Predicting prescriptions

Professor Colleen Jonsson, Director of the Center for Predictive Medicine for Biodefense and Emerging Infectious Disease at the University of Louisville, talks about approaches in identifying new viruses, molecular imaging and discovery of new therapeutics for these currently untreatable diseases

To begin, could you give us a brief insight into your life and work up to this point?

My work has focused on viral and host determinants of disease caused by pathogens; initially in plants and then in humans. I made the switch from plants to human systems in 1990 as a postdoctoral fellow with Dr Monica Roth. My research approaches have encompassed very mechanistic questions that target the macromolecular level (eg. proteins, enzymes, and nucleic acid) and the viral life cycle. In moving into research questions of hantaviruses I became intrigued with the ecology of viruses.

You are the Director of the Center for Predictive Medicine at the University of Louisville. Are there any projects or findings to date that you would like to highlight? What are some of the aims for the Center's future?

Over the past two years, the Center has led the hiring of new faculty members to the University who will be focused on mechanisms of pathogenesis and host response of emerging and biodefense pathogens as well as how to translate their basic research findings into useful therapeutics and/or diagnostics. I have great expectations for these scientists as they build their own research programmes and synergise across others to create much-needed translational science.

Your laboratory is working at developing predictive animal models of infectious diseases using molecular imaging modalities that until now have not been available. Could you elaborate on this and its applications in emerging diseases such as SARS?

Molecular imaging has been successfully employed in cancer research and patient care for many years. New research facilities in the U.S. have increasingly incorporated one or more imaging modalities to study the progression of pathogen infection in animal models. Current efforts focus on the discovery of new biomarkers as well as those already available that can be employed to understand the progression of disease. These markers will be used in the respective animal models to accelerate the discovery of more effective therapeutics. Translation of markers discovered in these basic and translational research efforts to patient care will require new, cost-effective approaches in imaging that are now underway.

Many people may find it surprising to know that the majority of human viruses have no treatment, vaccine or antiviral. What are some of the obstacles against controlling these viruses?

The approaches my laboratory and collaborations have employed are the screening for small molecule compounds against various viruses in predominantly cell-based assays although we have also developed biochemical based screens. The major obstacles in this research field are having access to small molecule libraries that have sufficient diversity, funding screening of assays that are expensive, and lack of animal models for efficacy studies. These obstacles drive the viral targets one focuses on for drug discovery. Finally, implementation of any therapeutic requires a diagnostic for detection in patients and typically these two efforts are not coupled together.

How do you find the transition from working in the field to working in a laboratory and vice versa? What are some of your favourite/least favourite aspects of each?

The results garnered from our field work take many years of data collection in most cases which is very different from the laboratory research. The transition is not apparent since both are ongoing efforts. Perhaps for me it is not so much the transition but the wider berth of scientific articles I have to keep up with to maintain current approaches in both areas.

What has been your experience as a woman working a in a largely male-dominated field?

In the beginning, it was a bit awkward and intimidating when I was the only female research faculty in the Department of Chemistry and Biochemistry at New Mexico State University (NMSU). I realised that I simply needed to engage which happened over time. I was lucky to have a mentor at NMSU in the Department who provided me with guidance and assurance.

What do you consider to be your principal achievements thus far?

In all my endeavours, my principal achievement has been being part of the scientific maturation process of the students I have trained as undergraduates, graduates and postdoctoral fellows. Being part of this process was predominantly what led me back to my current position at University of Louisville.

Suppressing emergent viruses

For over 20 years, Professor Colleen Jonsson's research into deadly viruses has taken her from the lab to South American jungles. Now she aspires to prevent future outbreaks of deadly emerging diseases in humans

THERE ARE ONLY a handful of labs in the U.S. equipped to provide researchers with a safe environment to study the most dangerous and life threatening agents. Biosafety level 4 (BSL4) requires the highest level of biocontainment precautions, since the agents under the microscope have the potential to cause fatal disease if exposed to humans and there are no vaccines or treatments available. The diseases often infect humans through inhalation or animals, with smallpox, hemorrhagic fevers and the Ebola virus all categorised as BSL 4. These labs are multi-million dollar investments, manned with airlocks, air and water decontamination units, Hazmat suits and self-contained oxygen supplies for lab members.

With strict safety procedures in place, lab members are protected from deadly infection. However, many emerging viruses that can only be worked with at BSL4 are found out in the open in nature in the ecological field setting. In this case, researchers like Professor Colleen Jonsson will often travel far from the safety of their lab to get to the source of the diseases into the jungles of South America where many emerging viruses are prevalent.

It is a significant challenge for researchers to understand how these viruses emerge in nature given the dangerous consequences of exposure, and Jonsson explains that staying safe is always the number one priority: "We spend a great deal of care and training in making sure all of the participants working with the capture of the rodents understand the risks involved and use proper protect equipment during sample collection when potential exposure to the virus is the highest".

WINDING PATH TO DISCOVERY

Jonsson has been the Director of the Center for Predictive Medicine for Biodefense and Emerging Infectious Diseases at the University of Louisville in Kentucky since 2008. She has established the Regional Biocontainment Laboratory (RBL) on the university's campus and focuses her work on developing treatments for emerging viruses and hantaviruses in particular. The RBL was set up at the University of Louisville as one of only 11 sites to be chosen to take part in an NIH programme that encouraged universities to work with BSL3 pathogens shortly after September 11th to meet the need for secure biosafety research. It is ready for use by internal and external investigators through direct use, collaboration or as a service.

For over 20 years, Jonsson's research has delved into highly pathogenic, emerging human viruses including investigations of hantaviruses, influenza viruses, SARS, filoviruses, and retroviruses. Efforts at the Center currently focus on developing treatments for emerging viruses and bacteria and bring together a range of disciplines to conduct research, including synthetic chemistry, animal models, and high-throughput screening technologies to identify small molecule inhibitors and new targets for these deadly pathogens.

Conducting research on some of the world's most potent viruses was not Jonsson's initial ambition. In fact, she was originally interested in being an artist, but got her degree in plant biology before moving into the field of virology. She dedicated a decade of her research to studying retroviruses and gradually merged her work into examining hantaviruses. This interest has lead to her field work in Honduras, Paraguay and Brazil.

Hantaviruses are mainly identified with Asia and Europe and result in hemorrhagic fever with renal disease. Stateside, however, hantaviruses became well known in 1993 when an outbreak struck the southwestern region of the country. Humans most often contract the viruses through rodent excretion. Some strains have proven deadly in humans and symptoms are characterised by severe complications of the respiratory system. While hantaviruses are known to be harboured by rodents, scientists have been unable to develop any prevention or treatments for humans.

Working at New Mexico State University at the time, Jonsson was close to the epicentre of the 1993 outbreak and her interest was immediately sparked: "The more I read about the virus, the more I became intrigued that a virus could be so prevalent in the environment and yet go undetected until that time," she recalls. Along with her colleagues, she investigated the hypothesis that landscape could be affecting the pervasiveness of hantavirus and concluded that landscape and variations in the seasons did indeed influence the emergence of these viruses. Her team also examined correlations between the virus and climate, but found the region's neotropical system was not as affected by rain as

other desert regions in the southwest corner of the country.

INTO THE WILD

Jonsson's research into hantaviruses has also led her to studying the rodent reservoirs of New Mexico and further south into Mexico and South America. In 2001 she was awarded an American Society of Microbiology International Professorship to Tegucigulpa, Honduras. The Professorship supported Jonsson in her work to provide faculty and students at the local university with the tools needed to screen for hantaviruses in the country.

Her time in Latin America taught Jonsson the benefits and satisfaction that can be garnered from international collaboration and scholarship. "I learned from this and other experiences how much I enjoyed meeting scientists and students from other countries," she reflects. "I realised I enjoyed field research and I began to look for

ıding to

s during
research
ıey tried
ɔllection
the lab
e frozen,
l before
ıents on
creasing
become

increasingly difficult for scientists to collaborate in sharing of specimens for basic and applied research". Consequently, she has since adapted her approach to fieldwork to accommodate for conducting as much work in laboratories in the local area and when shipping is necessary, arranging for smaller packages.

RESEARCH ALLIANCES

Whether in the lab or out in the field, Jonsson notes that collaboration has always been the cornerstone of her work. Describing the advantages of working with other scholars, she comments: "In general, my collaborators and I work on different approaches to a particular question and work to integrate the information garnered into a mathematical and biological description of the ecology of the system". Incorporating expertise from different fields into virology research has proven fruitful and provides a comprehensive understanding.

For example, the research undertaken in Paraguay benefited from collaborations with experts in mathematical modelling, mammalogy, and geospatial imaging. Working at high biosafety levels with hantaviruses also requires mentoring, which equipped Jonsson with the experience and expertise necessary to understand the intricacies of the virus. She concludes: "All of my collaborations have been inspirational and our discussions over these years led me to new concepts in viral emergence and antiviral drug discovery. I cannot imagine my career without these interactions".

INTELLIGENCE

CENTER FOR PREDICTIVE MEDICINE FOR BIODEFENSE AND EMERGING INFECTIOUS DISEASE

OBJECTIVES

The Center for Predictive Medicine's mission is to support basic and translational research to promote understanding of newly emerging and re-emerging pathogens and diseases for the development of therapeutics.

Deciphering the basic mechanisms of newly recognised diseases such as swine flu, West Nile encephalitis, hantavirus pulmonary syndrome, glanders and plague is a core feature of the Center, with an aim to turn research into diagnostic methods, antivirals, antimicrobial drugs, and vaccines for these diseases.

KEY COLLABORATORS

Dr Linda J S Allen, TTU
Dr Jeffry Arterburn, NMSU
Dr Douglas G Goodin, KSU
Dr Daniel Mollura, NIH
Robert Owen PhD, TTU
Dr Connie Schmaljohn, USAMRIID
Dr Luis Tadeu Figuerido, USP, Brazil

FUNDING

NIH/NSF – FIC
DOD

CONTACT

Colleen B Jonsson, PhD
Professor of Microbiology

Director, Center for Predictive Medicine For Biodefense and Emerging Infectious Disease
Clinical & Translational Research Building
Sixth Floor, 505 South Hancock
Louisville, KY 40202
USA

T +1 502 852 1339
E cbjons01@louisville.edu

http://louisville.edu/predictivemedicine/

COLLEEN JONSSON is Professor and Director of the Center for Predictive Medicine at the University of Louisville. She completed her PostDoc in Biochemistry-Virology at the University of Medicine and Dentistry in New Jersey. Jonsson was awarded the Distinguished Alumni Award from Purdue University where she received her PhD in Biochemistry.

Her research on neglected and rare diseases and hantaviruses has led to the development of high-throughput screening approaches for several viruses for the discovery of small molecule inhibitors.