



MED • VET • NET NEWS

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This month MVN News provides information about Workpackage 7 - Pathogenesis of verocytotoxin-producing *Escherichia coli* infection: a new paradigm for VTEC

Diane Newell updates us with information about the Co-ordination Forum meeting and tells us of her rather unfortunate visit to Russia, and the network has a new Thematic leader for Epidemiology, Bob Adak who will introduce himself.

There's information about the Med-Vet-Net exchange programme and the new Med-Vet-Net Website which was launched at the end of March. Visit www.medvetnet.org to keep up to date with developments in the network and the latest news stories about zoonoses.

Med-Vet-Net Communications Unit

VTEC (WP7) OVERVIEW

Pathogenesis of verocytotoxin-producing *Escherichia coli* infection: a new paradigm for VTEC

Background: *Escherichia coli*

The bacterium *Escherichia coli*, which commonly live in the intestine, is a potential pathogen and can be responsible for gastrointestinal illnesses, sepsis, meningitis, and urinary tract infections. Its presence in food or water supplies is used as an indicator of faecal pollution. *E. coli* is also a favourite tool of microbial biochemists and geneticists and is the major organism used in recombinant-DNA studies.

Verocytotoxigenic *Escherichia coli* (VTEC) are pathogenic *E. coli* which produce potent toxins that can cause severe disease in man. They are so called because they were first recognized for their ability to kill the monkey tissue culture cell line 'Vero'.

Verocytotoxins

Verocytotoxigenic *Escherichia coli* may belong to many serotypes, but the majority of the reported cases of severe disease worldwide are caused by strains belonging to serotype O157:H7 and other serogroups, such as O26, O111, O103, and O145. The production of verocytotoxins (VT) represents the main virulence property of VTEC. Expression of these toxins appears to be essential, but not solely responsible, for the pathogenic effects in humans. Strains of VTEC, associated with severe human disease, are often also capable of colonizing the intestinal mucosa with a characteristic adherence mechanism known as attaching and effacing (A/E).

Infection in humans

Infection in humans can result in a range of illness including bloody diarrhoea (haemorrhagic colitis) which may be accompanied by mild-to-severe stomach cramps, but is generally present without fever. In about 5-10 per cent of cases of infections with VTEC belonging to serotype O157 and the serogroups mentioned above, this can progress to haemolytic uraemic syndrome (HUS), characterized by the rupture of red blood cells (haemolysis) leading to anaemia, low platelet count and

acute kidney failure. Haemolytic uraemic syndrome is responsible for the majority of cases of acute renal failure in children in the UK and other countries. Some patients with VTEC O157 infection develop thrombotic thrombocytopenic purpura (TTP) in which the clinical features of HUS are seen together with neurological complications. The incubation period of VTEC infection can range from 1 – 14 days and the reservoir of these organisms is the gastro-intestinal tract of ruminants, mainly cattle. Beside VT production, many other virulence factors have been described. However, several key aspects of the pathogenesis of VTEC infection are not yet understood.

Aims and objectives of Workpackage 7

The aim of Workpackage 7 is to set up a task force of key European scientists to review Med-Vet-Net expertise and to develop a catalogue of research activities into VTEC. A consultation meeting will generate a report with recommendations for further research into this pathogenic organism and joint research proposals will be prepared and submitted to Med-Vet-Net and/or the sixth framework programme (FP6) for further funding. The overall objective of Workpackage 7 will be to define the combination of virulence genes and the mechanisms that make a VTEC strain fully pathogenic to humans, govern the evolution of commensal *E. coli* toward virulence, and contribute to the animal reservoirs.



The primary reservoir of VTEC is the gastro-intestinal tract of cattle

Understanding the pathogenesis of VTEC

Despite the large amount of scientific work carried out during the last decade, several key aspects of the pathogenesis of VTEC infection have yet to be understood, in particular:

- The role of known, and still unknown, virulence genes, including VT and intimin gene variants.
- Plasmid-encoded factors and pathogenicity islands (PAIs).

Current Approaches

Approaches currently under investigation include:

- DNA arrays and genome sequence comparisons of O157/non O157 strains.
- Host/pathogen relationships are under investigation, including specificity and tissue tropism, the molecular dialogue between the host and the pathogen and the carriage of VT by blood cells and delivery to the target tissues.
- The study of host defences and responses, including the immune response in humans and animals during the course of disease or natural carriage, vaccination and immunotherapy.
- The mechanisms of cattle colonisation, including the effects of probiotic administration, various feeding regimens and differences in calf management at weaning.
- The development and use of animal models of disease and colonization.
- The understanding of pathogen evolution, including the establishment of the role of phages, plasmids, antimicrobial drug resistance elements, and PAIs in gene transfer.

Thus the development of a new paradigm for VTEC strains, based on their real pathogenic potential, will be pivotal to improving the efficacy of both the diagnostics of human infections and the surveillance of animal reservoirs and the assessment of public health risks.

Task 1. Set up the Task Force

Participants will initially be drawn from Med-Vet-Net but will later involve other European Institutes key scientists. The purpose of the Task Force will be to review Med-Vet-Net expertise in the context of international expertise

Task 2. Develop a catalogue of research activities within Med-Vet-Net

This catalogue will provide an electronic database of key scientists, research and surveillance activities, expertise and facilities.

Task 3. Organise a consultation meeting

This meeting will last for three days with about 20 invited key scientists, who will generate a report with recommendations for future research.

Task 4. Prepare joint research proposals

On the basis of the report in Task 3, joint grant proposals will be generated for submission, for example, to Med-Vet-Net or new sixth framework package calls.

The EU Descartes Prizes for Research and Science Communication 2005

The Descartes Prize is awarded to teams of researchers who have achieved outstanding scientific or technological results through collaborative research in any field of science, including the economic, social science and humanities.

Proposals for the Descartes Prize for research may be submitted by the research teams themselves, or by appropriate public or private organisations. Research teams or nominating bodies can only present one project per proposal and can make a maximum of 5 proposals. If more than five proposals are sent by the same proposing organisation, only the last five to arrive at the Commission will be evaluated.

Candidates for the prize must designate a co-ordinator that will submit the proposal and will take the leading role in representing the proposal during the selection process. The application co-ordinator must be a national of a Member State, an Associated State or someone who has been residing in the EU for at least the last five years.

Applications must have been completed through a collaboration involving at least two mutually independent legal entities in two different Member States or in a Member State and an Associated State. However, provided these minimum requirements are met, research collaborations can involve teams outside the European Union.

The prize is not restricted to projects which were originally financed by the European Community RTD programmes. The Laureates and Finalists of the prize are invited to participate in the award ceremony. The Descartes prize for Science Communication, is aimed at organisations or individuals who have achieved outstanding results in science communication. Nominees should have been selected as winners by European and/or national organisations which present science communication prizes of any kind.

A joint call for proposals for both Descartes Prizes was published on 15 December 2004, with a closing date of 10 May 2005. More information on both prizes can be found on the following website: <http://www.cordis.lu/descartes> or by e-mail: rdt-descartes@cec.eu.int

PEOPLE

Dr Alfredo Caprioli
ISS representative and Leader of Workpackage 7



Alfredo Caprioli graduated in Biology from the University "La Sapienza" in Rome in 1974, and between 1975-1977 completed a Fellowship in molecular microbiology (PhD) at the Biophysics Department of the Istituto Superiore di Sanità (ISS) in Rome. In 1978 he began his career as a scientist at ISS, undertaking research into the laboratory diagnosis of gastrointestinal infections and drug resistance in *Salmonella*. In 1983 he became head of the Unit of Electron Microscopy of Infectious Agents, and began his research into the pathogenesis and epidemiology of *E.coli* infections, with particular focus on *E.coli* O157 and other VTEC. In 1996 he became head of the Unit of Foodborne Zoonoses and Veterinary Epidemiology in the Department of Veterinary Public Health, which is the position he still holds today. His main research interests include surveillance and molecular epidemiology of VTEC infections in humans and animals, virulence markers and evolution of *E.coli* O157 and other VTEC, molecular epidemiology of antibiotic resistance in *Salmonella* and enterococci. He is among the Italian representatives in other EU networks and projects on zoonoses, for example, Enter-net and the COST 920, and is the co-ordinator of several national research projects. Alfredo is a member of the EMEA Scientific Advisory Group on Antimicrobials, of the National Committee on Novel Foods, and of the National Advisory Committee for Veterinary Drugs. He is Scientific Editor of Research in Veterinary Science and acts as reviewer for many journals of veterinary and clinical microbiology. He has published about 100 articles in peer-reviewed journals.

MED-VET-NET'S NEW WEBSITE

Med-Vet-Net launched its new public website late last month at <http://www.medvetnet.org>. The website will provide a gateway for public information on zoonoses. Current news, an overview of research topics, information on partner institutes, as well event announcements feature on the site. As work within the Network progresses, it will also provide research results and publications. The entire Communications Unit have been working on the design and content of the new site for the last six months. Special thanks go to Staffan Tamm, Med-Vet-Net webmaster (SVA) who built the site (CMS) and to Lars Boström (SVA) who created the graphics and implemented the design. Teresa Belcher (SFAM) and Jean-Claude Gnanou (AFSSA) have been responsible for content.

Med-Vet-Net Business Card ordering service

You can now order Med-Vet-Net business cards online. Visit: <http://www.webprint.nu/> and use the following username and password to access this great facility:

Username: medvetnet

Password: visitkort

If your logo is not available (those available are: SVA, AFSSA, VMRI, SfAM, VLA, UCM), then send your logo to us (as a vector file), and this can be incorporated into the template (see above for an example of the SfAM logo). You can then order your business cards and

MED-VET-NET »MED-VET-NET is a European network of excellence, working for the prevention and control of zoonoses and food borne diseases«

The entry page to Med-Vet-Net's public website

ADMIN BUREAU UPDATE

This has been a key month for the Administration Bureau, as three important meetings were prepared and implemented.

Budgetary Conference

From 14-15 March a budgetary exercise took place to assess the use of funds by each workpackage and make any necessary adjustments. So far eleven partners have drafted a financial statement and the forms from the five remaining partners are expected soon. The administration Bureau will then contact each of the partners' financial officers to discuss possible problems with their financial report and to talk about their level of expenditure. This budgetary exercise gave us a trial run before the first annual report which is to be sent to the EC next October. It has allowed us to target any stumbling blocks in the way the budget is allocated to, and used by partners, and has enabled us to set measures for future budgetary management. This budgetary exercise has given rise to financial procedures which were proposed and validated at the last Coordinating Forum meeting at the Health Protection Agency (HPA), London.

Coordinating Forum

The Coordinating Forum meeting at the HPA was jointly organised by a team from the HPA and the Administration Bureau. It took place on 31 March and was preceded the evening before by an informal dinner, allowing participants to meet in a friendly atmosphere. A schedule was discussed and defined at the meeting, to ensure that the content and budget for all new workpackages was ready before the beginning of September. Two procedures were presented by the Administration Bureau to the Co-ordinating Forum to respond to fund management issues which have been identified across the network, and to facilitate fund management for the second JPA. The first one allows the misallocation of funds to be amended through invoicing between partners. This will be especially valuable in the management of the travel and subsistence expenses, as the needs of partners will vary throughout the workpackage period. The second procedure defines the way training will be organised and financially managed. These procedures allow workpackages a more workable budget for the second JPA. The Administration Bureau will work closely with appointed workpackage teams to draft this budget.

Governing Board

From 4-11 April the first electronic Governing Board meeting took place in the form of a forum of discussion on the Med-Vet-Net private website. This Governing Board meeting commented on decisions taken during the Coordinating Forum meeting. It was technically implemented thanks to active collaboration with and invaluable support from Staffan Tamm, Webmaster of Med-Vet-Net (SVA). This electronic Governing Board meeting is the first attempt to test the functionality of the Virtual Institute under virtual conditions. An assessment of this exercise will be carried out afterwards, with the aim of defining the best combination of tools to enable the most efficient method for remote collaboration within our Network.

Administration Bureau

PEOPLE

Dr G K (Bob) Adak, Leader of the Epidemiology Thematic Group

Bob Adak graduated in microbiology from Imperial College London and has postgraduate qualifications in toxicology and microbiology from the University of Birmingham and the University of Surrey. He has worked at Communicable Disease Surveillance Centre (CDSC) since 1989 on both surveillance and research into the epidemiology of salmonellas, *Campylobacter* sp., Vero-cytotoxin *Escherichia coli* O157, norovirus and the development of models for measuring the burden of foodborne infections.

In addition he has been heavily involved in designing and conducting investigations into recent national outbreaks of foodborne disease. Bob has also served on World Health Organisation expert groups on enterohaemorrhagic *E. coli* and the burden of foodborne disease. Before working for the HPA, Bob worked at Great Ormond Street Hospital on a study on cerebral palsy in London Children. He also spent three years working for the Ministry of Agriculture Fisheries and Food on the development of methods for the detection of toxins in foodstuffs. Bob is currently Head, Environmental and Enteric Diseases Department, HPA Centre for Infections.



Bob Adak

PROJECT MANAGEMENT

Co-ordinating Forum meeting and Commissioning new workpackages

On 31 March the Co-ordinating Forum met at the HPA, Colindale, London. The Forum discussed a number of important issues. In particular the group approved the progress of the current workpackages and new financial procedures to enhance flexibility. The forum also discussed plans for the next Joint Programme of Activities (JPA) including the commissioning of new scientific workpackages. The new JPA will start in April 2006 and must be submitted for approval to the EC in September 2005. The three overarching workpackages (Virtual Institute, Strategic Integration and Spreading Knowledge) will be continued to ensure integration throughout the network. A new programme of scientific workpackages will be developed to deliver the scientific strategy generated by the Med-Vet-Net Thematic Representatives. To this end a list of workpackage concepts was developed at the Thematic Meeting in Rome in March and these concepts have formed the basis of a Requirements Call. The Requirements Call Document has now been published on the private website (see your Institute Representative for access). The initial step will be for network scientists to register interest in specific topics and then, by collaboration, develop a team approach to submit a brief proposal by 8 May 2005. Brief proposals will be assessed by a Subcommittee of the Co-ordination Forum, using published criteria, and selected proposals invited to submit a detailed proposal with budgets by 1 July 2005.

General Meeting

The General Meeting is the primary integration event of the network and all scientists employed by Med-Vet-Net partners are eligible to attend. This first General meeting will be held in Winchester and we expect 200 delegates. Winchester is a historically important site in England so you may consider taking a few days sightseeing.

The local organiser is Claire Cassar who has been working hard on the meeting programme. Details of the meeting have been distributed to all Institute Representatives and on-line registration and abstract submission

is now available on the website. We welcome presentations in any topic related to zoonoses and there are four major thematic areas: Epidemiology and Risk Research; Detection and Control; Host pathogen Interaction and Microbial Ecology; and New and Emerging Zoonotic Diseases. To date we have received confirmation from two internationally renowned keynote speakers Professor Nina Morano (CDC Atlanta) and Professor Corrie Brown (University of Georgia) so we anticipate that this is going to be a scientifically exciting meeting with the added advantage of networking with colleagues across Europe.

From Russia without much love!

Finally, as several of you will know I was invited by the EU to attend, on behalf of Med-Vet-Net, an important EU-Russia meeting in Moscow this month to discuss possible future collaborations. Having dutifully completed all the required formalities (visa, abstracts, registration, hotels etc), I decided to also take the opportunity of a few well-deserved days holiday. I arrived at the airport to a wintery reception of several inches of snow but that was my only view of Russia as I was arrested at immigration and deported immediately. The reason was a simple error on the visa dates by the Russian Embassy but no amount of logical and reasoned debate made any impression with the immigration official. In fact the only Russian word I learnt was "impossible"!!! I am sure that James Bond did not have such problems!! Does anyone else want to be the Med-Vet-Net ambassador to Russia?

Diane Newell

EXTERNAL PRESENTATIONS

Roundtable Discussion

Med-Vet-Net Communications Director, Teresa Belcher, will be attending a roundtable discussion with communication managers of other Sixth Framework Programme projects and networks in Brussels on 26 April. Each participant will present their project and the related communication work, stakeholders, visions and infrastructure. The afternoon session will allow discussion of what works well and what does not work well, obstacles or problems with fulfilling partners' needs and the needs from the European Commission regarding dissemination.

EXTERNAL CONGRESSES

Society for Applied Microbiology (SfAM) Summer Conference on Spore forming bacteria - emerging and re-emerging issues. The Old Ship Hotel, Brighton, UK 4-7 July 2005

The conference will consider recent advances and understanding in health, industrial and environmental issues associated with spore formers and will consider the physiological aspects, particularly those associated with spore structure and resistance. The health implications will be considered with respect to common infections caused by spore formers in both animals and man, the persistence of spores in food products and also recent developments facilitating the use of spores as vaccine vehicles, probiotics and tumour targeting vectors. The environmental applications of spores will also be reviewed. There will be sessions on:

1. Spore formers the great survivors - a taxonomy and physiology update
 2. Spore formers in food microbiology
 3. Spore formers: human health issues
 4. Environmental applications of spore formers
- All are welcome and there are opportunities for poster presentations on **all aspects of Applied Microbiology**.

Visit www.sfam.org.uk/sumconf.html or contact the Events co-ordinator Marisa Ramsay at marisa@sfam.org.uk

Wild Mammals and Disease - Mammals Trust UKs 2005 International Conference, Zoological Society of London Meeting Rooms, 21 May 2005

Infectious diseases can have profoundly damaging consequences for mammal populations, particularly those that are already small or isolated. Some of the diseases affecting wildlife also pose potential threats to human health. Mammals Trust UK and WildCRU, University of Oxford, are jointly hosting an international conference to consider these issues and have invited a host of leading authorities to speak about and to discuss the implications of their work. Tickets cost £50 (£40 for PTES/MTUK supporters) and include lunch, tea and coffee and entry to London Zoo during the lunch break. Please contact Zoë Greenwood at Mammals Trust UK on 020 7498 5262 or enquiries@mtuk.org for more details

COST 920, WG 3 Workshop on Microbiological Risk Assessment and MC meeting, Hotel "President" Dubrovnik, Babin Kuk, Croatia, 26-28 June, 2005

This year's workshop will give updates on advancements in microbiological risk assessment. The first day's topics are dose-response modelling and "The pathogen - from farm to carcass - quantified". The second day will address the concepts of Food Safety Objectives, Performance Objectives, Appropriate Level of Protection etc. and how can they be derived from RA models. The third day is a half day when participants can choose between a technical session and MC meeting. Visit: www.babinkuk.com/cro/hoteli.aspx For useful information about Dubrovnik, see the following web sites:
www.dubrovnik-online.com,
www.dubrovnik-area.com/eng.asp or
www.htz.hr

EXCHANGE PROGRAMME

Do any of your scientists wish to visit other institutes to promote technology transfer and assist in your collaborative approach to research? The Med-Vet-Net exchange programme allows Med-Vet-Net members to apply for short-term exchange visits - usually between one week and two months in length - to facilitate the sharing of skills and experience between institutions. These programmes will strengthen the network by building relations among members and will also allow members the opportunity for personal development, presentation of data and sharing of knowledge.

To apply please contact Henrik C Wegener, Danish Institute for Food and Veterinary Research, Mørkhøj Bygade 19, DK-2860 Soborg. Tel: +45 72 34 70 75. Email: hwc@dfvf.dk

Details

Participants will be required to produce a detailed report of the outcomes of their visit at the end of the trip. Applicants must provide the following information:

1. Academic degrees
2. Current affiliation
3. Position held
4. Name of the institute you plan to visit
5. Name of the scientist you plan to visit
6. Dates and duration of stay
7. Purpose of visit
8. Detailed plan of the professional activities during the visit (max. two pages)
9. Relevance to Med-Vet-Net
10. Relevance to the fellows' career development
11. Detailed budget (max. one page)
12. Letter of recommendation from home institute
13. Letter of recommendation from host institute
14. Curriculum Vitae
15. List of Publications

An electronic form will soon be available on the internal website.



European Conference on Probiotics and Their Applications, Krakow, Poland 6 - 8 October 2005

The conference aim is to present and discuss the latest achievements in the field of probiotics, including: the mechanisms of their action, laboratory research, regulation and approval of probiotics as drugs or food supplements, specialised sessions devoted to the different medical fields as well as to the technology of probiotics in dairy and food industry, probiotics as a tool to alleviate global health hazards, data and future perspectives for probiotics.

The conference is aimed at participants from the European Union and outside, with a strong predilection for the ten new member states and the countries of Eastern Europe associated with the EU.

All lectures will be presented by prominent and distinguished representatives of the scientific, industrial and administrative sectors, who are experts in probiotics in the EU and globally. For further information, please visit <http://confer.uj.edu.pl/euprobio> or contact: EUPROBIO Conference Secretariat Ms Agnieszka Sito, Ms Agnieszka Kawalec The Centre of Innovation, Technology Transfer and University Development, 25/3 Straszewskiego Street, 31-113 Krakow, Poland Telephone: +4812 421 83 04 Fax: +4812 422 60 18 E-mail: euprobio@uj.edu.pl

60th International Conference on Diseases in Nature Communicable to Man (INCDNCM), University of Calgary, Alberta, Canada 7-9 August, 2005

For information contact: K.Fonseca@provlab.ab.ca

Salmonella and Salmonellosis Symposium, Saint-Malo, France, May 10-12, 2006.

The deadline for submission of abstracts is September 2005.

Visit: <http://www.zoopole.com/ispai/i3s2006> or contact Pierre Colin

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