



JDIP Issues Request for Applications for Year 3 of Program

JDIP has issued a request for applications (RFA) for consideration for funding in year 3 of the program. A variety of interacting projects which meet JDIP's objectives will be funded in order to maximize integration that facilitates the advancement of successful John's Disease research.

Approximately \$1.1 million will be available for integrated proposals (projects and core groups) as well as developmental projects. Approximately 10% will be awarded exclusively to JDIP members who are not currently funded through the JDIP mechanism.

In year 2, the approximate funding provided by JDIP included six core groups (\$881,000), five continuation projects (\$501,000), and five developmental projects (\$117,000). Anticipated funding in year 3 will approximate these levels. Based upon the review process and availability of funds, JDIP may fund selected projects at levels which differ from original proposed amounts.

JDIP's project and core leaders (see list and contact information on page 7) are coordinating the development of the integrated proposals. Applicants for integrated projects are encouraged to contact the project or core leaders at their earliest opportunity to ensure that their ideas are incorporated for the development of strong proposals.

If you are an investigator considering submission of an individual developmental grant, it is not required to work with a project leader prior to the submission of the proposal. However, making contact is encouraged so as to ensure that you have all of the relevant support for the development of your proposal.

Applications must be received by 4:30 PM CDT on May 1, 2006. All applicants must be a JDIP member, or request membership, on or before that date. To learn more about JDIP, our current membership directory, and the RFA (including application forms), please visit www.jdip.org. New member inquiries and requests should be directed to Bob Schroeder (schro488@umn.edu).

JDIP's 2nd Annual Conference Receives High Marks

Over 60 people attended JDIP's 2nd Annual Conference at the University of California – Davis, January 26 – 29, 2006. The conference highlighted ongoing research and new developments, and provided an opportunity to meet with collaborators and network, and to help plan for the future of JDIP.

(continued on page 2)

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Visit our website at:

<http://www.jdip.org>

JDIP News is published periodically to enhance intramural communications and ensure that JDIP participants and stakeholders are updated on news of relevance to our community.

Suggestions, comments and contributions should be directed via email to Bob Schroeder at schro488@umn.edu.

JDIP Scientific Advisory Board

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JDIP 2nd Annual Conference (continued from page 1)

In a post-conference evaluation survey completed by attendees, over 95% indicated that they thought the conference was well-organized and that the content was appropriate and informative, and nearly 85% responded that they plan to attend again next year.

The survey also provided valuable feedback on a wide range of considerations that will help improve this conference in the future, including advance notification to members, the location of the conference hotel, space available for poster sessions, and changes that could help to facilitate networking.

Mark your calendars now for JDIP's 3RD Annual Conference, to be held January 19 – 21, 2007! More information will be sent out as it becomes available.

(See page 8 for more pictures from the 2nd Annual Conference.)

JDIP Scientific Advisory Board Changes

In accordance with its policy of rotating membership, JDIP's Scientific Advisory Board (SAB) recently underwent several membership changes.

Departing from the group are Yrjo Grohn (Cornell), Ian Gardner (UC-Davis), Mike Collins and Adel Talaat (U Wisc), and John Bannantine and Judy Stabel (NADC). Grohn, Gardner and Bannantine will continue to serve on JDIP's Executive Committee.

Joining the group are Luiz Bermudez (OR State U), Jeannette McDonald (U Wisc), Ynte Schukken (Cornell), Murray Hines II (U GA), and Michael Paustian (NADC).

The current composition of the SAB is shown in the panel on the left side of this page.

Thank you to all of these individuals for their hard work and proactive service to JDIP.



Annual Conference Breakout Sessions Help To Chart Future of JDIP

As a part of our 2nd Annual Conference in Davis, California, attendees were invited to participate in one of four breakout sessions. These breakout sessions were project-focused in the areas of: epidemiology and transmission of Johne's disease; diagnostics and strain differentiation; *Map* biology and pathogenesis; and, *Map* immunology and vaccine development.

These sessions were an excellent opportunity for participants to network and establish or develop relationships, and also for them to provide their input regarding the future of JDIP. Two of the goals of these breakout sessions included:

- prioritizing knowledge gaps on a short-term (less than one year), medium-term (1-5 years) and long-term (more than five years) basis; and,
- exploring new collaborations by identifying individuals or groups, inside and outside of JDIP, for inclusion within the project and/or JDIP.

Each group provided a summary or highlight of their session, and these summaries are found on the following pages.

Please contact Vivek Kapur at vkapur@umn.edu, or Bob Schroeder at schro488@umn.edu, if you have any questions about this information.

Summary/Highlights of Breakout Session - Epidemiology & Transmission of Johne's Disease Group

Short-term and medium term

- Value of the national JD program
 - Resource allocation issues – where is the best place to put \$\$\$
- Economic effects of JD (regulatory and biological)
 - National level
 - Value of herd being in level 4 of the status program
 - Producer/processor involvement needs to be increased
- Critical evaluation of interventions (available today)
 - Vaccination – current and future
 - Use of Monensin
- NAHMS/USDA-CEAH data
 - Risk assessments
 - National demo herd data
 - Assist in planning of 2007 study (prioritized list of choices needs to be provided)

General comments

- Need to bring in more economists to the group
- Proactive in contacting/involving other industry groups
 - Organic producers
 - Professional heifer growers
- Increased interactions
 - Agri-politicians
 - Researchers in Canada and Mexico
- Interactions with National Johne's Working Group
 - Development of more unified strategy for outreach
- Investigation of "supershedding" provides opportunity to interact better with other project teams

Summary/Highlights of Breakout Session - Diagnostics & Strain Differentiation Group

Priorities

Short term (1 year)

- Fecal polymerase chain reaction (PCR)
- Milk PCR (milk filters)

Medium Term (1-5 Years)

- Cell mediated immunity-based assays
 - Detect early infection status by peripheral blood mononuclear cell gene expression signatures
 - gamma-IFN studies
 - Liquid culture (add on confirmation with PCR)

Long term

- Fluorescence polarization
- Fluorescence-activated cell sorter
- Recombinant protein and other MAP-specific antigen-based ELISAs

Collaborations

- Continuation and increased involvement with a number of identified investigators
- Identified potential new members; encourage them to submit proposals for yr 3
- Identified others who could be encouraged to join JDIP to contribute to diagnostics project

Summary/Highlights of Breakout Session - *Map* Biology & Pathogenesis Group

Knowledge gaps priorities

Short-term (<1 year)

- *Map* survival in the environment and under different stress conditions.
- Genetic basis of animal susceptibility to infection.
- Virulence gene regulation.

Medium-term (1-5 years)

- Bacterial-Intestinal interactions.
- Genetic factors associated with different stages of JD.
- Association of level of shedding with tissue changes and gene expression profiles.

Long-term (>5 years)

- Genetic basis of chronic/persistent infection.
- Transcriptional factors and regulatory networks.

Summary/Highlights of Breakout Session - Map immunology & Vaccine Development Group

Discussion/comments related to future direction and program renewal

- Using cells from infected animals or experimentally infected animals, begin looking at the >100 expressed Map proteins at NADC for how well they elicit T cell response; develop comparative framework and define which cytokines and chemokines should be measured to be used in determining effector activities associated with cells proliferating to particular antigens
- Begin looking at response of different strains to vaccine, and look at mutants to determine if decreased virulence elicits same or slightly different response pattern
- Develop methodology to determine, in vitro, interaction of memory T cells and macrophages
- In collaboration with private industry, simplify and reduce cost of vaccine testing by developing in vitro system that correlates well with potency in animals and helps determine vaccine efficacy
- Utilize both fractionating and proteomics to develop early immune response knowledge
- Show good vaccine candidate(s) for evaluation, and develop vaccines using parallel approaches
- Short term goal: Determine usability by observing reactivity of subunits (fractionated lipids, DNA)
- Medium term goal: Analyze mutant, attenuated strains
- Long term goal: Vectored approach
- Advance development of an effective Johne's vaccine by having a specific vaccine that doesn't need TB testing (difficult), or by working for USDA acceptance of a highly specific TB test
- Integrate well with European programs
- Do not issue subcontracts from lead laboratory, but directly from University of Minnesota
- Conduct workshop in near future to discuss these and related issues

Strategies for developing collaborative grants

- Submission of individual grants to respective projects.
- Submission of single joint proposal with sub budgets to be managed through JDIP.
- Workshop considered but not yet arranged. An agenda needs to be developed.

Future directions

- Develop and test vaccines.
- What is the role of dendritic cells in disease progression?
- Is disease progression modulated by T regulatory cells and/or Th17 cells?
- What is the role of *Map* in Crohn's Disease pathogenesis?

Johne's Disease Education – Virtually, Anytime



Since its debut in March, 2004, over 850 people have registered for the Online Johne's Disease Veterinary Certificate Program. Developed at the University of Wisconsin with funding from the USDA through both JDIP, and the Wisconsin Department of Agriculture, Trade and Consumer Protection, 38 states have adopted this program as a part of their veterinarian training for Johne's certification, and USDA includes it in their annual training for Designated Johne's Coordinators (DJCs).

The online training provides a common foundation in Johne's disease basics, such as the microbiology, pathology, and epidemiology of the disease, tests and test interpretation, control, and rules and regulations, all of which allows instructors to reach deeper levels of training and problem-solving in the face-to-face sessions.

Johne's-certified veterinarians must be recertified every three years. At last year's United States Animal Health Association meeting, the National Johne's Working Group determined that the recertification training should: provide a quick review of key points; cover common problems in risk assessments and management plans identified by DJCs; highlight changes in the Program Standards; and, provide updates of new and emerging tests and research findings. These requirements are satisfied by the online Recertification module which was unveiled on April 4, 2006. It has been added to the Johne's certification program as a seventh required module, entitled *Johne's Update and Review*, so that veterinarians being newly certified have this information as part of their initial certification. An additional course that was recommended and is currently in development will include updates on special topics, such as vaccine use and zoonotic potential.

Online Johne's disease education offerings are expanding. For veterinarians who provide care and advice for small ruminant producers, a goat module is available and a sheep module is being developed. Another module for cervidae, camelids, and bison is planned.

Veterinarians can also make virtual farm visits. The first available farm takes veterinarians to a Midwest dairy. Virtual farm visits that are currently being produced include a large western dairy and two beef operations: cow-calf and seedstock. These visits provide veterinarians with the opportunity to conduct a risk assessment, develop a management plan, and then compare it to what two experts would have done on the same farm.

There are also modules for producers that explain how Johne's disease enters and spreads within herds, provide details about the national control program, and offer Johne's management principles and herd strategies. Modules are available for producers of dairy, beef, goat, and sheep, and a final module is being developed that will include cervidae, camelids, and bison. The dairy module has also been translated and narrated in Spanish.

The online Johne's disease education effort is being led by Dr. Jeannette McDonald, veterinarian and distance educator at the University of Wisconsin (UW). The primary content expert for the modules for veterinarians and the dairy producers is Dr. Mike Collins, from UW's School of Veterinary Medicine. Dr. Becky Manning, also from UW, is the primary author of the other producer modules. Editors and narrators include Dr. Frank Garry, Colorado State University; Dr. Allen Roussell, Texas A & M; Dr. Don Hansen, Oregon State Veterinarian; Dr. Michael Carter, National Johne's Disease Control Program Coordinator; and Dr. Beth Patton and Dr. Tom Schomer, DJC's from Wisconsin and Nebraska, respectively. Access to the online Johne's disease education is available at www.vetmedce.vetmed.wisc.edu/jdvcp/.

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Other news

Do you need help planning your study for the year 3 RFA for JDIP?

The Epidemiology and Biostatistics Core is available to advise JDIP members who are submitting applications for year 3 JDIP funding (deadline May 1, 2006).

Through its post-docs at the University of California – Davis, and Cornell University, the Core can provide advice in two main areas:

- design of laboratory experiments, observational studies, and randomized trials including sample size calculations; and,
- statistical methods for analysis of these studies.

If you are interested in using this *free* service, you are encouraged to contact them as soon as possible. Although they will attempt to respond to all inquiries within 24 hours, their response time may increase as the deadline approaches based upon the number of requests that they receive.

Please direct all inquiries to:

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JDIP's 2nd Annual Conference

Top row, l. to r.: **Dean Bennie I. Osburn**, UC-Davis, delivers opening address; panelists discuss JDIP goal accomplishment

Middle row, l. to r.: **Larry Hutchinson**, EAB Chair, enjoys a light snack; **Brian O'Shea**, Texas A&M University, discusses AFLB generated polymorphic regions; **Judy Stabel**, NADC, discusses animal models and facilities

Bottom row: **Peter Johnson**, USDA, presents travel award certificate to **Chong Wang**, Cornell University. In addition to Chong, four other students were selected to receive a travel award from JDIP, enabling them to make oral or poster presentations at the conference.



Upcoming meetings and conferences that may be of interest

JDIP External Advisory Board

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Mark Tizard
(AUSTRALIAN ANIMAL
HEALTH LABORATORY,
AUSTRALIA)

Cynthia Wolf
(U. OF MINNESOTA)

- 2nd International Symposium on Animal Functional Genomics, The Center for Animal Functional Genomics of Michigan State University
East Lansing, MI May 16 - 19, 2006
<http://www.isafg.msu.edu>
- American Society for Microbiology 106th General Meeting.
Orlando, FL May 21 - 25, 2006.
<http://gm.asm.org/>
- American Veterinary Medical Association 143rd Annual Convention.
Honolulu, HI July 15 - 19, 2006.
<http://avmaconvention.org/>
- University of Wisconsin School of Veterinary Medicine and USDA Animal and Plant Health Inspection Service 4th Biennial Foreign Animal Diseases Training Course.
Madison, WI July 30 - August 4, 2006.
<http://www.vetmed.wisc.edu/pbs/courses/FAD2006>
- 11th International Symposium on Veterinary Epidemiology and Economics (ISVEE XI).
Queensland, Australia, August 6 - 11, 2006.
<http://www.isveexi.org/>
- American Association of Bovine Practitioners 39th Annual Convention.
St. Paul, MN Sept. 21 - 23, 2006.
<http://www.aabp.org/meeting/default.asp>
- 46th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy.
San Francisco, CA September 27 - 30, 2006.
<http://www.icaac.org/>
- Infectious Diseases Society of America 44th Annual Meeting.
Toronto, Ontario, Canada October 12-15, 2006.
<http://www.idsociety.org/Template.cfm?Section=Meetings>
- United States Animal Health Association 110th Annual Meeting.
Minneapolis, MN October, 12 - 19, 2006.
<http://www.usaha.org/meetings/>
- Conference of Research Workers in Animal Diseases.
Chicago, IL December 3 - 5, 2006.
<http://www.cvmb.colostate.edu/microbiology/crwad/index.htm>



JD ON THE WEB

Johne's Disease-related Websites

Organization	URL
American Association of Bovine Practitioners	http://www.aabp.org
American Society for Microbiology	http://asm.org/
American Veterinary Medical Association	http://avma.org
Conference of Research Workers in Animal Diseases	http://www.cvmb.colostate.edu/microbiology/crwad/index.htm
Infectious Diseases Society of America	http://www.idsociety.org
International Association for Paratuberculosis	http://paratuberculosis.org/
Johne's Disease Integrated Program	http://www.jdip.org
National Johne's Education Initiative	http://johnesdisease.org/
National Veterinary Services Laboratory	<p>Approved labs for fecal culture: http://www.aphis.usda.gov/vs/nvsl/labcertification/johnesculture.htm</p> <p>Approved labs for serology: http://www.aphis.usda.gov/vs/nvsl/labcertification/johnesserology.htm</p>
United States Animal Health Association	http://www.usaha.org
University of Wisconsin Johne's Information Center	http://www.johnes.org
USDA Johne's disease website	http://www.aphis.usda.gov/vs/naahps/johnes/
USDA-APHIS-VS-National Center for Animal Health Surveillance	http://www.aphis.usda.gov/vs/ceah/ncahs/index.htm

For Your Information

Late last year, USDA-APHIS issued its Uniform Program Standards for the Voluntary Bovine Johne's Disease Control Program. This publication can be found at: <http://www.aphis.usda.gov/vs/naahps/johnes/johnes-umr.pdf>

JD IN PRINT

Johne's Disease-related Publications – January, 2006 through March, 2006

- **Bartos, M., P. Hlozek, P. Svastova, L. Dvorska, T. Bull, L. Matlova, I. Parmova, I. Kuhn, J. Stubbs, M. Moravkova, J. Kintr, V. Beran, I. Melicharek, M. Ocepek, and I. Pavlik.** 2006. Identification of members of *Mycobacterium avium* species by Accu-Probes, serotyping, and single IS900, IS901, IS1245 and IS901-flanking region PCR with internal standards. *J Microbiol Methods* **64**:333-45.
- **Basler, T., S. Jeckstadt, P. Valentin-Weigand, and R. Goethe.** 2006. *Mycobacterium paratuberculosis*, *Mycobacterium smegmatis*, and lipopolysaccharide induce different transcriptional and post-transcriptional regulation of the IRG1 gene in murine macrophages. *J Leukoc Biol* **79**:628-38.
- **Berger, S. T., and F. T. Griffin.** 2006. A comparison of ovine monocyte-derived macrophage function following infection with *Mycobacterium avium* ssp. *avium* and *Mycobacterium avium* ssp. *paratuberculosis*. *Immunol Cell Biol*.
- **Berghaus, R. D., T. B. Farver, R. J. Anderson, C. C. Jaravata, and I. A. Gardner.** 2006. Environmental sampling for detection of *Mycobacterium avium* ssp. *paratuberculosis* on large California dairies. *J Dairy Sci* **89**:963-70.
- **Bhide, M., E. Chakurkar, L. Tkacikova, S. Barbuddhe, M. Novak, and I. Mikula.** 2006. IS900-PCR-based detection and characterization of *Mycobacterium avium* subsp. *paratuberculosis* from buffy coat of cattle and sheep. *Vet Microbiol* **112**:33-41.
- **Brey, B. J., R. P. Radcliff, D. L. Clark, Jr., and J. L. Ellingson.** 2006. Design and development of an internal control plasmid for the detection of *Mycobacterium avium* subsp. *paratuberculosis* using real-time PCR. *Mol Cell Probes* **20**:51-9.
- **Chamberlin, W. M., and S. A. Naser.** 2006. Integrating theories of the etiology of Crohn's disease. On the etiology of Crohn's disease: questioning the hypotheses. *Med Sci Monit* **12**:RA27-33.
- **Clark Jr, D. L., J. L. Anderson, J. J. Koziczowski, and J. L. Ellingson.** 2006. Detection of *Mycobacterium avium* subspecies *paratuberculosis* genetic components in retail cheese curds purchased in Wisconsin and Minnesota by PCR. *Mol Cell Probes*. Epublication ahead of print.
- **de Juan, L., J. Alvarez, A. Aranaz, A. Rodriguez, B. Romero, J. Bezos, A. Mateos, and L. Dominguez.** 2006. Molecular epidemiology of Types I/III strains of *Mycobacterium avium* subspecies *paratuberculosis* isolated from goats and cattle. *Vet Microbiol*. Epublication ahead of print.
- **Dorshorst, N. C., M. T. Collins, and J. E. Lombard.** 2006. Decision analysis model for *paratuberculosis* control in commercial dairy herds. *Prev Vet Med*.
- **Eckstein, T. M., S. Chandrasekaran, S. Mahapatra, M. R. McNeil, D. Chatterjee, C. D. Rithner, P. W. Ryan, J. T. Belisle, and J. M. Inamine.** 2006. A major cell wall lipopeptide of *Mycobacterium avium* subspecies *paratuberculosis*. *J Biol Chem* **281**:5209-15.
- **Elzo, M. A., D. O. Rae, S. E. Lanhart, J. G. Wasdin, W. P. Dixon, and J. L. Jones.** 2006. Factors associated with ELISA scores for *paratuberculosis* in an Angus-Brahman multibreed herd of beef cattle. *J Anim Sci* **84**:41-8.
- **Ewer, K., P. Cockle, S. Gordon, H. Mansoor, M. Govaerts, K. Walravens, S. Marche, G. Hewinson, and M. Vordermeier.** 2006. Antigen mining with iterative genome screens identifies novel diagnostics for the *Mycobacterium tuberculosis* complex. *Clin Vaccine Immunol* **13**:90-7.

- **Gioffre, A., K. Caimi, M. J. Zumarraga, V. Meikle, C. Morsella, F. Bigi, A. Alito, M. P. Santangelo, F. Paolicchi, M. I. Romano, and A. Cataldi.** 2006. Lpp34, a novel putative lipoprotein from *Mycobacterium avium* subsp. *paratuberculosis*. *J Vet Med B Infect Dis Vet Public Health* **53**:34-41.
- **Grewal, S. K., S. Rajeev, S. Sreevatsan, and F. C. Michel, Jr.** 2006. Persistence of *Mycobacterium avium* subsp. *paratuberculosis* and other zoonotic pathogens during simulated composting, manure packing, and liquid storage of dairy manure. *Appl Environ Microbiol* **72**:565-74.
- **Gumber, S., G. Eamens, and R. J. Whittington.** 2006. Evaluation of a Pourquier ELISA kit in relation to agar gel immunodiffusion (AGID) test for assessment of the humoral immune response in sheep and goats with and without *Mycobacterium paratuberculosis* infection. *Vet Microbiol*. Epublication ahead of print.
- **Gwozdz, J. M.** 2006. Comparative evaluation of two decontamination methods for the isolation of *Mycobacterium avium* subspecies *paratuberculosis* from faecal slurry and sewage. *Vet Microbiol*. Epublication ahead of print.
- **Horan, K. L., R. Freeman, K. Weigel, M. Semret, S. Pfaller, T. C. Covert, D. van Soelingen, S. C. Leao, M. A. Behr, and G. A. Cangelosi.** 2006. Isolation of the genome sequence strain *Mycobacterium avium* 104 from multiple patients over a 17-year period. *J Clin Microbiol* **44**:783-9.
- **Janagama, H. K., K. I. Jeong, V. Kapur, P. Coussens, and S. Sreevatsan.** 2006. Cytokine responses of bovine macrophages to diverse clinical *Mycobacterium avium* subspecies *paratuberculosis* strains. *BMC Microbiol* **6**:10.
- **Jones, P. H., T. B. Farver, B. Beaman, B. Cetinkaya, and K. L. Morgan.** 2006. Crohn's disease in people exposed to clinical cases of bovine *paratuberculosis*. *Epidemiol Infect* **134**:49-56.
- **Judge, J., I. Kyriazakis, A. Greig, R. S. Davidson, and M. R. Hutchings.** 2006. Routes of intraspecies transmission of *Mycobacterium avium* subsp. *paratuberculosis* in rabbits (*Oryctolagus cuniculus*): a field study. *Appl Environ Microbiol* **72**:398-403.
- **Koets, A., A. Hoek, M. Langelaar, M. Overdijk, W. Santema, P. Franken, W. Eden, and V. Rutten.** 2006. *Mycobacterial* 70 kD heat-shock protein is an effective subunit vaccine against bovine *paratuberculosis*. *Vaccine* **24**:2550-9.
- **Kostoulas, P., L. Leontides, C. Billinis, G. S. Amiridis, and M. Florou.** 2006. The association of sub-clinical *paratuberculosis* with the fertility of Greek dairy ewes and goats varies with parity. *Prev Vet Med*. Epublication ahead of print.
- **Lehtola, M. J., E. Torvinen, I. T. Miettinen, and C. W. Keevil.** 2006. Fluorescence in situ hybridization using peptide nucleic acid probes for rapid detection of *Mycobacterium avium* subsp. *avium* and *Mycobacterium avium* subsp. *paratuberculosis* in potable-water biofilms. *Appl Environ Microbiol* **72**:848-53.
- **Losinger, W. C.** 2006. Economic impacts of reduced milk production associated with epidemiological risk factors for Johne's disease on dairy operations in the USA. *J Dairy Res* **73**:33-43.
- **Lyche, J. L., H. J. Larsen, J. Utne Skaare, A. Tverdal, G. M. Johansen, and E. Ropstad.** 2006. Perinatal exposure to low doses of PCB 153 and PCB 126 affects maternal and neonatal immunity in goat kids. *J Toxicol Environ Health A* **69**:139-58.
- **Marsh, I. B., J. P. Bannantine, M. L. Paustian, M. L. Tizard, V. Kapur, and R. J. Whittington.** 2006. Genomic comparison of *Mycobacterium avium* subsp. *paratuberculosis* sheep and cattle strains by microarray hybridization. *J Bacteriol* **188**:2290-3.

- **McKenna, S. L., H. W. Barkema, G. P. Keefe, and D. C. Sockett.** 2006. Agreement between three ELISAs for *Mycobacterium avium* subsp. *paratuberculosis* in dairy cattle. *Vet Microbiol*. Epublication ahead of print.
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