



ISNV

Oct 2010
Special Issue

International Society for NeuroVirology

Editor: Dianne Langford, Ph.D.
Associate Editor: Michael Nonnemacher, Ph.D.
Assistant: Leslie Marshall, Ph.D.

James Kronstad Gives the 2010 Inaugural Neurological Infections Lectureship

Dianne Langford Ph.D., Philadelphia, PA

The ISNV is proud to honor James Kronstad who will present the 2010 Neurological Infections Lecture at the 10th International Symposium on NeuroVirology in Milan, Italy. Dr. Kronstad received a Ph.D. in Microbiology and Immunology from the University of Washington, which was followed by two years of postdoctoral studies with ZymoGenetics in Seattle and two years as a research biologist with the USDA at the University of Wisconsin. Currently, he is a Professor in the Department of Microbiology and Immunology at the University of British Columbia and serves as the Director of the Michael Smith Laboratories, an interdisciplinary research unit founded by the Nobel Prize-winning chemist Dr. Michael Smith. Dr. Kronstad is a Burroughs Wellcome Fund Scholar, a Fellow of the American Academy of Microbiology, and a Fellow of the American Association for the Advancement of Science. In addition to these accomplishments, he previously served as chair of the NIH study section on AIDS, Opportunistic Infections, and Cancer (AOIC) (2008-2010).

As a leader in the field of fungal pathogenesis, Dr. Kronstad has contributed significantly to our understanding of the virulence mechanisms of fungal pathogens, their responses to anti-fungal therapeutics and aspects of fungal co-infection with HIV. In addition, work from Kronstad's laboratory has uncovered important fungal survival adaptations to the host environment. Dr. Kronstad's research program focuses on the molecular genetic and genomic analysis of virulence in the fungal pathogens *Cryptococcus neoformans* and *Cryptococcus gattii*. *C. neoformans* is the causative agent of meningoencephalitis in people with a compromised immune system such as AIDS patients. Recent estimates place the global burden of cryptococcosis in AIDS patients at 1 million cases per year, with approximately 600,000 deaths. In contrast, *C. gattii* tends to infect otherwise healthy people as demonstrated by the ongoing outbreak of cryptococcosis in immunocompetent people in western North America. Current projects in the Kronstad group include:



BOARD OF DIRECTORS

JOSEPH BERGER, USA
SHILPA BUCH, USA
ROBERT FUJINAMI, USA
STEVEN JACOBSON, USA
MAHENDRA KUMAR, USA
LYNN PULLIAM, USA
DAVID VOLSKY, USA

JOAN BERMAN, USA
JANICE E. CLEMENTS, USA
JENNIFER GORDON, USA
PETER KENNEDY, UK
MONIQUE LAFON, FRANCE
WALTER ROYAL, III, USA
BRIAN WIGDAHL, USA

RUTH BRACK-WERNER, GERMANY
ANTONINA DOLEI, ITALY
IGOR GRANT, USA
KAMEL KHALILI, USA
EHUD LAVI, USA
MINEKI SAITO, JAPAN

BRUCE BREW, AUSTRALIA
PASQUALE FERRANTE, ITALY
ALAN JACKSON, CANADA
IGOR KORALNIK, USA
AVINDRA NATH, USA
ISRAEL STEINER, ISRAEL

Metabolic and nutritional adaptation to the mammalian host environment. The Kronstad group found that the GATA transcription factor Cir1 is a major regulator of iron uptake functions in *C. neoformans*. These functions include siderophore iron transporters, components of a high affinity iron uptake system, cell surface reductases, and extracellular proteins involved in iron acquisition from heme. Remarkably, Cir1 also regulates all of the known virulence factors in the pathogen, including the polysaccharide capsule that plays a major role in interactions between the fungus and phagocytic cells. In parallel, the Kronstad laboratory is also investigating the remodeling of central carbon metabolism in cryptococcal cells during pulmonary infection. In this case, functions for the production and utilization of acetyl-CoA have been found to influence the structure of the capsular polysaccharide.

Nutrient sensing and virulence. A second major ongoing project in the Kronstad laboratory involves analyzing the role of cAMP-dependent protein kinase (PKA) in the regulation of the secretory pathway and delivery of virulence factors to the cell surface. PKA activation is dependent on glucose and amino acids, and previous transcriptional profiling identified a regulatory connection with secretion. Proteomics approaches are being used to

identify targets of PKA phosphorylation and to define the PKA-dependent phosphoproteome. In addition, genetic approaches have identified downstream targets of PKA that regulate capsule size.

Genome plasticity during infection and in response to antifungal drug treatment. The Kronstad group has also been involved in constructing physical maps and sequencing the genomes of three strains of *C. neoformans* and two strains of *C. gattii*. The genome sequences were employed in comparative genome hybridization experiments to discover that strains of *C. neoformans* and *C. gattii* show variability in chromosome copy number. For example, strains recovered from the cerebral spinal fluid of AIDS patients have been found to be disomic for specific chromosomes. In addition, strains of *C. neoformans* and *C. gattii* that display high-level heteroresistance to the antifungal drug fluconazole have multiple disomic chromosomes, when compared with non-resistant parental strains. A set of engineered strains has been developed that are monosome or disomic for chromosome 13, and these have been used to demonstrate that disomy influences virulence in a mouse inhalation model of cryptococcosis.

Overall, Dr. Kronstad has had a highly active and diverse career experience and the ISNV is pleased to have him deliver the 2010 Neurological Infections Lecture.

**Request for Nominations for
The Neurological Infections Lectureship**

The 11th symposium will be held in New York, New York, 2012

International Society for NeuroVirology
ISNV
LectureShip Series

The International Society for NeuroVirology will accept nominations for the 11th International Symposium on NeuroVirology for Spring 2012, sponsored by the Journal of NeuroVirology. Please send all inquiries and nominations to mail@isnv.org

**JOURNAL OF
NEUROVIROLOGY**

The Journal of NeuroVirology (JNV) provides a unique platform for the publication of high-quality basic science and clinical studies on the molecular biology and pathogenesis of viral infections of the nervous system, and for reporting on the development of novel therapeutic strategies using neurotropic viral vectors. The Journal publishes original research articles, reviews, case reports, coverage of various scientific meetings, along with supplements and special issues on selected subjects.

For information on submitting abstracts, subscribing to newsletters, and general information about the Journal of NeuroVirology, please visit www.jneurovirol.com

Contact the ISNV Administrative office at:

Tel: (215) 707-9788 Fax: (215) 707-9838

Email: mail@isnv.org www.isnv.org

**Center For
Scientific
Communication & Outreach**

Drexel University College of Medicine

ISNV Newsletter printed by the Center for Scientific Communication and Outreach: Director, Michael Nonnemacher, Ph.D.