, are exposed to similar environments, and have been reasonably well studied in terms of physiology and genetics. To overcome substantial variables that complicate studies of privately-owned household dogs, we have focused on a more uniform population composed of retired Alaskan sled dogs that shared similar lifestyles, including exposure to natural stresses, and are less prone to breed-specific biases than a pure breed population. To reduce variability even further, we have collected a population of 103 retired (8-11 years-old) sled dogs from multiple North American kennels in a specialized research facility named Vaika. Vaika dogs are maintained under standardized conditions with professional veterinary care and participate in a multidisciplinary program to assess the longitudinal dynamics of aging. The established Vaika infrastructure enables periodic gathering of quantitative data reflecting physical, physiological, immunological, neurological, and cognitive decline, as well as monitoring of aging-associated genetic and epigenetic alterations occurring in somatic cells. In addition, we assess the development of age-related diseases such as arthritis and cancer. In-depth data analysis, including artificial intelligence-based approaches, will build a comprehensive, integrated model of canine aging and potentially identify aging biomarkers that will allow use of this model for future testing of antiaging therapies.

Poster Title

Canine Nasal Tumors as a Sentinel for Environmental Exposure and Human Cancer Risk in Kansas and Surrounding States

Authors

Chieko Azuma, DVM, PhD, DACVR (Radiation Oncology), CPIA, Clinical Associate Professor, Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University

Mary Lynn Higgnbotham, DVM, MS, DACVIM (Oncology), Associate Professor, Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University

Raghavendra Amachawadi, BVSc, MS, PhD, Associate Professor, Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University

Timothy Walsh, DVM, DACVP, Clinical Professor, Kansas State Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Kansas State University

Presenting Author

Chieko Azuma (virtually)

https://bit.ly/3crIkZY

Abstract

The nasal cavity is a common site for malignant tumor development in dogs and has potential to be a valid model for the study of environmental exposure effects and human cancer susceptibility. Dogs and humans share the same environment, but the route of exposure to chemicals may be different. Dogs aggressively sniff fields for long periods of time, especially working and herding breeds, potentially resulting in highly concentrated chemical exposure during their life-time. Kansas and surrounding States offer unique geography suitable for large-scale farming which may provide opportunities to examine effects of chemical use and cancer incidence. The purpose of this on-going study is to investigate geographic distribution and change of incidence of canine nasal tumors in the state of Kansas and surrounding areas.

We hypothesize that dogs that live in Kansas and near-by states have exposure to field chemicals and have an increased risk of developing nasal tumors. Dogs histologically diagnosed with nasal malignancy in the States of Kansas, Nebraska and Missouri were searched in the Kansas State Veterinary Diagnostic Laboratory (KSVDL) database and Veterinary Health Canter database between 2005 and September 2021. All histology reports were reviewed and clinical information was utilized to supplement patient information when available. Other data collected included breed of dog, age at tumor identification and zip code location of the owner. Nasal tumor cases were mapped using the zip code data using Geographic Information System (GIS) software (Esri Software). A total of 387 nasal tumor cases were identified. The study is ongoing and association between canine nasal tumor incident and GIS public information on chemical use, human cancer incidence and other environmental data will be examined to identify environmental exposure effects and cancer susceptibility.

Poster Title

Once-Daily Feeding is Associated with Better Cognitive Function and Health in Companion Dogs: Results from the Dog Aging Project

Authors

Emily E. Bray – Postdoctoral Research Associate, University of Arizona and Canine Companions for Independence

Zihan Zheng – Graduate Student, University of Washington

M. Katherine Tolbert – Clinical Associate Professor, Texas A&M University

Brianah M. McCoy – Graduate Student, Arizona State University

Dog Aging Project Consortium

Matt Kaeberlein – Professor, University of Washington

Kathleen F. Kerr – Professor, University of Washington

Presenting author

Emily E. Bray (virtually)

https://bit.ly/3Fwta23

Abstract

A variety of diets have been studied for possible anti-aging effects. In particular, studies of isocaloric time-restricted feeding in laboratory rodents have found evidence of beneficial health outcomes. Companion dogs represent a unique opportunity to study diet in a large mammal that shares human environments. The Dog Aging Project has been collecting data on thousands of companion dogs of all different ages, sizes, and breeds since 2019. We leveraged this diverse cross-sectional dataset to investigate associations between feeding frequency and cognitive function (n = 10,474) as well as nine broad categories of health outcomes (n =24,238). Controlling for sex, age, breed, and other potential confounders, we found that dogs fed once daily rather than more frequently had lower mean scores on a cognitive dysfunction scale, and lower odds of having gastrointestinal, dental, orthopedic, kidney/urinary, and liver/pancreas disorders. Therefore, our findings suggest that once-a-day feeding in dogs is associated with improved health across multiple body systems.

Poster Title

Dogs of Chernobyl: A Model for Human Health Effects Arising from Chronic Exposure to Radiation, Heavy Metals, and Other Environmental Toxins.

Authors

Megan N. Dillon[1], Norman J. Kleiman, PhD[2], Martha O. Burford Reiskind, PhD[1], Tim Mousseau, PhD[3], Matthew Breen, PhD[4,5,6]

[1]Department of Biological Sciences at North Carolina State University, Raleigh, NC 27695, USA
[2]Department of Environmental Health Sciences, Mailman School of Public Health, ColumbiaUniversity Irving Medical Center, New York, NY 10032, USA
[3]Department of Biological Sciences, University of South Carolina, Columbia, SC 29208, USA
[4]Department of Molecular Biomedical Sciences, College of Veterinary Medicine, ComparativeMedicine Institute, Center for Human Health and the Environment North Carolina State University, Raleigh, NC 27695, USA
[5]Cancer Genetics, UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC 27514, USA
[6]Duke Cancer Institute, Durham, NC 27710, USA

Presenting author

Megan N. Dillon

https://bit.ly/3Hrp5xI

Abstract

In 1986, a steam explosion at the Chernobyl Nuclear Power Plant (NPP) destroyed reactor 4, releasing hundreds of tons of radioactive debris into the atmosphere, and contaminating surrounding regions of Ukraine, Belarus, and Russia with more than 10^{18} Bq of various radioisotopes. Within 48 hrs, authorities evacuated ~50,000 residents of Pripyat, and thousands of others from dozens of towns and villages within a 30 km radius of the NPP. To limit the spread of radiation, teams of "Liquidators" eliminated agricultural livestock and pets left behind. Nevertheless, some dogs escaped destruction. Today, a population of several hundred semi-domesticated animals live around the NPP and Chernobyl City, receiving handouts from several thousand workers still employed there. The region is still heavily contaminated by 137-Cs, 90-Sr, heavy/toxic metals, organics, and chemicals left over from decontamination efforts, deconstruction, and 35 years of decay of this former industrial complex as well as a nearby military base. Genetic effects of these toxic exposures on the resident canine population are still unclear. Two populations of semi-feral dogs; one living around the NPP and another living ~18 km away in Chernobyl City are being studied. Preliminary analyses highlight genetic differences between these populations. We hope to 1) identify local adaptations, methylation differences, and differential expression across the exposure gradient and, 2) relate these genetic impacts of chronic exposures on animal health. The subsequent Fukushima nuclear disaster, as well as potential future large-scale nuclear or industrial accidents, highlights an urgent need to better understand how such exposures can adversely impact the genome and epigenome. Findings from the dogs of Chernobyl study are likely to provide vital insights concerning identification of biomarkers of human exposure that can predict subsequent adverse health outcomes after future environmental disasters.

Poster Title

A Study of Citizen Science Supported Wearable and Non-Contact Systems for Quantifying Canine Behavioral and Physiological Response Profiles to Potential Risk Factors of Cancer and Aging in Humans

Authors

Timothy Holder, Emily Summers, Evan Williams, Marc Foster, Zach Cleghern, James Dieffenderfer, Parvez Ahmmed, David Roberts, Alper Bozkurt

Presenting Authors

Timothy Holder and Emily Summers (virtually)

https://bit.ly/3wWY40i

Abstract

Animal companions are becoming increasingly common in human life and carry great potential to serve as sentinels to detect potential risk factors for aging and cancer complications, especially in oncology units. Some canines are even reported to detect cancer in patients and many pet dogs can sense decreased health or affect in their owners. This detection can lead to increased sniffing and licking in addition to other behavioral and physiological responses in the dog. These response profiles from the dog can warn the dyad to potential early warning signs and, if given access to the relevant information, alert medical staff to an incipient risk event.

There is a critical need for engineering methods and novel technologies that can enable a quantified understanding of human and canine physiological states. These allow us to objectively probe the dog's ability to identify the aforementioned potential risk behaviors more accurately and efficiently. Here, we present our preliminary efforts towards the development of wireless sensor systems to simultaneously detect the related behavioral (activity level, movement, vocalizations), physiological signals (heart rate, respiratory rate and their variability), and environmental factors (ambient sound, light, temperature and humidity levels, barometric pressures) around and of humans and animals during their normal interactions. These systems are comprised of both wearable and non-contact electronic devices and provide three categories of signals (i.e. behavioral, physiological, environmental) that have profound immediate and potential implications for detecting aging and cancer related phenomena. In our preliminary exploration, we assessed these relevant parameters successfully and identified the design challenges towards deployment of these systems in larger clinical studies aimed at instrumenting animals to act as sentinels.

Poster Title

Golden Retriever Lifetime Study: Progress and Prospects

Authors

Julia Labadie[1], Mara DePena[2], Rodney Page[3], Kathy Tietje[4], Janet Patterson-Kane[5]

[1]Veterinary Epidemiologist, Morris Animal Foundation, Denver, CO; presenting author

[2]Veterinary Research Manager, Morris Animal Foundation, Denver, CO

[3]Director, Flint Animal Cancer Center, Colorado State University, Fort Collins, CO

[4]Vice President of Scientific Operations, Morris Animal Foundation, Denver, CO

[5]Chief Scientific Officer, Morris Animal Foundation, Denver, CO

Presenting Author

Julia Labadie (virtually)

https://bit.ly/3oCigkt

Abstract

The Golden Retriever Lifetime Study is the largest, most comprehensive longitudinal veterinary cohort study, following 3,044 golden retrievers in the contiguous United States. The primary aim of the study is to investigate nutritional, environmental, lifestyle, and genetic risk factors for cancer and other common diseases in dogs, with an emphasis on four cancer types: lymphoma, osteosarcoma, hemangiosarcoma, and high-grade mast cell tumors. Rolling enrollment of dogs aged 6 months through 2 years was conducted from June 2012 through April 2015. Extensive annual questionnaires completed by owners and veterinarians obtain information about lifestyle, environmental exposures, physical activity, reproductive history, behavior, diet, medications, and diagnoses. Dogs also have annual veterinary examinations and biospecimen collection (whole blood, serum, hair, nails, feces, urine) for laboratory analysis and biobanking. As of June 1, 2021, there have been 224 diagnoses of the primary cancers of interest: 120 hemangiosarcomas, 85 lymphoma/leukemias, 10 high-grade mast cell tumors, and 8 osteosarcomas. Many other disorders common in golden retrievers have also been diagnosed, such as otitis externa, atopy, hypothyroidism, cataracts, and orthopedic disorders. The study has had high retention, with 2,251 dogs remaining in the study, 441 lost to follow-up, and 352 deceased. Among the deaths, 70% (n=248) have been attributed to cancer and 62% (n=218) have had a full or partial necropsy. The biorepository currently contains baseline DNA for all participants as well as approximately 19,000 of each sample collected: whole blood, serum, urine, feces, hair, and nails. A subset of questionnaire data is freely available to researchers with approved credentials who agree to a data use agreement. In addition, both academic and private sector researchers can apply to access data and/or biospecimens through our request for proposal process. More information can be found at https://www.morrisanimalfoundation.org/golden-retriever-lifetime-study.

Poster Title

The Link Between Environment, Age, and Health in a Large Cohort of Companion Dogs from the Dog Aging Project

Authors

Brianah M. McCoy (Ph.D. Student) – School of Life Sciences, Arizona State University, Tempe, AZ, USA
Layla Bressington (Masters Student) – School of Life Sciences, Arizona State University, Tempe, AZ, USA
Dr. Kelly Jin – Allen Brain Institute, Seattle, WA, USA,
Devin Collins (Masters Student) – Department of Sociology, University of Washington, Seattle, WA, USA
Dr. Matthew Dunbar – Center for Studies in Demography & Ecology, University of Washington, Seattle, WA, USA
Sandi Shrager – Collaborative Health Studies Coordinating Center Department of Biostatistics, University of Washington, Seattle, WA, USA
Dr. Noah Snyder-Mackler – School of Life Sciences, Arizona State University, Tempe, AZ, USA

Presenting Author

Brianah McCoy

https://bit.ly/3FqVx1j

Abstract

Exposure to social environmental adversity strongly predicts health and survival in many species such as non-human primates, wild mammals, and humans. However, little is known about how the health and mortality effects of these social determinants vary across the lifespan. Using the companion dog, which serves as a powerful comparative model for human health and aging due to our shared biology and environment, we examined which components of the social environment impact health, and how the effects vary with age, in dogs. We first drew on detailed survey data from owners of 27,547 dogs from the Dog Aging Project and identified six factors that together explained 27% of the variation in dog's social environment. These factors all predicted measures of health, disease, and mobility, when controlling for dog age and weight. Factors capturing measures of financial and household adversity were linked to poorer companion dog health, while factors associated with social companions, like dogs and adults, were linked to better health. Interestingly, some of these effects differed across a dog's lifespan: for instance, the effect of owner age on general health was strongest in younger dogs. Together, our findings point to similar links between adversity and health in companion dogs and set up future work on the molecular and biological changes associated with environmental variation in order to identify ways to mitigate or even reverse the negative environmental effects.

Poster Title

Subjective Assessment of Companion Dog Vision Shows an Age-Related Decline: Preliminary Findings

Authors

Freya Mowat, BVSc. Ph.D., Assistant Professor[1,2,]
Leah Russell[1], Ceylan Ersoz[1], Michele Salzman, BS, MS[1]

[1]Surgical Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI
[2]Ophthalmology and Visual Sciences, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI

Presenting Author

Freya Mowat

https://bit.ly/3npxzNY

Abstract

There are well-validated visual function questionnaires for humans that are associated with a clinically measurable decline in visual ability with age, most notably in low luminance vision. The purpose of our study was to examine the association between companion dog age and subjective assessment of visual function using a previously validated human owner canine visual function questionnaire and a novel human owner canine visual function questionnaire that enquired about dog visually mediated behavior in different lighting conditions.

We disseminated a questionnaire by mail or digital means to previous participants in a human longitudinal study of aging. Of the 899 responses to-date, 53% (n = 487) disclosed they did not currently own a dog, and 24% (n = 212) consented to participate. In this preliminary analysis, we performed multivariate analysis (JMP 15.0) comparing age with visual function questionnaire scores.

Purebred dogs represented 45% of the sample, and females represented 50% of the sample. Median age was 92 months (7.7 years; range 6-202 months). The previously validated canine visual function questionnaire score positively correlated with age (R^2 0.2, $P < 0.0001$). The newly developed visual function questionnaire scores for behavior in different lighting intensities also correlated with age (overall score R^2 0.15, $P<0.0001$). The association between age and owner assessment score in bright lighting conditions (R^2 0.11, $P<0.0001$) was poorer than that in dim lighting conditions (R^2 0.13, $P < 0.0001$) and dark lighting conditions (R^2 0.15, $P<0.0001$).

In this preliminary analysis, subjective human-owner assessment of canine visual function declines in association with dog age. Similar to aging humans, dim light vision in dogs subjectively declines with age. Future studies will examine the age-related decline in clinically measurable visual ability, retinal structure and function, in addition to exploring potential environmental risk factors that might exacerbate visual decline with aging.

Poster Title

Dog Size and Patterns of Disease History Across the Canine Age Spectrum

Authors

Yunbi Nam, Department of Biostatistics, University of Washington, Seattle, WA, USA. (Presenting author)
Michelle White, Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA, USA., The Broad Institute of Harvard and MIT, Cambridge
Elinor Karlsson, Bioinformatics and Integrative Biology, University of Massachusetts Chan Medical School, Worcester, MA, USA., Broad Institute of MIT and Harvard, Cambridge, MA, USA.
Kate E. Creevy, Department of Small Animal Clinical Sciences,Texas A&M University College of Veterinary Medicine & Biomedical Sciences, College Station, TX, USA.
Daniel Promislow, Department of Laboratory Medicine and Pathology, University of Washington School of Medicine, Seattle, WA, USA., Department of Biology, University of Washington, Seattle, WA, USA.
Robyn McClelland, Department of Biostatistics, University of Washington, Seattle, WA, USA.

Presenting Author

Yunbi Nam

https://bit.ly/3CuRr6G

Abstract

It is widely known that both age and size are major predictors of risk of many diseases in dogs. However, more studies on which conditions manifest differently across age and size has been needed. The Dog Aging Project provides a unique opportunity to address these issues in a large community-based population of companion dogs. We used data from the curated 2020 release of the data containing 27,541 survey records collected on or before December 31st, 2020. Dog owners are asked questions if their dogs have ever been diagnosed with various medical conditions. Among those conditions asked, we focused on thirteen conditions of interest that were present in 500 or more dogs. For skin conditions, each SD increment (4 years) of age was associated with a 29% greater relative prevalence of a reported history of skin conditions (PR 1.29, 95% CI 1.27-1.31, $p<0.001$). Prevalence also increased with the owner-reported weight of the dog, with each SD increment (13 kgs) associated with 12% higher relative prevalence of skin condition history (PR 1.12, 95% CI 1.10-1.14, $p<0.001$). There was no significant interaction between age and weight ($p=0.02$) indicating that larger dogs reported skin conditions more often by a similar relative margin across the age spectrum. On the other hand, dog weight was inversely associated to prevalence of a history of cardiac conditions, with each SD increment in size reducing prevalence by a third (PR 0.67, 95% CI 0.63-0.71, $p<0.001$). Additionally, we observed a significant interaction where the prevalence was not only higher for smaller dogs but was associated with a significantly steeper increase in prevalence across age groups. Several disease categories and individual diagnoses vary in prevalence across size groups. These differences will help us understand the trend of decreasing longevity with increasing size in the domestic dog.

Poster Title

Detecting Low-Frequency Precancerous Mutations in Companion Dogs Using Duplex Sequencing Technology.

Authors

Ashley Paynter, Maria Partida-Aguilar, Rosana Risques, Scott Kennedy, Daniel Promislow
Institution: University of Washington

Presenting Author

Ashley Paynter

Abstract

Neoplastic disease is the leading cause of canine mortality in the United States. The most common type of cancer is lymphoma, with ~ 80,000 cases diagnosed annually. Breeds vary tremendously in the relative risk of cancer. However, we are far from understanding the underlying causes of this variation despite considerable effort to identify the genetic determinants of cancer risk and progression in dogs. Cancer typically arises from the accumulation of somatic mutations. However, variation among breeds in cancer risk could be due to breed-specific variation in the types of mutations, the rate of accumulation of mutations, or the downstream effects of mutations in healthy dogs. Lack of clear support from a specific hypothesis represents a major gap in our understanding. Here we took advantage of cutting-edge Duplex Sequencing technology to test the hypothesis that breed-specific variation in lymphoma risk is due to variation in the frequency and type of rare precancerous mutations. Normally, detecting these very low-frequency mutations is beyond the range of sensitivity of standard sequencing technology. This technology will allow us to compare precancerous mutation frequency in blood lymphocytes of healthy high-risk versus low-risk companion dogs. Duplex Sequencing is an extremely high-accuracy sequencing approach with an error rate of approximately 5 x 10-8/base, a more than 10,000-fold improvement over standard sequencing technologies. This work has the potential to shed light on the mechanisms that underlie breed-specific variation in lymphoma risk, and in the long term, could lead to the development of novel tests for the early diagnosis and prognosis of canine lymphoma.

Poster Title

Dogs and Humans Share Unique Gene Expression Signatures in the Macular and Peripheral Retina

Authors

Michele M. Salzman[1], Tetsuya Takimoto[2], Melanie Foster[3], and **Freya M. Mowat[1,4]**

[1]Surgical Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI

[2]Medical Genetics, University of Wisconsin-Madison, Madison, WI

[3]College of Veterinary Medicine, North Carolina State University, Raleigh, NC

[4]Ophthalmology and Visual Sciences, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI

Presenting Author

Michele M. Salzman

https://bit.ly/32iEMaF

Abstract

BACKGROUND

The macula is a photoreceptor-enriched region of the central retina in humans, critical for high quality vision, and susceptible to age-related disease. The tissues that support the retina include the retinal pigmented epithelium (RPE) and choroid. Previous work using normal human donor eyes determined the macula has unique gene expression signatures compared to the periphery, with 2,051 differentially expressed (DE) genes in the macular retina and 926 DE genes in the macular RPE/choroid. We have shown that the dog also has a central photoreceptor-enriched macula-like region, whereas laboratory rodents lack a similar region. We hypothesized that the dog macula would also have unique gene expression signatures.

METHODS

We performed RNASeq on dog macular and peripheral retina and supporting tissues from post-mortem eyes (n = 4 eyes), then performed quantitative RT-PCR of key pathway genes that were differentially expressed (n = 5 eyes).

RESULTS

The photoreceptor-enriched macula-like region in the dog has unique gene expression signatures, with 1,490 DE genes in the macular retina and 767 DE genes in the macular RPE/choroid. The majority of DE genes were up-regulated in the macula compared to the periphery. In both the retina and RPE/choroid, the top KEGG pathway (DAVID-WS) was neuroactive ligand-receptor interaction. In addition, genes involved in drug metabolism and the visual cycle were DE. Quantitative RT-PCR confirmed the up- or down-regulation of key genes important for vision, including cytochrome P450 (***CYP24A1***), and genes involved in retinol recycling (***ALDH1A1, RDH10***).

CONCLUSIONS

Our work adds to the growing body of evidence drawing similarities between canine and human neurologic tissues. Future directions include the study of structural and functional decline in the canine visual system with aging and in association with environmental neurodegenerative risk factor exposure such as heavy metals.

Poster Title

Lifetime Prevalence of Malignant and Benign Tumors in Companion Dogs: Analysis of Dog Aging Project (DAP) Baseline Survey

Authors

Stephen M. Schwartz,[1,2] PhD, MPH; **Silvan R. Urfer,**[3] Dr. med. vet.; **Michelle White,**[4,5] DVM, PhD; **Kate Megquier,**[5] DVM, PhD; **Sandi Shrager,**[6] MSW; **The Dog Aging Project Consortium;**[3] **Audrey Ruple,**[7] DVM, MS, PhD

[1] Epidemiology Program, Fred Hutchinson Cancer Research Center, Seattle, WA, 98115

[2] Department of Epidemiology, University of Washington, Seattle, WA, 98195

[3] Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA, 98195

[4] Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA, 01605

[5] The Broad Institute of Harvard and MIT, Cambridge, MA, 02142

[6] Department of Biostatistics, University of Washington, Seattle, WA 98195

[7] Department of Population Health Sciences, Virginia-Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA 24061

Presenting Authors

Stephen M. Schwartz (virtually) and Audrey Ruple (in-person)

https://bit.ly/3FqvOGr

Abstract

Although cancer is a major contributor to canine morbidity and mortality, its frequency in companion dogs has not been robustly characterized. We analyzed data from the baseline survey of owners of 27,541 living companion dogs enrolled in the Dog Aging Project as of December 31 2020 to estimate the lifetime prevalence of malignant and non-malignant tumors and several potentially-associated characteristics. Survey questions elicited information on history of "cancer or tumors" including organ site and histologic type. Owners reported 819 malignant tumors (56% sited in the skin, muscle, or other soft tissue) and 404 benign tumors (69% sited in the skin, muscle, or other soft tissue). The lifetime prevalence of malignant tumors (29.7/1000 dogs) was approximately double the lifetime prevalence of non-malignant tumors (14.7/1000 dogs). Lifetime prevalence of both malignant and non-malignant tumors increased with dog age at survey completion. There were no statistically discernable differences in age-adjusted lifetime prevalence of malignant (prevalence ratio (PR) = 0.93 [95% confidence interval (CI) 0.82, 1.07] or non-malignant tumors (PR=1.10, 95% CI 0.91, 1.34) in mixed vs. purebred dogs. The lifetime prevalence of malignant tumors increased with increasing dog size class; compared to toy and small dogs, the age-adjusted PRs (95% CIs) for medium, standard, large, and giant dogs were 1.65 (1.28, 2.11), 2.92 (2.35, 3.64), 3.67 (2.92, 4.62) and 2.99 (1.23, 4.02), respectively. Similar though less pronounced patterns in relation to dog size were observed for non-malignant tumors. Our reliance on owner-reported histories of their dog's tumor organ site and histologic type most likely underestimates lifetime prevalence, particularly for animals with "internal" malignancies for which no definitive diagnostic procedure was performed or that were not successfully treated. Ongoing prospective data collection for these dogs (and additional dogs to be enrolled in the Dog Aging Project) will permit future studies on risk factors for canine tumor incidence.

Poster Title

Mutagenic Environmental Chemical Exposures in the Urine of Dogs and People Sharing the Same Households

Authors

Kaitlyn Craun,[1] Hannah Peterson,[1] Kristofer Ross Luethcke,[1] Martin Shafer,[2] Noel Stanton,[2] Chen Zhang,[2] James Schauer,[2] Kristen Malecki,[3] Lauren Trepanier[1]

[1] Department of Medical Sciences, School of Veterinary Medicine;

[2] Wisconsin State Laboratory of Hygiene;

[3] Department of Population Health Sciences, School of Medicine and Public Health, University of Wisconsin-Madison

Presenting Author

Lauren Trepanier

https://bit.ly/3codSQ6

Abstract

Urothelial carcinoma (UCC) develops in both humans and dogs and tracks to regions of high industrial activity. We hypothesize that dogs with UCC may act as sentinels for human urothelial carcinogen exposures. The aim of this study was to determine whether healthy people and dogs in the same households share urinary exposures to potentially mutagenic chemical carcinogens. We measured urinary concentrations of acrolein (as its metabolite 3-HPMA), arsenic species, 4-aminobiphenyl, and 4-chlorophenol (a metabolite of the phenoxy herbicide 2,4-D) in healthy dogs and their owners. Biomarkers of urinary exposure to acrolein, arsenic, and 4-chlorophenol were found in the urine of 42 pet dogs and 42 owners, with 4-aminobiphenyl detected sporadically. Creatinine-adjusted urinary chemical concentrations were significantly higher, by 2.8- to 6.2-fold, in dogs compared to humans. Correlations were found for 3-HPMA ($r = 0.32$, $P = 0.04$) and monomethylarsonic acid ($r = 0.37$, $P = 0.02$) between people and their dogs. Some healthy individuals (3 of 42; 7.1%) and dogs (2 of 42; 4.8%) had evidence of urinary exposure to concentrations of acrolein or inorganic arsenic that led to DNA damage, as measured by the H2AX assay, in human (HT-1376) and canine (K9TCC) urothelial cell lines ***in vitro.*** We conclude that healthy people and their pet dogs share urinary exposures to known mutagenic chemicals, with significantly higher levels in dogs. Higher urinary exposures to acrolein and arsenic in dogs correlate to higher exposures in their owners, and some individuals of both species reached concentrations that are mutagenic to urothelial cells. Ongoing studies will evaluate these chemicals in the urine of dogs with UCC as well as their owners.

Poster Title

Canine Fur: An Underutilized Specimen to Advance Companion Animals as Sentinels for Monitoring Environmental Exposure and Disease Susceptibility in Humans

Authors

Robert J. Turesky[1,2], Jingshu Guo[1,2], Joe Koopmeiners[1,3], Scott J. Walmsley[1,4], Paari Murugan[5], Jaime F. Modiano[1,6], and Christopher J. Weight[7,8]

[1]Masonic Cancer Center
[2]Department of Medicinal Chemistry,
[3]Division of Biostatistics,
[4]Institute for Health Informatics,
[5]Department of Laboratory Medicine and Pathology,
[6]Animal Cancer Care and Research Program, College of Veterinary Medicine, and
[7]Department of Urology, University of Minnesota, Minneapolis, MN,
[8]Department of Urology, Cleveland Clinic, Cleveland, OH

Presenting Author

Robert J. Turesky (virtually)

https://bit.ly/30DHbfb

Abstract

Hair is a non-invasive long-lived biospecimen that accrues illicit drugs and hazardous chemicals in the environment, foods and beverages, personal care products, packaging materials, pesticides, and herbicides. Some of these chemicals are neurotoxic, endocrine disruptors, or cancer-causing agents. We developed a sensitive mass spectrometry-based method to measure 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), a cooked meat carcinogen in the hair of omnivores. PhIP is a multisite rodent carcinogen. PhIP's target organs include the pancreas, colorectum, prostate, and mammary gland. Several epidemiological studies report that frequent consumption of well-done cooked meats containing PhIP increases the risk of developing human cancers at some of these target sites.

PhIP hair levels are significantly higher in prostate cancer patients than those with benign prostatic hyperplasia (BPH) or bladder cancer under treatment at the University of Minnesota. When prostate pathology biomarkers were categorized as binary variables, PhIP-hair levels were significantly higher in patients with elevated prostate-specific antigen blood levels above 4.0 ng/mL ($p = 0.030$) and higher in patients with intermediate and high-risk Gleason scores of 7 - 10 compared to patients with a lower-risk Gleason score of 6 and BPH patients ($p = 0.021$). The PhIP hair biomarker data support the paradigm for the role of cooked meat in PC risk.

PhIP is also present in the fur of dogs consuming high-temperature processed kibble pet foods, often occurring at higher levels than found in human hair. High-density fur covers approximately 90% of the body surface area of dogs. In contrast, high-density terminal hair covers significantly less of the body surface area of humans, encompassing primarily the scalp and pubis. The follicular binding data on PhIP is promising, suggesting that canine fur can serve as a biospecimen for screening other environmental toxicants, expanding the role of canines as sentinels for monitoring exposures in disease susceptibility in humans.

Poster Title

Cats as Canaries? Exploring the Connection Between Genetics, Environment, IBD, and GI Lymphoma

Authors

Tracy L. Webb, DVM, PhD, Research Scientist, Colorado State University
Emily Rout, DVM, PhD, DACVP, Research Scientist, Colorado State University
Anne Avery, VMD, PhD, Professor, Colorado State University
Craig B. Webb, DVM, PhD, DACVIM, Professor, Colorado State University

Presenting Author

Tracy L. Webb

Abstract

Inflammatory bowel disease (IBD) is the most common cause of gastrointestinal (GI) signs in middle-aged to older cats. Anecdotal evidence suggests that in many cats, IBD progresses to low-grade alimentary lymphoma (fLGAL), which is the most common feline cancer. The causes of either disorder have not been elucidated, nor has the mechanism of progression from IBD to cancer. fLGAL may serve as a useful model for understanding the pathogenesis of two human intestinal T cell neoplasms. Human enteropathy-associated T cell lymphoma (EATL) progresses from refractory celiac disease. Understanding the environmental and genetic risk factors that drive progression from IBD to fLGAL may inform this process in human EATL. Monomorphic epitheliotropic intestinal T cell lymphoma (MEITL) also shares some features with fLGAL, including a recently described activating mutation in STAT5. Case reports suggest that MEITL may also be preceded by IBD. In order to investigate the cat as a translational model, we have prospectively collected GI biopsies from 105 cats with suspected IBD or lymphoma (gastric, duodenal, ileal, and colonic) for gene expression profiling and mutation analysis. 56% of these cats were diagnosed histologically with fLGAL, but 73% of cases harbored clonal T cell populations. Remarkably, a subset of these cats carry different clonal populations in different sites, suggesting an intestinal environment that is conducive to the development of lymphoma. We have developed a comprehensive REDCap questionnaire to collect health history, medications, diet, environment, and lifestyle information from these cats and healthy controls. Blood is also being collected for the study of potential genetic risk factors. Through this work, the team hopes to better characterize feline IBD and fLGAL, explore the connection between chronic inflammation and cancer development in the intestinal tract, and identify environmental exposures that contribute to the development of gastrointestinal disease in cats and humans.

Poster Title

Community-Partnered Study Utilizing Passive Environmental Sampling and Blood Biopsy to Evaluate Risk Factors for Cancer in Pet Dogs

Authors

Michelle E. White[1,2], Kate Megquier[1], Marjie Alonso[3], Kim A. Anderson[4], Cheryl A. London[5], Elinor K. Karlsson[1,2]

[1]Broad Institute of MIT and Harvard; Cambridge, MA 02142, USA.

[2]University of Massachusetts Medical School; Worcester, MA 01655, USA.

[3]The International Association of Animal Behavior Consultants, Cranberry Township, PA 16066, USA.

[4]Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, OR 97331, USA

[5]Cummings School of Veterinary Medicine, Tufts University, Grafton, MA 01536, USA

Presenting Author

Michelle E. White (virtually)
https://bit.ly/3xi3WkW

Abstract

Cancer is a complex disease caused by genetic and environmental factors and their interaction. However, identifying exposures that increase cancer risk in human patients is difficult due to long latencies between exposure and disease development. Pet dogs offer a powerful model system for assessing contributions of environmental exposures and gene/environment interactions to carcinogenesis. Dogs develop many of the same cancers that humans do, with many clinical and genomic similarities to human cancers, while sharing an environment with humans. The shorter lifespan of dogs and shorter length of time to disease development makes the study of the impact of environmental exposures on disease risk more feasible than in human patients.

We have developed a community science approach to enable rapid enrollment of dogs and large-scale data collection, including owner-reported health information. We will soon begin enrolling dogs in our pilot study investigating environmental exposures and their correlation with cancer incidence and progression. Enrolled dogs will wear a silicone dog tag to enable passive sampling of environmental chemicals. These measurements will be used to estimate accuracy of environmental survey response, and to identify any correlations with cancer type and outcome.

In addition, to enable exploration of gene/environment interactions and mutational signatures associated with environmental exposures, we have developed a direct-to-dog owner process allowing for a blood biopsy to be taken by the dog's owner and shipped directly to the Broad Genomics Platform for sequencing of cell-free DNA and identification of tumor-derived somatic variants.

With methods designed to maximize sample size, we will assemble a cohort large enough to represent the diversity in environmental exposures, genetic variation, and clinical outcomes within canine cancers and thus greatly improve our understanding of canine and human cancers.

Poster Title

Analysis Of PBDEs in Canine Placental Tissues: Pet Dogs as a Model for Diseases of Developmental Origin

Authors

Catherine F. Wise [1], Claire A. Wiley[2], Matthew Breen[2,3,4,5] and Heather M. Stapleton[1,2]

[1] Nicholas School of the Environment, Duke University, Durham, NC 27708, USA.

[2] Duke Cancer Institute, Durham, NC, USA.

[3] Department of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, 1060 William Moore Drive, Raleigh, NC 27607, USA.

[4] Comparative Medicine Institute, North Carolina State University, Raleigh, NC 27607, USA.

[5] Center for Human Health and the Environment, North Carolina State University, Raleigh, NC 27607, USA.

Presenting Author

Catherine F. Wise

Abstract

Early life exposures to endocrine disrupting chemicals such as, polybrominated diphenyl ethers (PBDEs) can disrupt crucial developmental processes leading to chronic health issues later in life such as neurodevelopmental disorders and diabetes. Gestation is a critical window for development and the placenta is increasingly recognized as a key player in mediating fetal exposures to environmental contaminants. Previous human studies have shown that PBDEs accumulate in the placenta in a sex-and tissue-specific manner. Understanding the later-life consequences of early life exposures can be challenging due to the long latency periods for chronic human diseases. Pet dogs offer a unique opportunity to serve as a sentinel species for human environmental health studies because they share our environment, have similar genomes and diseases with similar clinical and biological features.

Importantly, dogs have a significantly reduced lifespan compared to humans, offering an accelerated path to investigate environmental exposures in utero and their potential associations with health outcomes that stem from developmental origins. We have previously demonstrated that people and their pet dogs have significant and positive correlations in their exposure to PBDEs in indoor environments. Our objective in this study is to demonstrate that pet dogs can act as a sentinel species to evaluate real-world environmental exposures in placental tissues. During the summer and fall of 2021, we collected 22 placenta samples from routine cesarean sections from five different dog litters.

Preliminary data from one placenta sample revealed the presence of PBDEs in canine placenta at a concentration of 0.8 ng/g and TBB at a concentration of 0.1 ng/g. Interestingly, we observed higher concentrations of BDE-209 in the fetal placenta tissue compared to maternal placenta tissue, which is similar to trends in human placenta. Our hypothesis is that sex-dependent and tissue-specific accumulation of PBDEs observed in human placental tissues is a conserved phenomenon and would be also found in canine placentas. Dogs are increasingly recognized for their value in translational research in cancer and aging, and thus we think are likely to offer similar value for chronic conditions of developmental origin.

Poster Title

Canaries in the Coal Mine, Canines on the Couch - A Model for Investigating Contaminant Exposures to Support Human Health Research

Authors

Catherine F. Wise[1,2], Stephanie C. Hammel[3], Nicholas Herkert[3], Jun Ma[4,5], Alison Motsinger-Reif[6], Heather M. Stapleton[3,7], Matthew Breen[1,2,7,8,9]

[1]Program in Toxicology, Department of Biological Sciences, North Carolina State University, Raleigh, North Carolina, 27606, USA

[2]Department of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina, 27607, USA

[3]Nicholas School of the Environment, Duke University, Durham, North Carolina 27708, USA

[4]Department of Statistics, North Carolina State University, Raleigh, North Carolina 27607, USA

[5]Bioinformatics Research Center, North Carolina State University, Raleigh, North Carolina 27607, USA

[6]Biostatistics and Computational Biology Branch, National Institute of Environmental Health Sciences, Durham, North Carolina 27709, USA

[7]Duke Cancer Institute, Durham, North Carolina, USA

[8]Comparative Medicine Institute, North Carolina State University, Raleigh, North Carolina 27607, USA

[9]Center for Human Health and the Environment, North Carolina State University, Raleigh, North Carolina 27607, USA

Presenting Author

Catherine F. Wise

Abstract

Only 5-10% of human cancers can be explained by genetics alone, suggesting the environment plays a strong role in disease etiology. Quantifying the impacts of exposures remains challenging due to latency issues that can take years to manifest after exposure. Dogs may provide valuable insights as a sentinel species for exposure-related human disease because they experience similar environment exposures, have a 6-8 fold shorter lifespan, share many clinical and biological behaviors, and have closely related genomes. We evaluated individual exposures among pet dogs and their paired human companions using silicone dog-tags and wristbands as personal passive samplers (n=30 pairs). Silicone samplers were analyzed for a suite of chemicals across multiple compound classes, including organophosphate esters (OPEs), polybrominated diphenyl ethers, polychlorinated biphenyls, phthalates, and pesticides. As a validation pilot study, we collected urine samples from each study participant and dog, and measured levels of OPE metabolites. 32 of the 41 compounds measured, with a detection frequency >50%, were significantly correlated between dog and human wristbands (r_s = 0.38-0.90; $p < 0.05$), indicating the dog could be a valuable One Health model and potential sentinel species for examining how exposure to consumer product chemicals impact health. The concentrations of several OPEs parent compounds measured on the dog tags were significantly correlated with their respective metabolites in urine (r_s = 0.50-0.71; $p < 0.01$). These data support the value of using the domestic dog as a sentinel species to investigate the potential long-term health impacts on humans from shared exposures.

Poster Title

Canines on the Couch: Using Silicone Passive Samplers to Evaluate Pesticide Concurrent Exposures in People and Their Pet Dogs

Authors

Catherine F. Wise[1], Stephanie C. Hammel[1], Nicholas Herkert[1], Matthew Breen[2,3,4,5] and **Heather M. Stapleton[1,2]**

[1] Nicholas School of the Environment, Duke University, Durham, NC 27708, USA.

[2] Duke Cancer Institute, Durham, NC, USA.

[3] Department of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, 1060 William Moore Drive, Raleigh, NC 27607, USA.

[4] Comparative Medicine Institute, North Carolina State University, Raleigh, NC 27607, USA.

[5] Center for Human Health and the Environment, North Carolina State University, Raleigh, NC 27607, USA.

Presenting Author

Catherine F. Wise

Abstract

People are chronically exposed to various pesticides through the diet, but also through herbicide applications in lawns and pesticide treatments around the home. Chronic household exposure to pesticides affects people and their pets, and some studies suggest pesticide exposure in dogs may be associated with cancer. Companion animals are recognized for their value in comparative health studies, and their shared daily environment with people suggests they are valuable in supporting environmental health research. In this study, we used wearable silicone passive samplers to support a comparative exposure assessment. We recruited 30 people and their pet dogs (living in the same household) to participate in a study to determine how well silicone wristbands (for human) and dog tags (worn on dog collars) can predict urinary pesticide biomarkers of exposure. Participants wore the silicone samplers for 5 days. They collected urine from themselves and their dogs on Days 1, 3 and 5 of the study. Urine samples were pooled for analysis of pesticide biomarkers. Using targeted GC-MS analyses, we quantified 8 pesticides in silicone samplers. Using a suspect screening approach, we additionally identified N,N-diethyl-m-toluamide (DEET), promecarb, flamprop-methyl and fipronil on the silicone samplers with high detection frequencies. DEET and fipronil were confirmed with authentic analytic standards and had statistically significant correlations between wristbands and dog tags (r_s=0.86 and 0.67, respectively, $p<0.01$). Pooled urine samples were quantified for 15 pesticide metabolite biomarkers. Several pesticides, including permethrin, DEET and chlorpyrifos, were detected with high frequency (>70%) in wristbands and urine of both humans and dogs, as corresponding biomarkers. Compared to adults evaluated in the U.S. g eneral population, these dog-owners had higher urinary pesticide metabolite concentrations. Significant and positive correlations were observed between silicone sampler levels of permethrin and DEET with their corresponding urinary metabolites (r_s= 0.50-0.96, $p<0.05$) in both humans and dogs. Dogs had significantly higher urinary concentrations of 2,4-D and ***para***-nitrophenol compared to humans in our study. Owners that reported using flea and tick products containing fipronil on their dog had significantly higher levels of fipronil in wristbands (~10X) and dog tags (~100X) compared to those who did not ($p<0.01$). This study demonstrates that pet dogs can act as proxies for human pesticide exposures in the home environment, potentially providing a new way to study relationships between environmental exposures and disease etiology.