Bat Lyssaviruses

Overview

Workpackage 5: Molecular Epidemiology of Bat Lyssaviruses

Bat variants of rabies virus: European Bat Lyssavirus

European Bat Lyssaviruses (EBLVs) are RNA viruses and are members of the lyssavirus genus of the family Rhabdoviridae. EBLVs are host-adapted to European species of insectivorous bat and are genetically different to the ‘classical rabies virus’ strains, historically isolated from dogs, cats and foxes.

European Bat Lyssavirus type-1 has been isolated principally from Serotine (*Eptesicus serotinus*) bats and EBLV type-2 from Myotis species (*Myotis daubentoni* and *M. daubentoni*) bats throughout Europe. Currently, there have been over 700 reported cases of EBLV in European bats; 95% of these have been EBLV-1 isolates from Serotine bats and the remainder have been EBLV-2. On rare occasions, these strains have been known to spillover between bats and other animals. On two occasions sheep have been infected with EBLV-1 in Denmark and the same strain was detected in a stone marten in Germany. The risk of EBLV exposure to humans is low, especially in individuals who do not handle bats, however, since 1977 there have been four (three confirmed; one suspect) human deaths from rabies in Europe attributed to EBLV infections. The latest human case was a bat conservationist from Scotland who was infected with EBLV-2 and later died of rabies. These cases all occurred in humans who had been exposed to bats, usually through a biting incident and exposure to an infected bat’s saliva. In all cases the infected individual had not received rabies vaccination either before or after being bitten. Bat handlers are advised to be immunised against rabies and even if they are not, post-exposure vaccination is known to be effective, if administered soon after exposure. Daubentons’ bats rarely roost in houses and so are unlikely to cause widespread problems in man. The public are advised to avoid handling bats and if bitten or scratched by a bat should immediately wash the affected area with soap and water and seek medical attention.

Where EBLVs are found

There are two types of EBLV: type 1 (geno-
type 5) which has subtypes a and b. Type 1a is the most common and has been found across northern and central Europe to Russia. Type 1b has been isolated in some Western countries down to Spain. EBLV type-2 (genotype 6) also has subtypes a and b but has rarely been identified, with one case of EBLV-2a found in The Netherlands and some cases found in the UK and Switzerland. Both types of EBLV cause similar rabies-like encephalitis (inflammation of the brain) in man, however it is possible that differences in their glyco-protein content may influence the origin and development of the disease.

How the virus replicates

The incubation period of lyssavirus is typically 20-90 days, although periods ranging from a few days to more than a year have been documented. The virus replicates in local muscle fibres and binds to receptors in the neuromuscular junction. It then travels rapidly to the central nervous system, replicates in the neurones of the spinal cord and dorsal root ganglia, infects brain neurones and then spreads along nerves to the major exit portals, the salivary glands. The first rabies-related viruses were isolated in Africa and Europe in 1956. Continuing developments in molecular biology allowed the identification of the lys-
savirus genus and the classification of several genotypes, six of which have caused rabies encephalomyelitis (inflammation of the brain and spinal chord) in humans and/or animal deaths in nature.

Re-emergence of the virus

It is possible that healthy bats may be infected and infectious before clinical signs appear. Some bats in Europe have been shown to recover from exposure, become seroposi-
tive and survive suggesting that an ‘atypical infection’ has occurred. Viral RNA has been detected in the brain of Spanish bats without evidence of viral replication. This suggests that re-emergence of the virus is possible.

Objectives

The overall objective of Workpackage 5 is to provide accurate information on the risk of bat-associated rabies in Europe to animal and human health. This is to be achieved by forging collaborations among rabies laboratories. Initially, the goal is to capture all of the genetic information we have from the various collaborating institutes across Europe and to store this information on a common database for use by all members of Med-Vet-Net and access by others outside of the network. Rabies is a notifiable disease throughout Europe and it is possible that under-reporting of bat rabies cases is common. The principal aim is to assess the risks that EBLVs pose and the risk of spillover to domestic livestock, which ultimately affects the food chain. This occurrence of events is common in Latin American countries where a genotype 1 bat variant of classical rabies virus will commonly spillover from the vampire bat host (*Desmodus rotundus*) to both cattle, horses and on rare occasions to man. This causes both economic losses and a risk to public health. Our working hypothesis is to question whether EBLVs are less viru-

tant than other bat variants of rabies virus and whether the risk of spillover is therefore smaller. Evidence from North America has shown that genotype 1 bat variants that have spilled over from bats to terrestrial mammals have caused minor epizootics of rabies. With the reduction of vaccination of foxes against rabies throughout Europe and the subsequent increase in fox numbers, the possibility exists that a rabies epizootic in wildife could occur.

The objectives of Workpackage 5 will be achieved by:
1. Collection of sequence data and archived material from EBLV isolates detected by Med-Vet-Net partner institutes
2. Setting up a database of sequence data for the EBLV isolates
3. Dissemination of the necessary information electronically via the internet

Workplan

Task 1. Agree optimum approaches
An initial meeting in The Netherlands was held in September 2004 between key sci-
etists to determine methods for collation of data and exchange of expertise. A second meeting will be held in the latter part of the project (Summer 2005) in Poland to review progress and present findings.
At present, there is no information on the impact of social behaviour on the transmission of EBLV or the mating behaviour of the European long eared bat. Therefore, further information about different environments / habitats and how they effect EBLV transmission is needed.

Problems with EBLV Reverse Transcription Polymerase Chain Reaction (RT-PCR) and Sequencing Methods
Currently RT-PCR is used to identify and sequence isolates, and the importance of using primers which will pick up ALL strains of EBLV was discussed. Currently the ‘N’ gene is targeted but it was suggested that this gene is too conserved so isolates within genotypes are not necessarily distinguished. Some suggestions to target the ‘G’ gene were mentioned and this was also discussed in Geneva. In the meantime a 400 base pair region of the G gene is to be used by everyone and use of the G gene will be discussed later.

Isolate and Sequence Collections
The number of isolates held by each institute is as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>EBLV-1</th>
<th>EBLV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLA (UK)</td>
<td>46</td>
<td>12</td>
</tr>
<tr>
<td>AFSSA (France)</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>ISCIII (Spain)</td>
<td>20+</td>
<td>0</td>
</tr>
<tr>
<td>SVA (Sweden)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>FRC (Germany)</td>
<td>160</td>
<td>2</td>
</tr>
<tr>
<td>DIV (Denmark)</td>
<td>200</td>
<td>0</td>
</tr>
<tr>
<td>PZH (Poland)</td>
<td>13+</td>
<td>0</td>
</tr>
<tr>
<td>RIVM (Netherlands)</td>
<td>50+</td>
<td>6</td>
</tr>
</tbody>
</table>

Database design and training initiatives
Information technology support provided through Med-Vet-Net has been used to set up a database of surveillance information and EBLV isolate sequences. The database requirements of Workpackage 5 have been agreed with the IT team from Uppsala and a prototype database is operative (from April 2005). We intend to go live before the end of May 2005 and begin accepting rabies sequences from each partner institute. Additional training opportunities and criteria are to be sourced as part of a possible application for workpackage 5.

Meetings
Governing Board forum of discussion
The first electronic Governing Board meeting was closed on the 13 April after 10 days of discussions. The minutes have been drafted and sent to the Chairman of the Governing Board, the Co-ordinator’s Representative and the Project Manager for the first review. They will then be disseminated to participants for review and validation.

Co-ordinating Forum at HPA
Minutes of the Co-ordinating Forum at HPA and its annexes have been drafted, reviewed and are now validated. They have been published on the private website.

Date of Upcoming Meeting
The next Governing Board meeting has been agreed as Friday 14 October. This and the Co-ordinating Forum and Advisory Panel meetings will take place at AFSSA Headquarters.

Preparation of the 2nd Joint Programme of Activities (JPA)
The recent Co-ordinating Forum and Governing Board meetings focussed on the preparation and organisation of the next round of Workpackages which will begin in March 2006 and will each last for 18 months. The Administration Bureau is involved with the commissioning of new workpackages and the definition of financial regulations to ensure better implementation and use of the budget among partners. We are also in negotiation with the EC to make adjustments to the way the budgets for the second grant are allocated. Procedures relating to training course organisation and budget reallocation were validated by the Co-ordinating Forum and actioned by the Governing Board. The Administration Bureau is now at the final stage of implementing these procedures. Rules for the use of budget reallocation are being defined and will soon be published on the website. Also, training request forms have been drafted in collaboration with Henrik Wegener of Workpackage 2a (training). These will ensure skilled management of training courses and short term exchange visits of scientists among the consortium. These training request forms will also ensure that allocated funds are set and followed-up accurately.

Admin Bureau
Andreas Hensel is the new Vice president of the Governing Board for Med-Vet-Net. Andreas graduated in 1988 with a degree in Veterinary Medicine, specialising in Microbiology, from the School of Veterinary Medicine in Hannover, Germany. In 1994 he graduated with a PhD from the University of Utrecht after which time he worked as a Senior Scientist in the Biocenter, Institute for Microbiology and Genetics, University of Vienna.

In 1997 he transferred to a different department of University of Vienna - the Institute for Bacteriology, Mycology and Hygiene – to work again as a senior scientist at the same time taking up a lectureship in Microbiology at the University of Hannover, and becoming a Full Professor for Animal Hygiene and Veterinary Health.

Between 2001 and 2003, Andreas was the director and held the Chair of the Institute for Animal Hygiene and Veterinary Public Health at the University of Leipzig and in 2003 he became President and Professor of the Federal Institute for Risk Assessment, Berlin.

Between 1990 and 2004 Andreas obtained further qualification as a veterinary specialist in: Microbiology, Animal Hygiene, Clinical Laboratory Medicine, Epidemiology and Food Hygiene.

- lessons from the past. Prof. Nina Marano, the Associate Director for Veterinary Medicine & Public Health at CDC, Atlanta, USA will talk about Future international challenges in Zoonotic diseases.

Diane Newell and Claire Cassar

GENERAL SCIENTIFIC MEETING

University College, Winchester, UK
Wednesday 29 June - Friday 1 July 2005

Two Band D Risk Analysts in the Centre for Epidemiology and Risk Analysis, Veterinary Laboratories Agency - Weybridge, Addlestone, Surrey

There are two positions available for Risk Analysts to work as part of a team undertaking work in all aspects of risk analysis with a focus on development of risk assessments in the fields of national and international veterinary and public health, but also to include varying amounts of research, methodological development and advice on hazard identification, risk communication and risk management. The main duties include:

- Developing and using risk analysis techniques and/or risk assessment models applied to current and international veterinary and public health.
- Undertaking methodological research for development of all aspects of risk analysis
- Presenting results by writing project reports, and papers, and giving oral presentations and advice
- Liaising with all those providing information and data for risk analysis work, including specialists, collaborators, policy makers and other stakeholders
- Writing project proposals to obtain funding, managing projects, line managing and supervising Pay Band E risk analysts
- Keeping up to date with developments in selected areas of the risk analysis discipline

The successful applicants should have a degree in a quantitative subject or which includes a substantive quantitative element and a demonstrated track record of experience and success in an aspect or aspects of risk analysis or mathematical modelling. Applicants should either have appropriate risk analysis experience or a higher degree. Other necessary attributes include a motivated, enthusiastic and flexible self-starter with the ability to work as part of a multi-disciplinary team, an organised methodological approach to data collection and recording and presentation of results; a confident and clear oral communicator with a strong interest in veterinary and/or public health. In addition, knowledge of, or experience in an aspect of agriculture, veterinary or public health, or biology would be an advantage, as would experience of project or staff management.

These posts are in Pay Band D - £22,300 to £32,100 per annum. These are full-time posts, although both could be undertaken by two part-time staff on a job-share basis.

If interested, please contact the VLA Personnel Department on +44 (0)1932 357257 an application form to be sent to you (quoting reference ADP 3373). Alternatively, go to the Job Opportunities link on the VLA website www.vla.gov.uk. The closing date for application forms is 31 May 2005.
Institute of Biology course on Intellectual Property, London, UK, 9 June 2005. This course is designed to help scientists understand and use the law to protect their research, discoveries, designs and inventions. Two top city lawyers who specialise in intellectual property, will give a practical guide to intellectual property in relation to scientists. Including what scientists should and should not do, the legal framework to intellectual property and how to protect your interests.

Call Rebecca Bradbury on 0207 581 8333 ext. 237 for more information

2nd European Conference Functional Genomics and Disease Oslo, Norway, 6 - 10 September, 2005

The conference will focus on the impact of functional genomics on disease-related research. The programme will include symposia and workshops on specific disease areas and functional genomics technologies. Topics include: • Neurogenomics and Disease • Ageing • Oncogenomics • Inflammation and Immunity • Diabetes and Metabolic Diseases • Emerging Infections and Poverty-Related Disseases • Cardiovascular Disease and Angiogenesis • Predictive, Preventive and Personalized Medicine • Molecular Phenotyping and Model Systems • Epigenomics and Genomic Landscape • Comparative Genomics • Systems Biology • Cell Signalling • Stem Cells • Expression of the Genome • Bioinformatics • RNAi • Molecular Tools • Free papers Early registration deadline 15 May 2005.

Bursaries available for younger researchers. E-mail: mailto:esffg2005@congrex.no


7th International Symposium on Cytokines and Chemokines, Montreal, Quebec, Canada, 8 - 9 September 2005

The symposium will evaluate the role of cytokines in diseases that occur in gastro-intestinal tract, and inflammation signalling for malignancies. This CIHR-Institute of Infection and Immunity sponsored symposium focuses on new technologies and strategies in diagnostic markers and therapies. Members of the clinical, pharmaceutical, and biotechnology community are invited to present their work in a poster session. You are encouraged to submit abstracts on a range of subjects including: Cytokines & Chemokines Basic and Translation Research; Alcohol and Drug-Induced Toxicities; Cytokine-chemokine therapies; Bio-technology; In vivo and in vitro models of inflammation and repair; Inflammatory Bowel Diseases and Cytokine therapy; and many more. For details of all the subject areas covered and more information about the meeting visit http://www.wcog2005.org/s2_postgcourses10.html#a1

Animal Circoviruses and Associated Diseases - European Society for Veterinary Virology (ESVV) Conference, Queens University, Belfast. 11 - 13 September 2005

This conference will provide an opportunity for scientists, veterinarians and other end-users to meet, debate and discuss important aspects of circovirus research with particular focus on pathogenesis, epidemiology and control of circovirus diseases of economic importance to the pork, poultry and feed industry. The deadline for Abstract submission is now 27 May 2005. The abstract form and guidelines on the format of the abstract are available to download from the website http://www.happen.co.uk/esvv2005/ You can also register on-line and if you book before 04/07/05 you’ll be eligible for the Early Booking Rate.

Health Protection Agency Annual Conference, Warwick University, UK, 12-14 September 2005

The main theme for this year is Health Inequalities, Patient and Public Safety. The conference will bring together over 900 health protection professionals from a variety of disciplines to meet, learn and share knowledge and expertise. The main themes - Health Inequalities and Patient and Public Safety - will be analysed and discussed by experts from the HPA and our national and international partner organisations. Alongside this, a full programme of parallel sessions and poster exhibition will showcase new research and developments in health protection, providing an opportunity to gain knowledge and insight into work on a wide range of health protection issues.

Visit the conference website for updates on the programme: http://www.hpaconference.org.uk/ Email: hpaconference@hpa.org.uk

OBITUARY

Henry Riddell Smith MA, PhD

Henry Smith received his early education at Harrogate Grammar School in Yorkshire, followed by undergraduate training at Gonville and Caius College, Cambridge. After graduating from Cambridge in 1968 with MA in Natural Sciences, he joined the Health Protection Agency, at that time the Public Health Laboratory Service. Here he worked in the Enteric Reference Laboratory at Colindale under Professor E. S. Anderson. At this time Henry registered for a PhD entitled ‘Studies in non-autotransferring plasmids in Escherichia coli and salmonellae’, under the jurisdiction of the University of London, and was awarded his PhD in 1975. Whilst with Anderson, Henry published several notable papers, particularly in relation to his PhD subject and also in the field of infectious drug resistance in salmonellae in general.

From the late 1970s Henry developed a major interest in research into the pathogenicity of E. coli, which soon became his lifelong interest. He rapidly gained an international reputation in this field, with numerous publications and presentations in areas ranging from colonisation factor characterization to the genetics of Vero cytotox in production in E. coli O157 and related strains. He has served on numerous professional committees and in 1998 became a joint project leader of the European Union-funded EnterNet project. He has also acted as a co-organiser of several international scientific meetings, including Food Safety Y2K and VTEC 2003. Throughout his career he worked in the Laboratory of Enteric Pathogens (LEP) of the HPA. Under the Directorship Dr Bernard Rowe he became Head of the Molecular Genetics Unit in 1978, and was appointed Deputy Director of the LEP in 1996 and Acting Director in 1999. His appointment as Director was confirmed in 2002. Henry has always taken a major interest in the welfare and development of his staff. In particular his encouragement of junior scientific staff has resulted in many young scientists leaving Colindale with a thorough grounding, not only in the subject but also in the ethos of scientific research. His integrity was widely appreciated by staff throughout the HPA and internationally.

Apart from microbiology his passion in life was his family and his interests in cricket and the local community in Bushley, Herefordshire, where he has lived for the last twenty years. His untimely and tragic death, on April 10th 2005, in a traffic accident, came as a devastating blow to friends and colleagues throughout the world. He leaves a wife, Geraldine, and a son, Thomas, who is currently in his second year at the University of Bristol.

“The perfect gentleman, his contribution to science and to the community will always be remembered”

Dr John Threlfall

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Contributions and suggestions are welcome.

Deadline for publication is 1st of each month.

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Med-Vet-Net is a European Network of Excellence on Zoonoses Research

Visit http://www.medvetnet.org
As part of its overarching ‘Spreading Excellence’ Workpackage 3, Med-Vet-Net is offering four positions for a Science Communication Internship.

The Internship is open to any current student, researcher or staff member of the Med-Vet-Net partner institutes. The Internship will consist of a 3-month period of full-time training / tutorials in various aspects of science communication including:

• Communicating with government and industry
• Communicating with the media
• Presentation skills
• Internet and website design
• Writing skills and publications
• Communicating with the public and children
• Organising events and exhibitions

Following completion of the 3-month period, it is expected that participants will return to their Institute and apply the skills learnt by communicating the work of Med-Vet-Net in their country, as well as assisting the Med-Vet-Net Communications Unit with the dissemination of information throughout Europe.

During the Internship, the candidates will be mainly located for 12 weeks at the offices of the Society for Applied Microbiology in Bedford, UK, with some additional travel throughout Europe to other partner institutes and Brussels. Accommodation, travel and associated expenses will be provided.

The first 3-month Internship will run from September - November 2005.

To apply, you will need:
• Good written and spoken English
• Degree in science (preferably biology, microbiology, clinical or veterinary science-related field), or relevant work experience in one of these fields
• Desire to become more involved in the communication of science
• Willingness to move from research into communication
• A flair for communication

In addition you will need to submit:
• Your Curriculum Vitae (CV)
• A one-page summary outlining why you want to learn about communicating science.
• A press release (250 words) describing some aspect of your (or your colleagues’) research Note: this must be written for a non-scientific audience (eg. media and public)

Before you apply, it is important that you have the full support of your Institute in this endeavour. They must support your 3-month secondment to the UK (while continuing to pay your salary), and also agree that for the first 3-months upon your return to your institute, at least 50% of your time is spent working on communications. The details of these arrangements are flexible, and will be agreed for each individual candidate and their circumstances.

APPLICATIONS DUE BY
FRIDAY 17 JUNE 2005

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