Bellwether Magazine

Volume 1
Number 80 *Fall 2013*

Article 2

10-1-2013

Harnessing the Power of Genomics: Introducing Penn Vet's Center for Research on Microbes in Health and Disease

Katherine Unger Baillie
University of Pennsylvania

bellwether

NUMBER 80 | FALL 2013

THE NEWSMAGAZINE OF THE UNIVERSITY OF PENNSYLVANIA SCHOOL OF VETERINARY MEDICINE







HARNESSING THE POWER OF GENOMICS:
Introducing Penn Vet's Center for Research on Microbes in Health and Disease

ALSO IN THIS ISSUE...

PennVet

OFFICE OF ADVANCEMENT, ALUMNI RELATIONS AND COMMUNICATIONS

ASSISTANT DEAN OF ADVANCEMENT, ALUMNI RELATIONS AND COMMUNICATIONS
CAROL POOSER

DIRECTOR OF ANNUAL GIVING AND ADVANCEMENT SERVICES
MARY BERGER

DIRECTOR OF DEVELOPMENT FOR MATTHEW J. RYAN VETERINARY HOSPITAL
HELEN RADENKOVIC

DIRECTOR OF DEVELOPMENT FOR NEW BOLTON CENTER
JANE SIMONE

DIRECTOR OF STEWARDSHIP AND SPECIAL PROJECTS
JILLIAN MARCUSSEN

DIRECTOR OF ALUMNI RELATIONS
KRISTEN McMULLEN

DIRECTOR OF COMMUNICATIONS
ASHLEY BERKE

ASSISTANT DIRECTOR OF ANNUAL GIVING AND ADVANCEMENT SERVICES
JOHN CAMPBELL

WEB COMMUNICATIONS MANAGER
CAROLE CLOUD

COMMUNICATIONS SPECIALIST FOR NEW BOLTON CENTER
LOUISA SHEPARD

COMMUNICATIONS COORDINATOR
JOHN DONGES

DEVELOPMENT COORDINATOR FOR NEW BOLTON CENTER
BARBARA BELT

SPECIAL EVENTS COORDINATOR
DARLEEN CALAHAN

ADMINISTRATIVE COORDINATOR
JUDI FRANCISCO

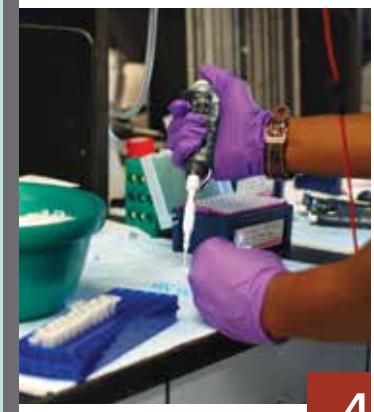
CONTRIBUTORS
KATHERINE UNGER BAILLIE
MARY BERGER
ASHLEY BERKE
JOHN DONGES
DR. LAWRENCE GERSON
JILLIAN MARCUSSEN
KRISTEN McMULLEN
HELEN RADENKOVIC
STACY RITCHEY
JANE SIMONE
MANASEE WAGH

DESIGNER
ANNE MARIE KANE

Please address your correspondence to:
Ashley Berke
University of Pennsylvania
School of Veterinary Medicine
3800 Spruce Street
Philadelphia, PA 19104-6010
(215) 898-1475
berke@vet.upenn.edu

PennVet

FALL2013
NUMBER 80



bellwether

FEATURES

DEPARTMENTS

ABOUT THE COVER:

Penn Vet launches the Center for Research on Microbes in Health and Disease. Penn Vet researchers are collaborating with Penn Med to answer questions about how microbes interact with their hosts and affect health and disease.

HARNESSING THE POWER OF • genomics

BY KATHERINE UNGER BAILLIE

Last summer Dean Joan Hendricks challenged Penn Vet's faculty to come up with a big idea to advance the profession. This wasn't just an idle "ask." She planned to put money where her mouth was.

"I said to the leadership – and the entire community – that while we had to be very disciplined and careful about routine spending, we actually had some reserves, and wise investments in exciting ideas with huge potential were possible," says Hendricks.

Dean Hendricks' challenge got the gears turning for Dr. Christopher Hunter, Chair of the Department of Pathobiology.

"I started to think about ways to make our faculty better; not in recruiting new faculty necessarily, but in improving the skills of the people already here," he says.

This idea, one that would invest in Penn Vet's already world-class faculty while simultaneously supporting cutting-edge research, has given birth to what is now known as the Center for Research on Microbes in Health and Disease. The Center is designed to teach, facilitate, and encourage collaboration on the use of genomics technologies to gain insights into

how bacteria, parasites, viruses, and other organisms interact with their human and animal hosts in ways that both maintain health and lead to disease.

"The proposal sparked my imagination," says Hendricks. "It would make us both a leader on the campus and a leader in our profession."

With support from Dean Hendricks, Associate Dean for Research Dr. Phil Scott, Executive Director of Finance and Administration Robert Schieri, and others, the Center has begun by funding five research projects, each led by Penn Vet faculty, which will probe these interactions. These pilots promise to augment society's understanding of the complex relationship between microbes and health, and carry Penn Vet's scientific enterprise to new heights.

HOT TOPIC

In retrospect, this proposal may seem obvious, as it capitalizes on the School's existing strengths in the study of microorganisms, including a focus on bacterial, viral, and parasitic pathogens, while addressing an aspect of science that has evolved rapidly over the last several years: genomics.

A decade ago, it cost 25 to 50 million dollars to sequence a genome. Today, that price has dropped to less than $10,000. As a result, genome sequencing has become a relatively accessible scientific tool, one that has the potential to open up new realms of research. Studies of the microbiome, or the collection of microorganisms that reside on the skin, in the gut, or in other specific environments, have exploded thanks to these techniques.

"We always knew there were microbes there, but we didn't know what they were. You couldn't grow them, nor could you work with them," explains Hunter. "But the genomic approach now allows you to look at them and associate them with disease."

Yet despite genome sequencing dropping in cost and rising in availability, Hunter realized that many faculty members lacked the

> "We always knew there were microbes there, but we didn't know what they were. You couldn't grow them, nor could you work with them. But the genomic approach now allows you to look at them and associate them with disease."
>
> *—Dr. Christopher Hunter*
> *Chair of the Department of Pathobiology*

training and familiarity with these approaches to use them, or to make the most of their power. Even those faculty members with knowledge of how to utilize genomics tools can easily be overwhelmed by the vast amounts of data that the techniques can generate.

"Many faculty, especially more established faculty who set up their labs 15 or 20 years ago, may be unfamiliar with these techniques, or reluctant to invest in new technologies," adds Hunter.

EDUCATE, UNIFY, FACILITATE

To overcome these hurdles, one of the first steps toward creating the Center involved hiring Dr. Daniel Beiting, an immunologist by training who gained expertise in genomics methods during a postdoctoral fellowship at Penn, in the lab of Dr. David Roos in the School of Arts and Sciences' Department of Biology. Beiting's goal is to demystify the scientific approaches required to set up, conduct, and analyze genomics-based studies.

"There are people at Penn who have never used these technologies, there are people who dabble with them, and there are people who use them routinely," says Beiting. "As a center, we have to act as a catalyst to help make it easier for everyone in all three of these groups."

Indeed, even those faculty and students familiar with genomics can use assistance in the latter stages of experimentation – after the tests are over and data has poured in. If one imagines the quantity of information that can arise from one genome is extraordinary, the quantity that comes from an analysis of all the microbes living on a portion of a dog's skin, for example, would be astronomical. Issues of data storage, management, and analysis have become some of the most challenging elements of experimentation.

"If you're looking at microbes, you could be dealing with 30,000 different genomes in a patch of skin," says Hunter. "How do you parse out what is meaningful? How do you even store that amount of data? Those are the challenges that Dan is helping our community address."

An early strategic decision was *not* to invest in hardware, as sequencing equipment is expensive and can quickly become obsolete. In addition, Penn has facilities, particularly within the medical school, that Penn Vet researchers can utilize. Beiting has been able to help to connect vet school students and faculty with the resources around campus that would best fulfill their needs while training them in the most effective ways to set up experiments and analyze data.

Partnering with the Perelman School of Medicine has also been a key facet of the Center, as certain Penn Medicine faculty are already engaged in studying the host-microbe interactions and using genomics regularly to address questions of basic science and clinical importance.

"Our School is in a unique position in that we have a medical school across the street and a dental school down the road," Hunter says. "We're ideally positioned to take advantage of their expertise and collaborate in ways that further everyone's research aims."

LAUNCHING RESEARCH

In the first year of the Center's existence, five projects have received full funding – $50,000 a piece – to pursue their aims, while three others received partial funding.

The five fully funded pilots include a multi-investigator study at Penn Vet's Philadelphia campus, examining the role of microbes in canine atopic dermatitis, and another at New Bolton Center, which is studying how the rumen microbiome of dairy cows impacts their productivity and health (read more on pages 9 and 12). While not the sole focus of the Center, the microbiome also serves as the primary focus of the three additional projects.

One of these will be led by Dr. Christopher Lengner, Assistant Professor of Animal Biology at Penn Vet. A stem cell geneticist, his prior work has shed light on the idea that most cases of colorectal cancer may originate from a mutation in a stem cell that leads to unregulated growth. Yet other research has indicated that chronic inflammation, inspired by an immune response to gut bacteria, may also play a leading role in increasing cancer risk.

"With our project, we want to reconcile these two ideas," Lengner says.

The pilot work will involve experimentally manipulating expression of the protein Msi, which Lengner's lab has previously found to bind directly to RNA molecules that are involved in regulating immune responses.

"We believe these genes might provide a link between the transformation of the stem cell and regulation of the immune response to microbes," Lengner adds.

Lengner and colleagues will track the response of the microbial communities as Msi levels are either knocked down or overexpressed. What they find may lead to the pursuit of other questions, such as how tumor development progresses in the presence or absence of various microbial communities.

"This is really just a first step to get a little bit of a handle on a very complex problem," Lengner says. "As a relatively junior faculty member, I might have otherwise been reluctant to divert resources to a new project like this one. But because these resources are here now and the expertise is here, it lowers the barrier and makes it much more tenable for me to head down this path."

Dr. Julie Engiles, Assistant Professor of Pathology at Penn Vet's New Bolton Center, is the primary investigator on another Center-funded effort. Her project will investigate the effect of pre-operative antibiotics on the gut microbiome of horses that come to New Bolton Center for elective surgeries.

Previous research has linked high-carbohydrate feed to the development of colitis. The mechanism may have to do with how a change in diet leads to alterations in the population of microbes living in the gastrointestinal tract, causing disruptions and illness. Likewise, administering pre-operative antibiotics could also lead to gut microbiome imbalances.

Engiles and colleagues do not lack for potential study subjects at the busy New Bolton Center. Their study method is simple and non-invasive: They will take fecal and serum samples on admission and at certain time points after surgeries to track variations in the horses' gut microbiome. If, unfortunately, a horse develops an infection after its procedure, the researchers will evaluate whether the infectious agents match up to those in the gut or whether they match other microbes. The study will also track horses to see if they develop other post-operative complications, including two of the most troublesome maladies that strike horses: colic and laminitis.

Researchers from Penn Vet and Penn Med discuss the progress of their projects and share ideas and resources.

Using genomics in this study might help researchers identify the infectious microbes, which can be difficult to do using traditional culture-based approaches.

"I thought that this genomic approach would be a fantastic way to explore microbial shifts in horses that have been administered pre-operative antibiotics. We want to see if we can identify specific organisms or groups of organisms that may be associated with post-operative complications," says Engiles.

The data Engiles and colleagues collect may feed into other studies, including one she is partnering on with Dr. Hannah Galantino-Homer, Senior Research Investigator at New Bolton Center, to search for biomarkers associated with an increased risk of developing laminitis.

Through her project, Engiles hopes to not only help improve treatments and protocols for treating horses, but also draw conclusions that could potentially impact human medicine.

"We say it all the time but I truly believe in 'Many Species, One Medicine,'" she says. "As a pathologist, I see that, time and time again, we can bridge the species gap and get the bigger picture answer of how these infections arise."

For Dr. Tracy Bale, Professor of Neuroscience at Penn Vet, the Center's support provided an opportunity to explore connections between the microbiome and her primary area of focus: how maternal stress impacts the neurological health of offspring.

"While we are not immunologists or microbiologists, this is a novel way of thinking about a mechanism that might be contributing to outcomes in our maternal stress model," she says.

The project Bale is leading will examine how a mother's vaginal microbial community impacts her offspring's brain development. Bale's thinking is as follows: Because a baby's gut is first colonized by bacteria from the mother's vagina at birth, perhaps differences are produced in the population of microbes by a mother's stress, and can lead to changes in a baby's own gut microbiome. This altered microbial community could then lead to differences in how important nutrients are absorbed in the offspring's body, leading to differences in how the baby's brain develops.

"Some studies on the gut microbiome have found associations with risk factors for autism and schizophrenia," says Bale. "We're now trying to put two and two together."

Already Bale's lab has collaborated with Dr. Elizabeth Grice of Penn Medicine and Dr. Michael May of Penn Vet, and determined that a female mouse's vaginal microbiome is changed when she is stressed, and that these altered microbe populations are transferred to pups at birth. Further down the line, Bale hopes to determine whether experimentally manipulating the bacteria in the vagina leads to changes in brain development, and whether these changes could be "rescued" by various procedures like giving antibiotics or introducing particular types of bacteria into a baby's gut.

With hard work and a little luck, says Hunter, the results of these pilots will enable Penn Vet's faculty to produce preliminary findings that will give them a competitive edge in earning additional funding from outside sources. Already, a grant application submitted by Hunter describing the work of the Center was given a top ranking by the National Institutes of Health.

"This is an investment, with the expectation that it will pay off in the long run," says Hunter.

SUPPORT FOR THE FUTURE

All of the faculty with funded projects will be supported by monthly lab meetings where they will share data and provide each other with feedback. But the advantages of the Center do not end with the pilot projects. Beiting has made himself available to all of Penn Vet as a resource. Already he can be found in his office answering questions of students and faculty, or holding workshops to introduce or coach individuals in the techniques of genomics research.

Moving forward, Beiting is looking to design a course for postdoctoral researchers and graduate students in the area of genomics research. The Center is also considering creating a seminar series or sponsoring speakers to present in other established series around campus. Continuing to engage the medical school through learning partnerships and research collaboration will be an ongoing goal. And the Center plans to offer funding for another set of pilot projects next year.

"We strongly believe this innovative approach to health and disease will provide new insights into human and animal health," says Hendricks, "and will build on the One Health concept in a novel and very impactful fashion."

Adds Engiles: The Center is introducing me to techniques that I would not have had exposure to otherwise, but are very powerful and give you a different perspective. They allow you to answer questions that you would previously just scratch your head and wonder about."