The Virology Interest Group is sponsoring the following seminar
Thursday May 27th, 2010 12:30 PM Room 433, Building 4

Molecular Approaches Towards Understanding the Biology and Pathogenesis of Hepatitis E Virus

Shahid Jameel, Ph.D.
Senior Scientist and Group Leader
Virology Group
International Centre for Genetic Engineering and Biotechnology (ICGEB)
New Delhi, India

Description:
The hepatitis E virus (HEV) causes an acute, self-limited infection, which is responsible for over a third of all sporadic hepatitis and almost all the hepatitis outbreaks in endemic areas. The World Health Organization estimates that about 2 million people live in areas endemic for HEV infection, which include resource-poor countries found mainly in tropical and subtropical areas of the world. Following the discovery of animal HEVs and unusually high anti-HEV seropositivity in developed countries, this virus poses a global threat.

The lack of a good in vitro culture model has prevented basic studies on HEV biology and pathogenesis, but replicon-based approaches are now being developed. We have mainly used subgenomic and replicon-based expression strategies to study the role of HEV proteins in its biology and pathogenesis. HEV is a non-enveloped virus with a ~7.2 kb single-stranded, positive-sense RNA genome that encodes three proteins – ORF1, which is the viral nonstructural protein; ORF2, which forms the viral capsid; and ORF3, which is a small protein with host regulatory functions.

We have recently shown the ORF2 capsid protein to bind heparan sulfate proteoglycans (HSPGs) on the cell surface and propose these to act as attachment factors for virus entry. Our results over the past few years suggest that the HEV ORF3 protein modulates multiple host cell signaling pathways towards the promotion of cell survival. These include activation of the Erk/MAPK signaling pathway, attenuation of the mitochondrial death pathway through increased expression and oligomerization of the outer mitochondrial membrane porin, VDAC and hexokinase, and by prolonging endomembrane growth factor signaling. This protein also regulates energy homeostasis in the cells and regulates the inflammatory acute phase response.

In recent work we have used genomic, proteomic, peptidomic and metabolomic tools to understand HEV biology and pathogenesis. Working with cell line models and the body fluids (plasma and urine) of HEV-infected humans, we have looked at differentially expressed genes, proteins and metabolites during acute infection. This has allowed us to identify biomarkers of HEV infection and to propose a comprehensive model to explain the disease process. This coordinated approach has also allowed us important insights into severe/fulminant liver disease in hepatitis E patients, especially in pregnant women who experience increased mortality following infection.

Funding: The HEV research in my laboratory is supported by grants from The Wellcome Trust (UK) and The National Institutes of Health (USA).

Dr Jameel would be pleased to prolong the discussion after his seminar. You are welcome to stay if you wish to participate.
Also, if you are interested in meeting personally Dr. Jameel, you can request it by sending me an Email:
kolbg@mail.nih.gov<mailto:kolbg@mail.nih.gov