The Evolving Landscape for Precision Health and One Health: New Opportunities in Human and Veterinary Medicine

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No GAI Platforms Were Used in Content Selection, Design, Assembly and Formatting This Presentation
the evolution of the relationships between human and veterinary medicine

a new era of precision health
  - major opportunities for veterinary medicine from diffusion of new technologies from human medicine
  - imperative to reduce the unsustainable cost of high failure rates of new candidate human therapeutics in clinical trials
  - need for new animal models for preclinical testing of new human therapeutics that more accurately reflect the causal etiologies of the targeted human diseases
  - growing recognition of the appeal of many natural canine diseases as more predictive preclinical models of major human diseases

one health
  - complex inter-dependencies of human and animal health and global ecosystems
  - an underinvested core component of global biosecurity
The Historical Evolution of Relationships Between Human and Veterinary Medicine (1850-present)
## The One Medicine: One Health Concept
### A Long Intellectual Pedigree

<table>
<thead>
<tr>
<th>Image</th>
<th>Name</th>
<th>Contribution</th>
<th>Year(s)</th>
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<tbody>
<tr>
<td></td>
<td>Sir Ronald Ross</td>
<td>Anophelian mosquitoes and malaria transmission</td>
<td>1897</td>
<td>Nobel Prize</td>
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<tr>
<td></td>
<td>Sir William Osler</td>
<td>Concepts in comparative medicine</td>
<td>1870s</td>
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<tr>
<td></td>
<td>Elie Metchnikoff</td>
<td>Comparative immunology and host defense</td>
<td>1890s</td>
<td>Nobel Prize</td>
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<td></td>
<td>Paul Ehrlich</td>
<td>Antimicrobial chemotherapy</td>
<td>1870-80s</td>
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<tr>
<td></td>
<td>Robert Koch</td>
<td>Anthrax, cholera, TB, trypanosomiasis</td>
<td>1850</td>
<td>Nobel Prize</td>
</tr>
<tr>
<td></td>
<td>Sir Ronald Ross</td>
<td>Introduction of term zoonosis: T.spiralis</td>
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<td>[Image 256x503]</td>
<td>Rudolf Virchow</td>
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<td>[Image 319x477]</td>
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<td>1890s</td>
<td>Nobel Prize</td>
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<td>[Image 176x58]</td>
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<td>1870-80s</td>
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<td>[Image 235x24]</td>
<td>Sir Ronald Ross</td>
<td>Anophelian mosquitoes and malaria transmission</td>
<td>1897</td>
<td>Nobel Prize</td>
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<td>[Image 212x7]</td>
<td>Sir William Osler</td>
<td>Concepts in comparative medicine</td>
<td>1870s</td>
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<tr>
<td>[Image 230x26]</td>
<td>Elie Metchnikoff</td>
<td>Comparative immunology and host defense</td>
<td>1890s</td>
<td>Nobel Prize</td>
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<tr>
<td>[Image 244x24]</td>
<td>Paul Ehrlich</td>
<td>Antimicrobial chemotherapy</td>
<td>1870-80s</td>
<td></td>
</tr>
</tbody>
</table>
The Historical Evolution of Relationships Between Human and Veterinary Medicine

**One Medicine: (1850-1920)**

- identification of common mechanisms of disease pathophysiology between animal species and humans
- health of horses, oxen as vital transportation and agricultural resources and military campaign logistics
Reform of Food Safety in Early 20th Century

- Food-borne illness as major cause of morbidity and mortality
- Adverse economic impact on workforce needed to drive industrialized urbanization
- TB as dominant cause of reduced lifespan
- Food and Drugs Act (1906) and Meat Inspection Act (1906)
  - “prevent the manufacture; sale or transportation of adulterated or misbranded or poisonous or deleterious food drugs, medication and liquors”
The One Medicine: One Health Concept
A Fluctuating Momentum

James Steele
Founder,
Veterinary Public
Health Division, CDC
(1947)

Calvin Schwabe
UC Davis School of
Veterinary Medicine
(1967)

One Health
Initiative (2006)

Ronald M. Davis
AMA
One Health
Resolution (2007)

American Veterinary One Health Society

Quadripartite One Health Joint Plan of Action (2022-2026)
The Historical Evolution of Relationships Between Human and Veterinary Medicine

1910 Onwards: Progressive Uncoupling

- rise of the combustion engine and mechanized agriculture
  - closure of many Colleges of Veterinary Medicine and shift to focus on agriculture/food production and safety
- Flexner report on Medical Education (1910)
  - increased focus on basic sciences and laboratory courses in medical training
- parallel growth of basic research departments in academia
- inbred laboratory mouse established (1907) and adoption as predominant model for experimental studies
- concept of comparative medicine viewed increasingly through the scientific lens of rodent disease models
- 1950s onwards: increased societal affluence, discretionary income and rapid growth in companion animal populations
The Evolution of Laboratory Models of Human Diseases

- rise of inbred laboratory animal disease models as core element of biomedical research and regulatory standards for preclinical safety testing of Rx, vaccines, devices

- neglected opportunity for leadership by veterinary schools and void filled by new Departments of Comparative Medicine in University Medical Schools/Life Sciences Schools

- veterinarians relegated to lab animal husbandry support and service roles rather than integral intellectual contributors in driving of new research initiatives

- ‘lost opportunity’ for veterinary research scientists with veterinary schools focused increasingly on companion animals and agricultural livestock
Large-Scale Laboratory Rodent Facilities with Sophisticated QA/QC inventory and Biocontainment Controls

Expansion of Murine Genetics, the Design Specialized Animal Models and Targeted Genetic Modification
Large-Scale Use of Rodents in Biomedical Research

- multibillion dollar supply industry for academic, government and private sector research
- mandatory compliance with regulatory statutes for safety testing (and ideally also efficacy evaluation) of products/ingredients
  - human and veterinary medicine
  - diverse consumer products
  - environmental release and exposure risks
- targeted by animal welfare activists as part of broader campaign against toxicity testing of diverse animal-sourced products/ingredients
Precision Health

The Design of Health Interventions to Reflect the Unique Features of Disease Risk, Onset and Progression in Individuals and Populations
**Precision Health and Deep Phenotyping:**

Mapping The Molecular Signatures of Disease as the Intellectual Foundation of Rational Diagnosis and Treatment Selection

<table>
<thead>
<tr>
<th><strong>(Epi)Genomics</strong></th>
<th><strong>Proteomics</strong></th>
<th><strong>Molecular Pathways and Networks</strong></th>
<th><strong>Network Regulatory Mechanisms</strong></th>
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ID of Causal Relationships Between Molecular Network Perturbations and Disease

Disease Subtyping Patient-Specific Disease Signatures: Disease Predisposition; Rx Selection; Disease Monitoring
Technology Trends in Human Healthcare and Diffusion into Veterinary Practice

Consumer Expectations for Highest Quality Companion Animal Care as Powerful Economic Driver
How can genomics benefit your cancer patients?

Discover how SearchLight DNA can provide insights into a cancer’s origin, its behavior, and the optimal approach to treatment.

Finally, there is a blood test for early cancer detection in dogs.

What is cancer screening?

Just like in people, cancer screening should be an important part of preventive care in dogs. The goal is to detect cancer when your pet is feeling well, before they start to show any clinical signs. During wellness visits, your...
Genomic tumor analysis provides clinical guidance for the management of diagnostically challenging cancers in dogs

Esther Chon, DVM, DACVIM; Guannan Wang, PhD; Derick Whitley, DVM, DACVP; Sharadha Salthikumar, PhD; Manisha Warrier, MS, Shukmel Wong, MS, Natalie Duran, MS; Jonathan Adkins, BS; Martin Boateng, BS; Zhanyang Zhu, PhD; Salvatore Facista, BS; David Haworth, DVM, PhD; William Hendricks, PhD

Vidium Animal Health, Translational Genomics Research Institute, Scottsdale, AZ

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Canine Molecular Diagnostics:
Disease Subtyping and Rx Selection

- Rx

- Rx

- Rx

The Next Level of Large-Scale Holistic Data Integration for Comprehensive MultiOmics Profiling

- whole genome sequencing
- cell, tissue and individual-specific differential gene expression and transcription kinetics
- epigenetic modifications: DNA, histones and RNAs
- integrate effects of coding and non-coding regulatory variants across the entire genome
- transcription factor-promoter: enhancer interactions
- protein-RNA interactions
- RNA-RNA interactions
- chromosomical topologies/adjacencies chromatin interactions, gene neighborhoods and other long-range interactions (the 3-D genome)
The Rise of Blood-Based MultiOmics Profiling

The Liquid Biopsy

Liquid Biopsy, Lone SN, et al. Molecular Cancer 21, 79 (2022). Used under the Creative Commons license: creativecommons.org/licenses/by/4.0/
Minimally Invasive Canine Cancer Screening Platforms

OncoK9: The Liquid Biopsy Test for Dogs

As a first-in-class multi-cancer early detection (MCED) test, OncoK9 employs cutting-edge genomic analysis that leverages next-generation sequencing (NGS) technology and proprietary bioinformatics algorithms, empowering veterinarians to provide superior care to canine patients.

- Simple Blood Draw
- Multi-Cancer Coverage
- Cutting-Edge Technology
- Early Detection
Clinical validation of a next-generation sequencing-based multi-cancer early detection "liquid biopsy" blood test in over 1,000 dogs using an independent testing set: The CANcer Detection in Dogs (CANDiD) study


Published: April 26, 2022 • https://doi.org/10.1371/journal.pone.0266623

Clinical experience with next-generation sequencing-based liquid biopsy testing for cancer detection in dogs: a review of 1,500 consecutive clinical cases

Allison L. Grikel, DVM, MS, DACVIM®; Katherine M. Lytle, DVM, MPH, MS; Todd A. Cohen, DVM, DACVIM®; Lillian K. Wong, MS, DVM, LVT; Emily Sandford, RVT®; Jill M. Rafalko, MS; Gina Brandstetter, DVM; Lauren R. DiMarzio, DVM; Ashley Phelps-Dunn, DVM; Michelle C. Rosante, DVM; Chelsea D. Warren, DVM; Angela L. McCleary-Wheeler, DVM, PhD, DACVIM®; Patrick C. Flaux, PhD; Francesco Marass, PhD; Maggie A. Marshall, MSc; Carlos A. Ruiz-Perez, PhD; Kristina M. Kruglyak, PhD; John A. Tynan, PhD; Susan C. Hicks, MAST; Daniel S. Gross, MD, MBA; Jason Chibuk, MS; Ilya Chorny, PhD; Dana W. Y. Tsui, PhD; Andi Flory, DVM, DACVIM®

1PetDX, Medical & Clinical Affairs, La Jolla, CA
2PetDX, Customer Support & Success, La Jolla, CA
3Carson College of Veterinary Medicine, Oregon State University, Corvallis, OR
4PetDX, Research Programs, La Jolla, CA
5PetDX, Information Technology, La Jolla, CA
6PetDX, Analytical Production, La Jolla, CA
7*Corresponding author; Jill M. Rafalko, MS (rafalko@petdx.com)
The Liquid Biopsy:  
Comprehensive Blood-Based MultiOmics Profiling

- oncology as initial focus but potential utility in diverse disease settings
- area of intense competition in human molecular diagnostics
  - over 65 companies
- lack of standardized methods as obstacle to cross-platform comparison
- ambitious agenda for multicancer early detection (MCED) tests
  - criteria for performance metrics and regulatory oversight of clinical utility (fit-for-purpose)
The Use of Cancer Liquid Biopsy Assays in Clinical Case Management

Machine Learning and Image Analysis in Clinical Medicine

- large scale training sets and classification parameters
- standardized, reproducible and scalable
- 260 million images/day for $1000 GPU
101-Plex Spatial MultiOmics

N. Jhaveri et al. (2023) GEN Biotechnology 2:418-434; doi.org/10.1089/genbio.2023.0029
Predicted Cost Reduction in Automated Surgical Robotics: New Control Systems from Integration of Imaging with ML/AI Algorithms
3D Printing a Functional Tri-Leaflet Valve, Perfusable Vasculature, and Neonatal Scale Heart

Functional Tri-leaflet Heart Valve

Perfusable Multiscale Vasculature

Neonatal Scale Collagen Heart

Lee et al. *Science*. 2019

3D-One Process Manufacture of Sensorized Robotic Hand with Tendon-Driven Grip Capabilities

T.J.K. Buchner et. al. (2023) Nature 623:522–530; doi.org/10.1038/s41586-023-06684-3
DIGITAL REVOLUTION IN ANIMAL HEALTH

How Predictive, Monitoring and Diagnostics Technologies are Enabling Tailored Care and Better Welfare for Animals
The Connected Pet: Telehealth and Remote Health Monitoring

Top leading companies in the Pet Wearable Market:
- Avid
- PetPace
- Whistle
- FitBark
- GARMIN
- Loc8tor
- DATAMARS
- tractive

PET WEARABLE MARKET

GLOBAL STATISTICS

- Market value (2022): >$3 BN
- Market value (2032): >$15 BN
- CAGR (2023-32): >10%

- Smart Collar Product Segment
  - Market value (2032): >$4 BN

- Sensors Technology
  - CAGR (2023-32): >15%

North America Market value (2022): >$2 BN
Telehealth and Remote Health Monitoring

- new sensor technologies for real time monitoring of health status
- integrated networks of multiple sensors for increasingly comprehensive clinical assessment
- faster detection of clinical deterioration and intervention
- monitoring treatment compliance and unanticipated adverse events
- longitudinal record of health status
  - individuals and populations
- ever larger databases for automated ML/AI analytics
  - proactive predictive risk analysis and mitigation
  - the digital twin concept: best match of individual patient profile to larger cohorts to optimize treatment options
Social determinants of health and disease in companion dogs: a cohort study from the Dog Aging Project

Brianah M. McCoy\textsuperscript{1,2}, Layla Eastham\textsuperscript{1,2}, Kelly Jim\textsuperscript{1,2}, Creer A. Debby\textsuperscript{1,2}, Sandi Shragg\textsuperscript{1}, Devin Collins\textsuperscript{1,2}, Matthew Dunbar\textsuperscript{1}, Dog Aging Project Consortium\textsuperscript{1} and Audrey Ruple\textsuperscript{1}, Noah Snyder-Mackley\textsuperscript{1,2,3}
FDA to resume enforcement of all federal VCPR requirements for veterinary telemedicine

December 21, 2022

Telehealth bill advances in California Senate

Veterinary groups warn of unintended consequences to eliminating in-person requirement for establishing veterinarian-client-patient relationship

September 06, 2023
Updated November 1, 2023
Can ChatGPT diagnose my collapsing dog?

Samira Abani¹,²*, Steven De Decker³, Andrea Tipold¹,², Jasmin Nicole Nessler¹ and Holger Andreas Volk¹,²

¹Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover, Hannover, Germany. ²Centre for Systems Neuroscience, University of Veterinary Medicine Hannover, Hannover, Germany. ³Department of Veterinary Clinical Science and Services, Royal Veterinary College, University of London, London, United Kingdom
# GAI and the Rise of Chatbots in Healthcare

## For medical professionals
- Clinical documentation
- Radiology interpretation
- Creating discharge summaries
- Suggesting treatment options
- Generating clinical notes
- Designing treatment plans
- Insurance pre-authorization
- Diagnostic assistance
- Summarizing research papers
- Medical triage

## For Pet Owners
- Analyzing laboratory results
- Symptom assessment
- Disease descriptions
- Analyzing wearables' data
- Interpreting physician notes
- Mental health chatbot
- Personalized health recommendations
- Medication adherence
- Health risk prediction
- Rehabilitation guidance

Adapted from B. Meskó & E. J. Topol (2023) NPJ Dig Med 6:120; doi.org/10.1038/s41746-023-00873-0
Human and Veterinary Medicine as Data-Intensive Disciplines

Evolution of Large-Scale Multimodal Databases

New ML/AI Analytics for Increasingly Automated Diagnosis and Clinical Decision Support Systems
Precision Health and Deep Phenotyping: Multimodal Data Integration for Longitudinal Management of Health Risks
Veterinary Consolidators: North American Market Analysis

https://vetintegrations.com/insights/veterinary-consolidators/
Continued Consolidation of Companion Animal Veterinary Clinics and Practices

Leverage Economies of Scale in Adoption of New Technologies and Increased Standardization of Data Capture Integration, Database Design and Cloud-Based Computing Infrastructure
The Emergence of Big Data and ML-AI Platforms Changes the Questions That Can Be Asked

Isolated Siloed Data

Complex Networked Data

Complex Computational Data
Automated Learning Systems:
The Future of ‘Search’ and Decision Support

- Deeper understanding of content and context structured text plus automated language processing of unstructured inputs

- Search all things
  - Integrate traditional document semantic sources with video, objects, speech

- Why should you have to ask first?
  - Smart machines and understanding where/what the user is doing
  - Automated and proactive analytics

- Why wait for the slow brain to catch up to the fast machine?
Automated Context: Data Finding Data
“Intelligence at Ingestion” and Collapse Time to Decision

Feature Extraction and Classification

Context Analysis

Persistent Context

- Knowledge Topologies
- Learning Systems

- Data Fidelity
- Rapid, Robust Decisions
Building ‘Digital Twins’: Matching Individual Deep Phenotypes to ‘Best Fit’ Cohorts

- digital twins and siblings’ and imputed phenotypes
- risk predisposition and disease prevention
- earlier detection of subclinical disease and mitigation
- selection of optimum treatment regimen for overt disease
- improved outcomes
- RWE/RWD and synthetic control arms for clinical studies
Technology Acceleration and Convergence: The Escalating Challenge for Professional Competency, Decision-Support and Future Medical Education
MultiOomics and Elucidation of Disease Mechanisms at the Molecular Level

The Intellectual Driver of Innovation in Precision Health

The Escalating Technical and Regulatory Complexity, Cost and Risk of Translational Research

The Need for New Paradigms in Preclinical Testing of Investigational Drugs to Constrain the Unsustainable Cost of Development Failures and Pricing of Approved Products
Diseases as Complex Adaptive Biological Systems: System State Shifts (Phenomes) and Cumulative Perturbations in Molecular Signaling Networks in the Health to Disease Continuum

- Identification of biomarkers/diagnostics and therapeutic targets in dysregulated networks
- **DrugMechDB** (2023) 4583 Rx indications, 5666 pathways, 32,249 molecular interaction networks across 14 biological parameters
Identification of New Therapeutic Targets

- multiOmics and major expansion of candidate targets
  - coding and non-coding elements
  - circular DNA
  - epigenetic targets
  - transcription factors, enhancers
  - splice variants
  - multiple RNA species
  - protein PTCMs
  - protein degradation pathways
New Therapeutic Targets

- expansion of chemical drug classes
  - from small molecules to diverse biologicals

- biological drug classes
  - proteins
  - protein degraders (PROTACs), molecular glues
  - antibodies and antibody: drug conjugates (ADCs)
  - oligonucleotides and RNA therapeutics
  - gene therapies
  - cell therapies
  - exosomes
  - mRNA and saRNA vaccines
  - oncolytic viruses
The Persistent Achilles Heel in Proficient Translational Therapeutics Research

- the impressive research productivity in expansion of new drug targets and diversified drug classes has not been matched by advances in preclinical disease models to better predict drug efficacy in human clinical trials
- continued high rate of high-cost failure of investigational agents in Phase II/III clinical trials
- average cost of successful NDA/BLA now $1 to 3.8 billion
- inflation-adjusted cost has doubled every nine years
The High Failure of New Investigational Agents in Human Clinical Trials: Approval by Disease Area

![Graph showing likelihood of approval from Phase I by disease area](https://go.bio.org/rs/490-EHZ-999/images/ClinicalDevelopmentSuccessRates2011_2020.pdf)
16 inhibitors, 183 clinical trials, 12,000 patients in wide range of tumor types (2003 to 2021)

- no successful registrations
- estimated wasted clinical trial costs of $1.6 to 2.3 billion (plus risk exposure of patients)
- 50% of the preclinical rodent tests demonstrated less than 50% tumor growth inhibition
Failure and Waste in Biomedical Research:
Herd Mentalities in Scientific Research

“To kill an error is as good a service as,
and sometimes even better than,
the establishing of a new truth or fact.”
Charles Darwin 1879

“Animal research (or rodents) hasn’t worked
and its time we stopped dancing around the problem
We need new methodologies for use in humans
to understand disease biology in humans.
You’ve lost the debate if you lose sight
of the taxpayers and the patients.”
Elias Zerhouni, Director, NIH 2013
The Limitations of Widely Adopted Laboratory Research Models in Replication of Pathophysiology of Major Human Diseases

- inbred populations with constrained genetic heterogeneity
- truncated lifespans that do not reflect the biological heterogeneity of spontaneous disease processes in humans and outbred animal populations
- highly controlled laboratory environments and diets do not reflect real world environments
- failure to represent complex immune and CNS functions
- lack of pharmacological responses to human specific biologics
Trends in Preclinical Testing of Investigational Agents

- FDA Modernization Act 2.0 (December 2022)
- pre-clinical testing on “non-relevant animals” no longer required for IND submission
  - animal data still accepted but non-animal-based test platforms can be used as alternates
  - in vitro and in silico methods
Use of In Vitro and In Silico Methods for Pre-IND Evaluation of Safety and Efficacy of Investigational Agents

2D cultures → 3D organoids → microphysiological systems (MPS) → model multi-organ physiology

- cells
- culture media, dishes, plates, wells
- extracellular adhesive proteins

- multiple cell types
- cell-cell interactions
- extracellular proteins
- cell-induced extracellular remodeling

- organoid technology
- microfabrication of dedicated compartments
- microfluidic circulation of media

• interconnected systems
• physiological modeling of experiments and data
• steady state operation

brain
lungs
heart
vascular

muscle
liver
bone marrow
kidney
gut

long overdue recognition of historical evidence of poor predictability of rodent models of human disease

legitimate question as to how far the proposed new roster of in vitro methods will prove equally lacking due to failure to replicate complex histiotypic structures and multifunctional humoral and cell-mediated communication systems

higher probability of value in safety (toxicity) profiling than efficacy assessment?
Animal Models: Adcomm Exposes Internal Rift In How FDA Defines ‘Translational’ For Purposes Of Confirmatory Evidence

by Sue Sutter

FDA review staff consider the animal models used in development of US WorldMeds’ eflorenthine for neuroblastoma to be translational to humans, even though this does not align with the definition in a September 2023 draft guidance on types of confirmatory evidence.
Comparative Medicine 2.0

The Imperative for New Methods to De-Risk the Unsustainable High Cost of Failure of Investigational Products in Human Clinical Trials

Companion Animal Medicine as an Underleveraged Resource for Preclinical Profiling of New Human Investigational Products?
Arizona Comparative Medicine 2.0

- explore opportunities to build a comprehensive canine clinical trial network in Arizona
- validate testing in canine models to reduce unsustainable cost and frequency of failure of human candidate investigational agents in Phase II/III trials
- attract industry/regulatory funding
- increased revenue to clinics/practices from trial enrollment and monitoring
- reputational benefits with clients and expand client case
- enhanced professional clinical status from engagement in leading edge translational research in biomedicine
Companion Dogs as a Robust Translational Model for Biomedical Research

- shift away from traditional laboratory animal models to study more biologically relevant organisms that replicate pathophysiology of human disease
- appeal of companion dogs for systematic profiling of genetic (multiOmic), environmental and lifestyle factors affecting disease predisposition, disease onset and progression
- canine actuarial aging, aging trajectories and shared environmental exposure(s) as their human owners
Dog Aging Project

- interdisciplinary project involving over 20 academic institutions
- large scale longitudinal study
- diverse cohort of mixed breed and purebred dogs throughout their lifespan
- proactive engagement of dog owners and veterinarians
  - collection of biospecimens, clinical data, diet, physical activity, environment
- rigorous QA/QC of preanalytical variables in biospecimen analysis
- data from over 10,000 animals for low-pass WGS coverage
- residual samples archived at Cornell Veterinary Biobank with ISO 20387:28 compliance
Biospecimen Collection and Profiling in the Dog Aging Project

K.E. Creevy et. al. (2022) Nature 602:51–57; doi.org/10.1038/s41586-021-04282-9
Integration of Environmental Determinants with Biospecimen Profiling in the Dog Aging Project

American Community Survey
- Tract-level sociodemographic variables
- Neighbourhood economic variables

Center for Air, Climate and Energy solutions
- Tract-level air pollution variables
- Four gases: O$_3$, CO, SO$_2$, NO$_2$
- Two aerosols: PM$_{10}$, PM$_{2.5}$

National Oceanic and Atmospheric Association
- County-level temperature measures
- County-level precipitation measures

Neighbourhood walkability
- Walkscore
- Tract-level residential density

K.E. Creevy et. al. (2022) Nature 602:51–57; doi.org/10.1038/s41586-021-04282-9
Chronic Late Onset Diseases in Companion Dogs
As Clinical Trial Cohorts for Preclinical Evaluation of Candidate Interventions in Human Studies

- oncology
- obesity and diabetes (and cats)
- osteoarthritis and other orthopedic problems
- shortened lifespan
- cognitive decline
- decreased resilience to environmental warming
<table>
<thead>
<tr>
<th>Breed Name</th>
<th>2. Overall Relative Cancer Risk</th>
<th>3. Breed Popularity Rank</th>
<th>4. Average Age at First Cancer Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boxer</td>
<td>261%</td>
<td>8</td>
<td>7.6</td>
</tr>
<tr>
<td>Beagle</td>
<td>198%</td>
<td>18</td>
<td>10.5</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>195%</td>
<td>2</td>
<td>9.2</td>
</tr>
<tr>
<td>Rottweiler</td>
<td>183%</td>
<td>20</td>
<td>7.8</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>164%</td>
<td>1</td>
<td>9.5</td>
</tr>
<tr>
<td>Boston Terrier</td>
<td>148%</td>
<td>19</td>
<td>9.3</td>
</tr>
<tr>
<td>Doberman Pinscher</td>
<td>131%</td>
<td>25</td>
<td>7.4</td>
</tr>
<tr>
<td>Pug</td>
<td>129%</td>
<td>15</td>
<td>9.4</td>
</tr>
<tr>
<td>Schnauzer Miniature</td>
<td>118%</td>
<td>14</td>
<td>10.3</td>
</tr>
<tr>
<td>English Bulldog</td>
<td>106%</td>
<td>7</td>
<td>8.0</td>
</tr>
<tr>
<td>Maltese</td>
<td>96%</td>
<td>12</td>
<td>10.5</td>
</tr>
<tr>
<td>American Pit Bull Terrier</td>
<td>95%</td>
<td>10</td>
<td>8.3</td>
</tr>
<tr>
<td>Shih Tzu</td>
<td>94%</td>
<td>6</td>
<td>10.8</td>
</tr>
<tr>
<td>Australian Shepherd</td>
<td>86%</td>
<td>22</td>
<td>10.0</td>
</tr>
<tr>
<td>Dachshund Miniature</td>
<td>83%</td>
<td>11</td>
<td>10.7</td>
</tr>
<tr>
<td>Cavalier King Charles Spaniel</td>
<td>81%</td>
<td>21</td>
<td>9.5</td>
</tr>
<tr>
<td>Great Dane</td>
<td>81%</td>
<td>16</td>
<td>6.2</td>
</tr>
<tr>
<td>Pembroke Welsh Corgi</td>
<td>80%</td>
<td>23</td>
<td>9.9</td>
</tr>
<tr>
<td>German Shepherd</td>
<td>80%</td>
<td>4</td>
<td>8.5</td>
</tr>
<tr>
<td>Siberian Husky</td>
<td>78%</td>
<td>13</td>
<td>9.6</td>
</tr>
<tr>
<td>Poodle Toy</td>
<td>73%</td>
<td>24</td>
<td>10.5</td>
</tr>
<tr>
<td>Yorkshire Terrier</td>
<td>69%</td>
<td>5</td>
<td>10.3</td>
</tr>
<tr>
<td>French Bulldog</td>
<td>63%</td>
<td>3</td>
<td>6.8</td>
</tr>
<tr>
<td>Chihuahua</td>
<td>52%</td>
<td>9</td>
<td>10.4</td>
</tr>
<tr>
<td>Pomeranian</td>
<td>45%</td>
<td>17</td>
<td>10.0</td>
</tr>
</tbody>
</table>

Molecular phenotyping of malignant canine mammary tumours: Detection of high-risk group and its relationship with clinicomolecular characteristics

Mohamad Zamani-Ahmadmahmudi1 | Maziar Jajarmi2 | Saeedeh Talebipour1

Received: 9 May 2022 | Revised: 9 October 2022 | Accepted: 10 October 2022

DOI: 10.1111/vco.12863

Blood biomarkers for canine cancer, from human to veterinary oncology

Philippe Colombet1,2 | Jérémy Béguin3,4 | Ghita Bencheikroun3,4 | Delphine Le Roux5,6

Received: 31 January 2022 | Revised: 5 July 2022 | Accepted: 7 July 2022

DOI: 10.1111/vco.12848

Leading the pack: Best practices in comparative canine cancer genomics to inform human oncology

C. London1 | H. Gardner1 | S. Zhao2 | D. Duval5 | M. Chambers6 | E. Ostrander7 | J. Trent8 | G. Kuffel9

Received: 10 May 2020 | Revised: 17 August 2022 | Accepted: 18 August 2023

DOI: 10.1111/vco.12915

Standing in the canine precision medicine knowledge gap: Improving annotation of canine cancer genomic biomarkers through systematic comparative analysis of human cancer mutations in COSMIC

Sharadha Saktihikumar1 | Salvatore Facista2 | Derick Whitley1 | Sara A. Byron2 | Zeeshan Ahmed1 | Manisha Warrier1 | Zhiyang Zhu1

Received: 7 November 2020 | Revised: 26 April 2023 | Accepted: 9 May 2023

DOI: 10.1111/vco.12791


Willam P. D. Hendricks3 | Guanman Wang1

Received: 7 November 2020 | Revised: 26 April 2023 | Accepted: 9 May 2023

DOI: 10.1111/vco.12791
Imagine if we could make your joints heal themselves?

NITRO
Novel Innovations for Tissue Regeneration in Osteoarthritis
## Senior Life Stage Arthritis Relative Risk for 25 Highest-Risk and 5 Lowest-Risk Breeds

<table>
<thead>
<tr>
<th>Rank</th>
<th>Breed</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rough Collie</td>
<td>411%</td>
</tr>
<tr>
<td>2</td>
<td>Saintoyed</td>
<td>357%</td>
</tr>
<tr>
<td>3</td>
<td>Bernese Mountain Dog</td>
<td>350%</td>
</tr>
<tr>
<td>4</td>
<td>Old English Sheepdog</td>
<td>338%</td>
</tr>
<tr>
<td>5</td>
<td>Labrador Retriever</td>
<td>297%</td>
</tr>
<tr>
<td>6</td>
<td>Irish Setter</td>
<td>296%</td>
</tr>
<tr>
<td>7</td>
<td>Airedale Terrier</td>
<td>293%</td>
</tr>
<tr>
<td>8</td>
<td>Golden Retriever</td>
<td>291%</td>
</tr>
<tr>
<td>9</td>
<td>Newfoundland</td>
<td>286%</td>
</tr>
<tr>
<td>10</td>
<td>English Mastiff</td>
<td>280%</td>
</tr>
<tr>
<td>11</td>
<td>Belgian Malinois</td>
<td>278%</td>
</tr>
<tr>
<td>12</td>
<td>German Shepherd</td>
<td>277%</td>
</tr>
<tr>
<td>13</td>
<td>Keeshond</td>
<td>274%</td>
</tr>
<tr>
<td>14</td>
<td>Alaskan Malamute</td>
<td>270%</td>
</tr>
<tr>
<td>15</td>
<td>Greater Swiss Mountain Dog</td>
<td>267%</td>
</tr>
<tr>
<td>16</td>
<td>Mixed Breed (Large)</td>
<td>263%</td>
</tr>
<tr>
<td>17</td>
<td>Akita</td>
<td>255%</td>
</tr>
<tr>
<td>18</td>
<td>Rottweiler</td>
<td>253%</td>
</tr>
<tr>
<td>19</td>
<td>Weimaraner</td>
<td>251%</td>
</tr>
<tr>
<td>20</td>
<td>English Springer Spaniel</td>
<td>250%</td>
</tr>
<tr>
<td>21</td>
<td>Doberman Pinscher</td>
<td>250%</td>
</tr>
<tr>
<td>22</td>
<td>Dalmatian</td>
<td>249%</td>
</tr>
<tr>
<td>23</td>
<td>Chesapeake Bay Retriever</td>
<td>248%</td>
</tr>
<tr>
<td>24</td>
<td>Saint Bernard</td>
<td>240%</td>
</tr>
<tr>
<td>25</td>
<td>Siberian Husky</td>
<td>239%</td>
</tr>
<tr>
<td>79</td>
<td>Havanese</td>
<td>133%</td>
</tr>
<tr>
<td>80</td>
<td>Miniature Schnauzer</td>
<td>123%</td>
</tr>
<tr>
<td>81</td>
<td>Mixed Breed (Small)</td>
<td>122%</td>
</tr>
<tr>
<td>82</td>
<td>Shih Tzu</td>
<td>117%</td>
</tr>
<tr>
<td>83</td>
<td>Miniature Dachshund</td>
<td>75%</td>
</tr>
</tbody>
</table>
A one-health perspective: use of hemoderivative regenerative therapies in canine and equine patients

Andris J. Kaneps, DVM, PhD, DACVS, DACVSMR*
Kaneps Equine Sports Medicine and Surgery LLC, Beverly, MA
*Corresponding author: Dr. Kaneps (ajkaneps@kanepssequine.com)
Received December 13, 2022
Accepted January 16, 2023
doi.org/10.2460/javma.22.12.0556

Use of mesenchymal stem cells for tendon healing in veterinary and human medicine: getting to the “core” of the problem through a one health approach

Lauren V. Schnabel, DVM, PhD, DACVS, DACVSMR12*, and Drew W. Koch, DVM, PhD, DACVS12
1Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC
2Comparative Medicine Institute, North Carolina State University, Raleigh, NC
*Corresponding author: Dr. Schnabel (lvschnab@ncsu.edu)
Banking on a new understanding: translational opportunities from veterinary biobanks

D. LaLonde-Paul · L. Mouttham · Dog Aging Project Consortium · D. E. L. Promislow · M. G. Castelhano

Received: 25 May 2022 / Accepted: 3 January 2023 / Published online: 8 March 2023
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Best Practices for Veterinary Clinical Studies

- **federally funded animal research**
  - Office of Laboratory Animal Welfare (OLAW)
  - assurance and oversight by Institutional Animal Care and Use Committee (IACUC)

- **FDA Center for Veterinary Medicine**
  - GCP guidelines
  - 9/14/23 draft guidance for informed consent for enrollment of client-owned companion animals

- **AVMA**
  - Use of Veterinary Clinical Studies Committee

- **CASTR Alliance**
  - Companion Animal Studies for Translational Research Alliance
One Health

- an integrated, systems-based approach to optimize the health of people and animals, availability of crucial food resources and sustainable environmental ecosystems
The ‘One Health’ Concept

- Intimate and ever-shifting interactions between human and animal hosts and environmental changes as drivers of risk:
  - Human health, agricultural productivity, food security
  - Climate change: heat, drought, floods
  - Socio-economic dislocations, political instabilities, conflict and geopolitical tensions

- Still largely siloed operational activities and investment in different domains:
  - Public health for human populations
  - Livestock and crop protection
  - Environmental resiliency initiatives

- Slow integration of one health as a core element of national/international public health policies and investment
# The Relentless Ever-Changing Dynamics of Infectious Diseases

<table>
<thead>
<tr>
<th>Old Foes Resurgent: Rx – Resistance</th>
<th>Omnipresent Pandemic Threats</th>
<th>New Foes: Emerging Infectious Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
</tr>
<tr>
<td>Climate Change and New Vector Ranges</td>
<td>Bioterrorism and Bioweapons</td>
<td>Dual-Use Research of Concern</td>
</tr>
<tr>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
<td></td>
</tr>
</tbody>
</table>

- SARS-CoV-2
SARS-CoV-2

Agent-X

What’s Out There?
Comprehensive Global Biosurveillance and Preparedness
for Epidemic/Pandemic Threats
Urbanization and Mega-Cities in Developing Countries and the Increased Threat of Zoonotic EIDs

- High Population Density With Inadequate Biosurveillance
- Expanded Eco-niches and New Zoonotic Exposures/Risks
- Major Gaps in Health Infrastructure and Rapid Disease Reporting
Food Production Systems and Changing Infectious Disease Risks in Low-and Middle-Income Countries (LMICs)

- population growth, urbanization and consumer demand for meat-based diets
- intensification of livestock production
  - shift from rural smallholders to large periurban production units
- deforestation for livestock production expanded of encounters with zoonotic EID reservoir hosts
Expansion of Intensive Livestock Farming Processes and Inter-species Transmission of Antibiotic Resistant Plasmids

Fig. 3. From D.G.J. Larsson and C.F. Flach (2022) Nature Rev. Microbiol. 20, 261
Over Half of Known Human Pathogenic Diseases Can Be Aggravated By Climate Change

Vector Borne Diseases Projected to Increase in Southern Arizona and Maricopa County

- Chagas disease
- chikungunya
- dengue
- Ehrlichiosis
- Lyme disease
- malaria
- Rocky Mountain Spotted Fever
- St. Louis Encephalitis
- West Nile virus
- Yellow Fever
- Zika
Candida auris in Dog Ears

Anamika Yadav, Yue Wang, Kusum Jain, Vijay Amrit Raj Panwar, Hardeep Kaur, Vikas Kasana, Jianping Xu, Anuradha Chowdhary

PMID: 37504709   PMCID: PMC10381908   DOI: 10.3390/jof9070720
THE NEW PANDEMIC FUND AIMS TO:

- bring additional, dedicated resources
- incentivize countries to increase investments
- enhance coordination among partners
- serve as a platform for advocacy

WORLD BANK GROUP
World Health Organization

G20 PRESIDENCY OF INDONESIA
RECOVER TOGETHER
RECOVER STRONGER
• renewed focus and funding to strengthen global public health is necessary but not sufficient

• without adoption of One Health as a core principle in global biosecurity then laudable aspirations for human and planetary health will be undermined by:
  - continued cycles of emergent novel zoonotic EIDs
  - increased infectious disease threats to agricultural livestock and crops
  - food insecurity and depletion of non-renewable natural resources and other ecosystem disruption and prospect of food and water shortages
  - increased risks of socio – cultural – economic instabilities as triggers of conflict
Precision Medicine and One Health: New Opportunities to Reverse the Historical Uncoupling of Human and Veterinary Medicine

- consumer expectations for advances in companion animal care and assimilation of precision medicine technologies from human medicine into veterinary practice
- major opportunities to leverage canine clinical trials as preclinical models to de-risk the current unsustainable cost of failure of investigational drugs in human trials
- one health: strengthening inter-dependencies between sustainable human, animal and environmental systems as a core element in future global biosecurity
The Looming Shortage in Veterinary Professionals (August 2023)

- 2030
  - projected shortage of 24,000 companion-animal veterinarians
  - even larger shortfall in credentialed veterinary technicians
Precision Health and One Health: Technology Acceleration and Implications for Professional Training and Competencies

- shared challenges between human and veterinary medicine
- contemporary curricula in both medical and veterinary schools not keeping pace with the breadth and complexity of technological innovation
- intensifying continuing education needs to sustain professional competencies
- burnout and concern over replacement of professional skills by automated ML/AI processes/decisions
Precision Health and One Health: Technology Acceleration and Implications for Professional Training and Competencies

- additional challenges in veterinary education
  - looming shortage of trained professionals (and credentialed technicians)
  - demographic imbalance between companion animal and livestock practitioners
  - inadequate role models and incentives for non-clinical careers in biomedical research, biotechnology industry and global biosecurity
  - rising educational debt and declining ROI
multiOmics and precision health

remote health monitoring

Big Data

improved translation

one health

the future veterinarian
multiOmics and precision health
remote health monitoring
Big Data
improved translation
one health
the future veterinarian

Slides Available @ http://casi.asu.edu/presentations