Learning Objectives

• Explain the One Health mission and research approach

• List the four One Health Priority Areas

• Discuss how One Health can support, extend, and validate translational research

• Explain the components of a successful One Health research proposal

• List the services Tufts CTSI and its One Health signature program can offer; explain how to request a One Health consultation
Clinical and Translational Science Awards (CTSA) Program

• National Institutes of Health (NIH) program
• Launched in 2006
• A national consortium of 64 institutions
• **Mission:** to develop innovative solutions that will improve the efficiency, quality and impact of the process for turning observation in the laboratory, clinic and community into interventions that improve the health of individuals and the public
Spectrum of Clinical and Translational Research

Bench to Bedside…  ...to Widespread Clinical Practice…  ...to Public Health…  ...to Health Policy

Translation (T1)  Translation (T2)  Translation (T3)  Translation (T4)
Tufts CTSI’s Mission & Purpose

Established in 2008 to translate research into better health

- Stimulate and expedite innovative clinical and translational research, with the goal of improving the public’s health
- *Entire spectrum* of clinical and translational research is critical to meeting the promise and the public’s needs of biomedical science
38 Tufts CTSI Partners

12 Tufts Schools & Centers
- Cummings School of Veterinary Medicine
- Fletcher School of Law & Diplomacy
- Friedman School of Nutrition Science & Policy
- Institute for Clinical Research & Health Policy Studies at Tufts Medical Center
- Jean Mayer USDA Human Nutrition Research Center on Aging
- Sackler School of Graduate Biomedical Sciences
- School of Arts & Sciences
- School of Dental Medicine
- School of Engineering
- School of Medicine
- Tisch College of Citizenship & Public Service
- Tufts Center for the Study of Drug Development

7 Tufts-Affiliated Hospitals
- Baystate Medical Center
- Lahey Clinic
- Maine Medical Center
- New England Baptist Hospital
- Newton-Wellesley Hospital
- St. Elizabeth’s Medical Center
- Tufts Medical Center

6 Industry/Non-Profit Partners
- Blue Cross Blue Shield of Massachusetts
- Eli Lilly and Company
- Institute for Systems Biology and P4 Medicine Institute
- Minuteman Health Network
- Pfizer, Inc.
- Tufts Health Plan

10 Community-Based Partners
- Action for Boston Community Development (ABCD)
- Asian Community Development Corporation
- Asian Task Force Against Domestic Violence
- Asian Women for Health
- Boston Chinatown Neighborhood Center
- Center for Information and Study on Clinical Research Participation
- Greater Boston Chinese Golden Age Center
- Health Resources in Action
- Museum of Science, Boston
- New England Quality Care Alliance

3 Academic Partners
- Brandeis University
- Northeastern University
- RAND Corporation
How Can CTSI Help?

• **Connections** with other researchers, industry, the community, and policy-makers across the Tufts CTSI network and national CTSA consortium via our Navigators & Research Collaboration team.

• **Consultations** on comparative effectiveness, one health, research process improvement and stakeholder and community engagement projects and grants, as well as regulatory issues and other areas of translation.

• **Study design and data analysis** (pre- and post-award) through the **Biostatistics, Epidemiology, and Research Design (BERD) Center**, including drop-in sessions.
How Can CTSI Help?

• 24/7 clinical trial support through our Clinical and Translational Research Center (CTRC).

• Informatics tools for electronic data capture (REDCap), resource sharing, and collaboration.

• Training & professional development including MS and PhD degrees, certificate programs, seminars & workshops, and paid career development awards and fellowships.

• Funding through one-year interdisciplinary pilot studies grants that support the initial stages of research.
How to Request Tufts CTSI Services

• Visit www.tuftsctsi.org and submit a request
http://ilearn.tuftsctsi.org/

Live seminars are recorded for our I LEARN site. Seminar videos can be viewed at any time, and are free!
Get Connected: CTSI Happenings

• Weekly e-newsletter with news, professional development and funding opportunities, resources, and success stories.

• Issued every Monday at 8AM

• Sign up on our website or at http://eepurl.com/C4d9X
For more information: www.tuftsctsi.org
Biostatistics, Epidemiology, and Research Design Center

Norma Terrin, PhD

Director, BERD Center
Tufts CTSI

Professor of Medicine
Tufts University School of Medicine
Biostatistics, Epidemiology, and Research Design Center
Study Planning & Grant Application

• Free services for investigator-initiated grants and protocols:
  – Grant critique/review
  – Development of aims and hypotheses
  – Study design
  – Power and sample size calculations
  – Analysis plans
  – Randomization plans
  – Pilot data analyses for inclusion in grants

• Submit a request at www.tuftsctsi.org
During Study or After Study Completion

• Free services:
  – Guidance on improving rejected manuscripts

• Free weekly drop-in sessions:
  – Guidance on data analyses
  – Statistical advice
  – Interpretation of results
  – Assistance with statistical software
  – Help with research process improvement
  – REDCap assistance
During Study or After Study Completion

- Services offered for a fee:
  - Pre-analysis
    - Analysis file creation
    - Data set organization and cleaning
  - Analysis
    - Statistical analyses
    - Interpretation of results
  - Manuscript
    - Table preparation and graphics
    - Drafting statistical methods and results section
    - Manuscript review

- Submit a request at www.tuftsctsi.org
Drop-in Sessions

• Tufts CTSI's Research Design Center/Biostatistics Research Center (RDC/BRC) offers Drop-in Sessions every Wednesday
  – 8:00 - 9:00am.
  – 35 Kneeland Street, 10th Floor Conference Room
• Drop-in Sessions are free and are staffed by Tufts CTSI epidemiologists and biostatisticians.
Integrating Human, Animal and Environmental Health: A One Health Symposium

Tufts Clinical Translational Science Institute (CTSI)

Tuesday, October 4, 9:00AM - 1:45PM
Boston, MA
One Health

The integrative effort of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals and the shared environment. (Modified from AVMA)
One Health Priority Areas

- Zoonotic infectious disease
- Naturally-occurring animal diseases
- Human-animal interactions
- Ecosystem health
Infectious and Zoonotic Disease
Human-Animal Interactions
Tufts Institute for Human-Animal Interaction

Mission Statement

Our mission is to promote the health, strengths, and well-being of humans and animals through transdisciplinary partnerships that foster innovative research, education, and service programs in human-animal interaction.

Vision Statement

To enhance the lives of humans and animals through mutually beneficial interactions.

How to Get Involved

Sign up for Updates
If you are either currently involved in HAI-related activities, or wish to become involved, please click here to sign up for updates about the Tufts Institute for Human-Animal Interaction. sign up now

Paws for People
Find out more about Tufts Paws for People, our volunteer program for disabled children, at pawsforpeople.org

About Us

Institute for Human Animal Interaction

Board of Advisors

Director: Lisa Freeman, DVM, PhD, Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine, Friedman School of Nutrition Science and Policy; and Jonathan M. Tisch College of Citizenship and Public Service, and Tufts Clinical and Translational Science Institute

Associate Director: Deborah Linder, DVM, Research Assistant Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine and Jonathan M. Tisch College of Citizenship and Public Service

Associate Director: Megan Mueller, PhD, Research Assistant Professor, Department of Clinical Sciences and Center for Animals and Public Policy, Tufts University
Natural animal models
Tufts Human-Animal Cancer Collaborative

Cancer does not discriminate—it is the number one cause of death in adult dogs and has become as common in cats as in humans. In fact, dogs and cats develop cancers that resemble the human disease and often experience a similar response to therapy. Cancer care for dogs and cats provides an opportunity for comparative oncology studies that may foster discovery and clinical translation that is relevant to humans as well as animals.

Human and veterinary oncologists are aligned in their pursuit of scientific discovery to find better outcomes and increase survival rates for their patients regardless of species—human, dog or cat.

Physicians, researchers and veterinarians who comprise Tufts Human-Animal Cancer Collaborative share a passion to revolutionize cancer care for humans and companion animals. They build collaborative bridges across Tufts Health sciences campuses, share knowledge and partner on research to help understand unique cancer biology, advance cancer treatments and improve patient care.

Mission:

Tufts Human-Animal Cancer Collaborative strives to advance mechanistic understanding of cancers leading to improved outcomes in humans and animals.

Partners in Healing

Veterinarians and physicians are poised to deliver a knockout blow to the cancers their patients share. Read more...

Member of the Tufts Human-Animal Cancer Collaborative

Sawhney, Anuwar, DMV, PhD, Professor and Associate Dean, Department of Biomedical Sciences, Cummings School of Veterinary Medicine

Lisa Stefan, DVMD, DACVIM, Assistant Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine

John Berg, DVM, BS, DACVS, Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine

Kathline Borgstrom, DVMD, MPA, DACVIM, Assistant Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine

Andrea Antin, D.O., D.Sc., Professor, Tufts University School of Medicine

Michele Kaperleia, Assistant Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine

Nick Frantz, DVM, PhD, DACVIM, Professor & Department Chair, Department of Clinical Sciences, Cummings School of Veterinary Medicine

Cinda Hebron, MS, VMD, DACVIN, Assistant Professor, Department of Clinical Sciences, Cummings School of Veterinary Medicine

Philip Hinds, PhD, Professor & Chair, Department of Developmental Molecular & Chemical Biology, Tufts University School of Medicine

Sam Jenkins, Assistant Professor, Department of Bio Medical Sciences...
Tufts CTSI One Health

- CTSI One Health Committee
- Tufts student One Health clubs
- CTSI One Health Alliance (COHA)
One Health Symposium

Project Presentations
A Safe, Inexpensive, Easily Administered enterohemorrhagic
\textit{E. coli} Vaccine for Cattle

John Leong, MD, PhD
Linc Sonenshein, PhD
Saul Tzipori, DVM, PhD, DSc, FRCVS

Tufts University School of Medicine
Tufts University Cummings School of Veterinary Medicine
Attaching and Effacing (AE) Pathogens

- Enterohemorrhagic *E. coli* (EHEC)
Attaching and Effacing (AE) Pathogens

- **Enterohemorrhagic E. coli (EHEC)**
  - ~100,000 cases annually
  - Encodes Shiga toxin on a lambdoid phage ($\Phi_{Stx}$)
    - Hemorrhagic colitis
    - 5-10% -> hemolytic uremic syndrome (HUS)
    - Antibiotic Rx -> increased Shiga toxin

![Attaching and effacing lesion](image)
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- **Citrobacter rodentium**
  - Efficiently colonizes conventional mice.
  - Lacks ΦStx and does not produce Shiga toxin.
  - Non-hemorrhagic colitis
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Cattle are major source of EHEC
Cattle are major source of **EHEC**

- **EHEC** colonization of mucosal surface at anorectal junction
Cattle are major source of EHEC

- EHEC colonization of mucosal surface at anorectal junction
Cattle are major source of EHEC

- EHEC colonization of mucosal surface at anorectal junction
Economic cost of EHEC


- 2015: an EHEC outbreak associated with Chipotle Mexican Grill resulted in cases in 11 states.
Potential vaccination strategy

• Gally: Three antigens, when used as an intramuscular vaccine cocktail, resulted in 1000-fold decrease in EHEC fecal shedding.
  – Tir
  – Intimin
  – EspA
Potential vaccination strategy

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Each is required for attaching and effacing lesions
Potential vaccination strategy

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  – Tir
  – Intimin
  – EspA

Each is required for attaching and effacing lesions

However, too expensive to be deemed practical.
Bacillus subtilis as a Heat-Stable, Needle-Free Vaccine Delivery System

Linc Sonenshein, PhD
Saul Tzipori, DVM, PhD, DSc, FRCVS

Tufts University School of Medicine
Tufts University Cummings School of Veterinary Medicine
Bacillus subtilis and sporulation

Growth

vegetative cell

sporulating cell

spore

Time

Tufts CTSI
Bacillus subtilis and sporulation

1. Produce antigens in vegetative cells
Bacillus subtilis and sporulation

1. Produce antigens in vegetative cells

2. Produce antigens on the surface of spores
**Bacillus subtilis and sporulation**

1. Produce antigens in vegetative cells

2. Produce antigens on the surface of spores

Cost: approximately $0.09 to $0.22 per dose
Test case

• Two prototype tetanus vaccine strains expressing the TetC antigen as
  – A fusion protein on the spore surface
  – In the vegetative cell cytoplasm
Mucosal delivery of B. subtilis vaccines

• In mice and piglets, intranasal administration of TetC-expressing B. subtilis induces a systemic protective immune response, both Th1 and Th2.

• Both vaccines are stable at 45°C for > 17 months.
Mucosal delivery of B. subtilis vaccines

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• Both vaccines are stable at 45°C for > 17 months.

• B. subtilis Rota virus vaccine also efficacious in animal model.
Challenge: EHEC does not efficiently colonize conventional mice

• Germ-free or streptomycin-treated mice have been used for EHEC infection, but well documented colonization factors are not required in these models.
Cr(ΦStx), a murine model for EHEC

C. rodentium

Joan Butterton  David Schauer
**Cr(ΦStx), a murine model for EHEC**

- Colonizes conventional mice, forms AE lesions on intestinal epithelium, causes lethal disease with renal manifestations.

Joan Butterton  David Schauer
Cr(ΦStx), a murine model for EHEC

- Colonizes conventional mice, forms AE lesions on intestinal epithelium, causes lethal disease with renal manifestations.
- Colonization and disease require Tir, intimin and EspA.
Aim 1: Generate *B. subtilis* vaccine strains that produce Tir, intimin or EspA.

- Several promoters and fusion partners will be tested and compared.
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Aim 1: Generate B. subtilis vaccine strains that produce Tir, intimin or EspA.

• Several promoters and fusion partners will be tested and compared
  – Utilize alleles from the four EHEC serotypes that comprise the major outbreaks, as well as from C. rodentium for proof-of-principle test in mice (see below).
Aim 2: Test B. subtilis Tir, intimin, and EspA vaccine strains for protection in mice.

- Using IN route, test *B. subtilis* strains with a panel of adjuvants for the ability to induce a robust, long-lived immune serum and fecal IgG and IgA responses.
Aim 2: Test B. subtilis Tir, intimin, and EspA vaccine strains for protection in mice.

• Using IN route, test B. subtilis strains with a panel of adjuvants for the ability to induce a robust, long-lived immune serum and fecal IgG and IgA responses.

• Test for protection from Cr(ΦStx) after immunization with mixture of B. subtilis harboring alleles specific to C. rodentium.
Aim 2: Test B. subtilis Tir, intimin, and EspA vaccine strains for protection in mice.

- Using IN route, test *B. subtilis* strains with a panel of adjuvants for the ability to induce a robust, long-lived immune serum and fecal IgG and IgA responses.
- Test for protection from Cr(ΦStx) after immunization with mixture of *B. subtilis* harboring alleles specific to *C. rodentium*.
- Test also for decolonization of mice pre-inoculated with *C. rodentium*. 
Aim 3: Test *B. subtilis* Tir, intimin, and EspA vaccine strains for protection in 3 m-old cattle.

- Establish the optimal dose, adjuvant, and number of immunizations for robust, long-lasting (>6 months) mucosal and systemic antibody production.
Aim 3: Test B. subtilis Tir, intimin, and EspA vaccine strains for protection in 3 m-old cattle.

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- Test efficacy prior to EHEC challenge (i.e., protection).
Aim 3: Test *B. subtilis* Tir, intimin, and EspA vaccine strains for protection in 3 m-old cattle.

- Establish the optimal dose, adjuvant, and number of immunizations for robust, long-lasting (>6 months) mucosal and systemic antibody production.
- Test efficacy prior to EHEC challenge (i.e., protection).
- Test efficacy following EHEC challenge (i.e., decolonization).
Thank You
Discussants

Caroline Genco, PhD
Deborah Linder, DVM, DACVN
Paola Massari, BS/MSc, PhD
Robin Ruthazer, MPH
Questions?
A One-Health Approach to Asthma Therapy: Decreasing Airway Smooth Muscle Mass Using Naturally Occurring Models of Disease in the Horse and Cat

Melissa R. Mazan, DVM, DACVIM
Heber Nielsen, MD
Daniela Bedenice, DVM, DACVIM, DACVECC
Elizabeth Rozanski DVM, DACVIM, DACVECC
Alisha Gruntman, DVM

Tufts University School of Medicine
Tufts University Cummings School of Veterinary Medicine
Asthma

- Afflicts 25 million in U.S., including 10 million children
- Leading cause of missed school days, ER visits, and hospitalizations
- 5,000 deaths per year in U.S., mostly children
- Current treatments only target inflammation
- 5-10% of asthma is poorly controlled with current therapies
- Severe asthmatics who are well-controlled still have significant loss of respiratory function due to smooth muscle cell proliferation
Pathophysiology of Asthma in Humans

- Allergic v. non-allergic
- Chronic airway inflammation
- Smooth muscle proliferation
- Heightened response to environmental triggers
- Episodes of bronchoconstriction with reversible airflow obstruction
Narrowed airway (limited air flow)
Tightened muscles constrict airway
Inflamed/thickened airway wall
Mucus

Muscle
Airway wall
Airway x-section

Thickened airway wall
Muscle
Mucus

Diana C. Doeing, and Julian Solway J Appl Physiol
2013;114:834-843
Airway Smooth Muscle and Asthma

Increased ASM Mass
Airway Wall Thickening

ASM Structure

ASM Function
Enhanced Contraction
Impaired Relaxation
Length Adaptation

Airway Inflammation
Cytokines/chemokines
Cell Adhesion
Cellular Infiltrate
Edema
Increased Mucus
Increased IgE

Diana C. Doeing, and Julian Solway J Appl Physiol
2013;114:834-843
Asthma Treatment

• Reverse acute bronchoconstriction – bronchodilators
• Decrease inflammation – corticosteroids
• Modulate environment – decrease exposure to triggers
Asthma is not just a human problem!

- Horses
  - Inflammatory airway disease
  - Heaves
- Cats
  - Feline asthma

Excess accumulation of airway smooth muscle cells is a prominent feature of airway wall remodeling in both animals and people.
Clinical Manifestations of Disease in Human, Horse and Cat

- Reversible airway obstruction
- Airway hyper-responsiveness
- Cough
- Wheeze
- Exercise impairment
Horse with Equine Asthma
Cat With Feline Asthma
Smooth Muscle Hyperplasia - Horse
Treatment – B2AR and corticosteroids does not address ASM hypertrophy
What makes horses and cats good models?

Horse
- LARGE – easy to sample airways tissues and secretions over time
- Direct visualization of airways with bronchoscopy
- Pulmonary function testing commonly performed

Cat
- SMALL – can readily assess with CT

Both have clinical signs similar to humans. Rodents do not.
Pharmacological Targeting of ASM

• No effective strategies to decrease ASM proliferation
• CCN5 protein inhibits proliferation of cultured human ASM, as well as human vascular and fibroid smooth muscle cell proliferation
• CCN5 expression is high in healthy airways and virtually absent in asthmatic airways in mice
• Human ASM treated with CCN5 or calcium channel blockers (CCBs) display similar gene expression profiles, based on Connectivity analysis
• CCBs are cheap and have a favorable toxicity profile
CCN5

CCN1 (CYR61)
CCN2 (CTGF)
CCN3 (NOV)
CCN4 (Wisp-1)
CCN6 (Wisp-3)

CCN5 (COP-1)

- 28kD, cystein-rich protein found in many cells and tissues
- Matricellular and nuclear protein

Confocal/DIC merge

Non-Permeabilized  |  Membrane Extracted

Confocal/DIC merge
Hypothesis

The use of clinically relevant animal models of human asthma will allow us to detect the clinical efficacy of CCN5 and CCN5-mimetic CCBs in limiting airway remodeling and damage by reducing ASM hyperplasia, acute bronchospasm, and inflammation, thus protecting pulmonary function.
Aim 1

Determine the differential expression of CCN5 in horses and cats with clinically documented naturally occurring asthma vs. non-asthma

- PFTs
- BAL
- Endobronchial biopsy
- Brush biopsy
Aim 2

Determine the effect of CCN5 and CCBs on cultured ASM from horses and cats with well-characterized asthma.

- Infect cultured ASM cells from horses and cats with:
  - Adenoviral vector expressing CCN5
  - Verapamil, diltiazem and nifedipine representing 3 classes of CCBs
- Measure cell proliferation and cell death
Thank You
Discussants

Sucharita Kher, MD
Alejandro Moreno-Koehler, MPH
John Castellot, PhD
Questions?
Break!
The Effects of Antimicrobial Therapy in Dogs on Owner Microbiota

Shira Doron MD, FIDSA
Kirthana R. Beaulac, PharmD BCPS
Tine Vindenes MD
Annie Wayne DVM, MPH

Tufts Medical Center
Foster Hospital for Small Animals at the Cummings School of Veterinary Medicine
Transmission of MRSA between Companion Animals and Infected Human Patients Presenting to Outpatient

Phylogenetic and Pathotypic Similarities between *Escherichia coli* Isolates from Urinary Tract Infections in Dogs and Extraintestinal Infections in Humans

James R. Johnson, Adam L. Stell, Parissa Delavari, Andrew C. Murray, Michael Kuskowski, and Wim Gaastra

1Medical Service and Geriatric Research, Education, and Clinical Center, Minneapolis Veterans Affairs Medical Center, and Departments of Medicine and Psychiatry, University of Minnesota, Minneapolis; 2Department of Bacteriology, Institute of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, University of Utrecht, Utrecht, The Netherlands


Commonly Prescribed Antibiotics

In dogs and cats:
• Amoxicillin and amoxicillin-clavulanic acid
• Cephalexin
• Doxycycline
• Enrofloxacin (fluoroquinolone)
• Clindamycin
• Metronidazole

In humans:
• Amoxicillin and amoxicillin-clavulanic acid
• Cephalexin
• Doxycycline, minocycline
• Ciprofloxacin (fluoroquinolone)
• Clindamycin
• Metronidazole
“It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body.”

- Alexander Fleming, 1945
Antibiotic Use Causes Resistance

Collateral Damage

Cephalosporins

- Vancomycin-resistant Enterococci
- Methicillin-resistant Staphylococcus aureus
- Extended-spectrum β-lactamase producing Klebsiella pneumoniae
- Multidrug-resistant Acinetobacter baumanii

Fluoroquinolones

- Methicillin-resistant Staphylococcus aureus
- Fluoroquinolone-resistant gram-negative bacilli
  - *E. coli* resistance in the community
  - *Pseudomonas aeruginosa* resistance in hospitals
- Extended-spectrum β-lactamase producing organisms

The Microbiome

- The GI microbiota serves many important functions including maintenance of nutrition, innate immunity, intestinal barrier function and preventing colonization by pathogens.
- Dethlefsen *et al.* showed that administration of ciprofloxacin decreased the taxonomic richness, diversity and evenness of the microbial community.
- Several taxa failed to normalize even six months later.

The GI microbiota serves many important functions including maintenance of nutrition, innate immunity, intestinal barrier function, and preventing colonization by pathogens.

Dethlefson et al. showed that administration of ciprofloxacin decreased the taxonomic richness, diversity and evenness of the microbial community, several taxa failed to normalize even six months later.

Figure 5. Diversity Statistics
(A) Observed taxon richness (number of V3 refOTUs) per sample; Cp-associated samples have significantly fewer OTUs than pre- and post-Cp samples for individuals A and B (p < 0.005) but not individual C (p = 0.129).
(B) Shannon diversity index; Cp-associated samples are significantly less diverse than other samples for all individuals (p < 0.001).
(C) Shannon equitability index; OTU abundance in Cp-associated samples is significantly less evenly distributed than OTU abundance in other samples for all individuals (p < 0.001 for A and B, p < 0.05 for C). Formulas for diversity and evenness are given in Methods; significance is assessed as the probability that the Cp-associated value is drawn from the lower tail of a normal distribution with mean and variance as calculated from the other samples.

doi:10.1371/journal.pbio.0060280.g005

Antibiotic Effects

• Jernberg et al demonstrated highly significant disturbances in bacterial communities that persisted over a two-year period after a seven-day course of clindamycin
• In particular, they found a sharp decline in the clonal diversity of Bacteroides and persistence of highly resistant clones
Jernberg et al demonstrated highly significant disturbances in bacterial communities that persisted over a two-year period after a seven-day course of clindamycin.

In particular, they found a sharp decline in the clonal diversity of Bacteroides and persistence of highly resistant clones.

Figure 1: Number of Bacteroides sp. clone types as assessed by rep-PCR and percent of clones that are highly resistant to clindamycin over a 2-year sampling period: (a) clindamycin exposed group; (b) control group. Day 0: day before clindamycin administration. Bars represent total number of clone types and filled circles represent percent of highly clindamycin-resistant clones (>64 mg/l).
Transfer of the Microbiome Between Pets and Humans

• Oh et al. used 16S rDNA pyrosequencing to compare the oral microbiomes of pets with their owners.

• Results were mixed. Owner-pet pairs with high “closeness scores” indicating oral contact were more likely to have similarities.
Methods

• Enroll 20 pet-owner pairs in which the pet is treated with an outpatient course of antibiotics for any indication
• Enroll 20 pet-owner pairs as controls (no antibiotics)
• Baseline oral/fecal samples, repeat after antibiotics
• Assess changes in microbial composition in the animal and the human
Hypotheses

• The bacterial composition of the mouth/stool will change in the pet as a result of antibiotic administration
• The bacterial composition of the mouth/stool will change in the owner as a result of antibiotic administration to the pet
Significance

• Pets consume 150,000 kg of antibiotics annually in the United States
Questions for the group

• Species: limit to dogs only?
• Human cohort: adults versus babies (microbiome not yet established)?
• Pyrosequencing versus culture-based versus repetitive sequence based PCR versus T-RFLP as outcomes?
• Limit to high “closeness score”
• Oral versus fecal microbial composition?
Questions for the group

• Antibiotic: limit to beta-lactams (most commonly used)? Include a fluoroquinolone arm?
• Duration of antibiotic therapy?
• Timing of follow-up specimen?
• Incentives for participation?
Thank You
Discussants

Cheleste Thorpe, MD
Farzad Noubary, PhD
Deborah Kochevar, DVM, PhD, DACVC
Questions?
Cohabitation with Production Animals, Gut Microbiota, and Stunting in Guatemalan Children

Marieke Rosenbaum, DVM, MPH (Co-I | TCSVM)
Janet Forrester, PhD, MSc (PI | PHPD)
Honorine Ward, MBBS (Co-I | SSBS)
Noel Solomons, MD (Co-I | Friedman, CeSSIAM)
Henry Rogalin, PhD (Post Doc | CTSI)
What Is Stunting?

Malnutrition comes in many forms:

- **Stunting**: (people are too short for their age)
- **Wasting**: (people are too thin for their height)
- **Obesity**: (people are overweight)

Global Nutrition Report 2015

#NutritionReport
What Is Stunting?

Low Height for Age (HAZ) <2 SD Below WHO Median for Optimal Growth.
Why Does Stunting Matter?

- Intellectual Development
- Educational Attainment
- Economic Development
- Longevity
- Immune Response
- Stunted Offspring
- Work Productivity
What Causes Stunting?
Associations With Stunting

- Maternal Health
- Parasitic Infections
- Gut Microbial Composition
- Poor Sanitation
- Impaired Intestinal Integrity
- Nutrition
Nutritional Status

Intestinal Integrity

Immune Response

Inflammatory Response

(a) Immunological equilibrium

Symbionts  Commensals  Pathobionts

Regulation  Inflammation

(b) Immunological dysequilibrium

Pathogens

Regulation  Inflammation

Impaired Intestinal Integrity

Microbial Translocation

Malnutrition
Preliminary Data by Dr. Ward and Dr. Kang from Vellore, India
Does exposure to animal feces, through alterations in the gut microbiota, promote stunting in children?
Map 1.1 Prevalence of Stunting by Country, 2011

### Recent Data on Stunting in Guatemala by Dr. Solomons and Colleagues, 2013

**Table 1: Average HAZ scores and proportion of stunted children by subgroups in children attending public health clinics in urban Quetzaltenango & suburban La Esperanza (n=299)**

<table>
<thead>
<tr>
<th>Age</th>
<th>HAZ score (mean, SD)</th>
<th>Proportion stunted (%)</th>
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</thead>
<tbody>
<tr>
<td>6-11 months</td>
<td>-1.70 (1.13)</td>
<td>41/114 (36%)</td>
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<td>(n=114)</td>
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<tr>
<td>12-17 months</td>
<td>-2.07 (1.16)</td>
<td>53/98 (54%)</td>
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<td>(n=98)</td>
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<tr>
<td>18-23 months</td>
<td>-1.93 (0.98)</td>
<td>41/87 (47%)</td>
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<td>(n=87)</td>
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</table>
Thank You
Discussants

Shibani Ghosh, PhD
Janis Breeze, MPH
Nicholas Frank, DVM, PhD, DACVIM
Breakout Sessions

Goals:

• Add, delete, change Specific Aims

• List of additional experiments/experimental approaches that would enhance project impact

• List of preliminary data needed before submission

• List additional collaborators needed for team

• List next steps for team
<table>
<thead>
<tr>
<th>Workgroup</th>
<th>Room</th>
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<tbody>
<tr>
<td>Development of a Safe, Inexpensive, Easily Administered EHEC Vaccine for Cattle</td>
<td>Room 1414</td>
</tr>
<tr>
<td>John Leong, MD, PhD</td>
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<tr>
<td>A Novel Approach to Asthma Therapy: Decreasing Airway Smooth Muscle Mass</td>
<td>Room 1503</td>
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<tr>
<td>Melissa Mazan, DVM, DACVIM</td>
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<tr>
<td>Antibiotic Stewardship and Infection Control</td>
<td>Room 1533</td>
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<td>Shira Doron, MD</td>
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<td>Cohabitation with Production Animals, Gut Microbiota, and Stunting in Children</td>
<td>Room 1521</td>
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<td>Marieke Rosenbaum, DVM, MPH</td>
<td></td>
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</table>
Report Back

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Thank you very much!
One Health Symposium