

October 18, 2007
USAHA / AAVLD / NJWG Meeting
Reno, NV

JDIP Updates: Focus on Phase II

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What is JDIP?

- J** – Johne's
- D** – Disease
- I** – Integrated
- P** – Program

What is JDIP?

A consortium whose mission is to promote animal biosecurity through development and support of projects that enhance knowledge, promote education, develop real-world solutions and mitigate losses from Johne's Disease.

More about JDIP

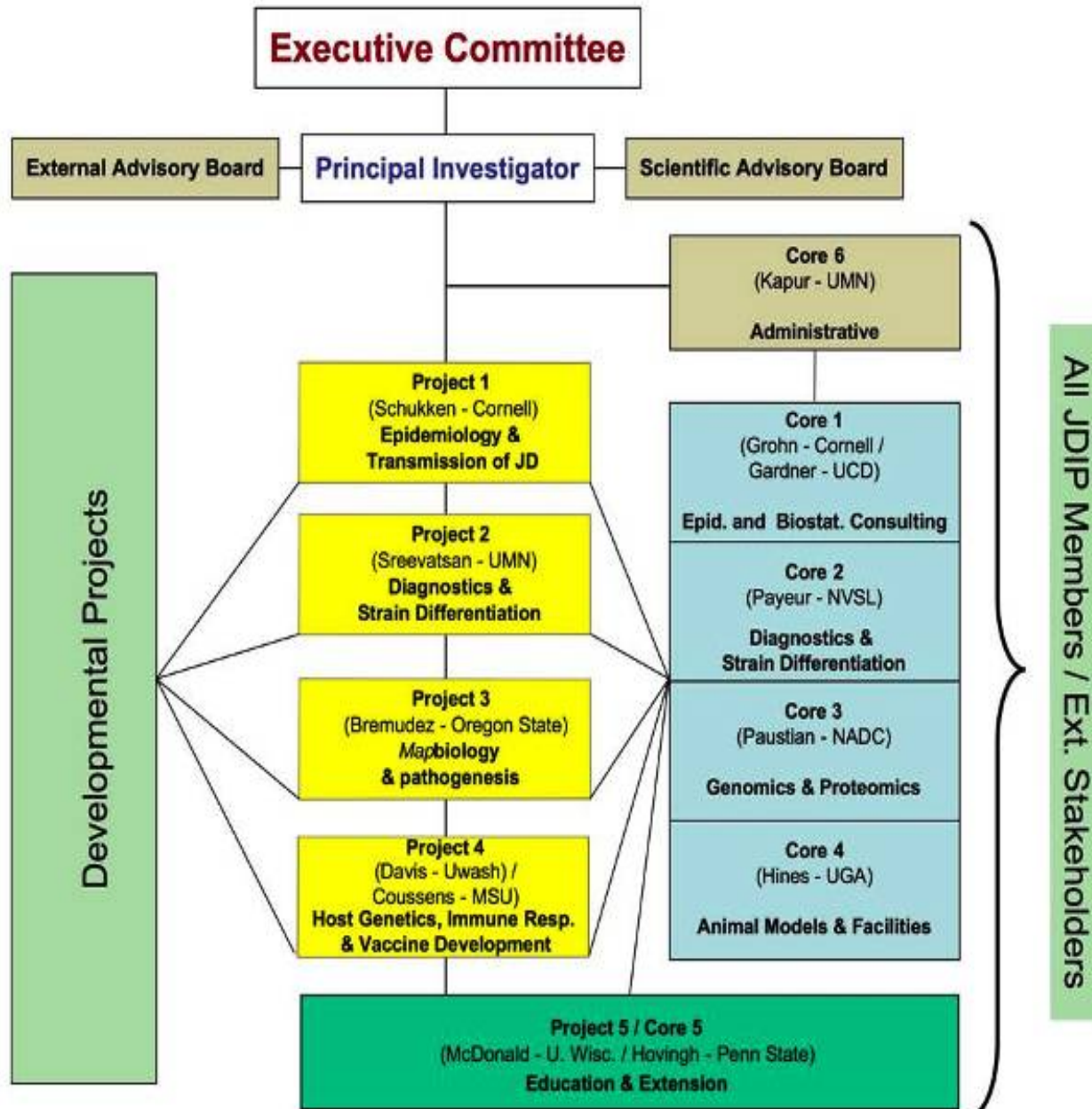
- Consortium of > 140 scientists from > 30 academic institutes, government agencies, and industry
 - Expanding membership
 - Establishing strong international collaborations
 - A similar European program was established in June of 2006
 - Strong links with industry

JDIP Strategic Objectives

- Support and facilitate investigator-directed research on JD
- Create and maintain comprehensive scientific core facilities to support JD research and training activities
- Establish translational research capacity for developing and validating diagnostic tests, vaccines, and disease management concepts for JD
- Provide scientific information and support for the development of JD education, prevention, and control programs

Background / Current Status

- Primary funding from USDA CSREES NRI CAP program grant - Phase I (\$4.4m) in year 3 of operations
- Renewed for 4 additional years (Phase II, \$4.8m) - funding start date April '08
- JDIP has been used successfully to leverage funds from other sources:
 - Federal and State programs
 - National and Federal Dairy Research Funds



JDIP Executive Committee

- John Bannantine – National Animal Disease Center
- Ian Gardner – University of California, Davis
- Yrjo Grohn – Cornell University
- Vivek Kapur – Penn State (PI)
- Scott Wells – University of Minnesota
- Ken Olson – Private Consultant, NIAA

JDIP Operations

- Regular conference calls of Executive Committee, Scientific Advisory Committee and External Advisory Committee oversee operations and monitor progress
- Annual Conference provides updates on activity during the year; present research results and set direction for coming year
- Annual RFA for research proposals

JDIP – Major Accomplishments (Years 1-3)

- Development of alternative sampling and testing strategies for detection of infected animals and herds.
- Optimization & standardization of lab protocols for *Map* culture & PCR to reduce time for detection of positives
- Characterization of genetic differences between *Map* isolates for molecular epidemiologic analysis and tracking strains in animals and the environment
- Identification of key genes, proteins and lipids in *Map* for development of new diagnostics and vaccines

JDIP – Major Accomplishments (Years 1-3)

- Better understanding of *Map* on-farm transmission dynamics to help identify critical control points
- Developed international standards for animal models
- Established transposon mutant libraries that are made available to other investigators
- Developed important community resources that are shared for the development of new diagnostics and vaccines
- Development and widespread use of on-line JD vet certification program and producer modules

Core 1 – Epidemiology & Biostatistics

Mission – Provide consulting support to laboratory and field-based investigations

Phase II Work plan

- Provide consulting on experimental design and data analysis
- Develop and implement statistical and epidemiological tools
- Provide workshops on epidemiological methods for infectious disease research

Core 2 - Diagnostics and Strain Differentiation

Goals

- 1) Provide standardized tools and services to support research on the basic biology, diagnostics, epidemiology, pathogenesis, immunology and control of JD.
- 2) Develop repository of fresh & frozen clinical samples from well characterized sources

Core 2 - Diagnostics and Strain Differentiation

Phase II Work plan

- Provide standardized routine diagnostic and strain differentiation tools and services
- Continue to develop repository of well-characterized fresh or frozen clinical samples
- Develop training programs and workshops on JD diagnostics and strain differentiation for *Map*

Core 3 - Genomics, Antibodies & Proteomics

Mission – To develop and distribute tools, reagents, and protocols that leverage recent technological advances

Phase II Work plan

- Continue to make available the ~24,000 gene disruption *Map* mutants to researchers
- Make available the oligonucleotide microarray that contains probes for all predicted coding sequences in the *MAP* K-10 genome and *M avium* 104 genome

Core 3 - Genomics, Antibodies & Proteomics

Phase II Work plan (Continued)

- Continue to identify, clone and express additional genes identified as unique to *Map* and make the fusion proteins available to researchers.
- Continue work on development of *Map*-specific mAb as well as additional mAbs against bovine T regulatory cell markers
- Provide a web portal for genomic tools and data

Core 4 - Animal Model and Facilities

Mission – Provide support to animal based JDIP projects, validate animal models & provide information on standardized protocols

Phase II Work plan

- Maintain listing of available BSL-2 certified animal facilities
- Validate experimentally the long term JD infection model and address key knowledge gaps on animal models
- Validate experimentally the long term JD infection model in goats and address knowledge gaps

Project 1 - Epidemiology and Transmission

Motivation – To better understand *Map* transmission patterns within and among dairy cattle herds

Phase II Work plan

- Intensive follow-up of existing commercial dairy production facilities of different sizes including sub-typing of *Map*
- Develop web portal for data and metadata from the herds
- On-farm randomized control trials as possible

Project 2 – Diagnostics and Strain Differentiation

Motivation – To develop and validate efficient tests and testing strategies to facilitate control of JD

Phase II Work plan

- Develop and validate optimal combination of highly immunoreactive lipids for identification of cattle with JD
- Develop a sensitive immunodiagnostic detection system for JD
- Develop and validate a reproducible internal calibration standard to enable quantitative detection of *Map* numbers
- Develop and validate cell mediated immune response signatures for JD

Project 3 - Basic Biology and Pathogenesis

Motivation – To better understand the basic biology and mechanisms of pathogenesis of *Map* so that strategies can be developed to prevent or limit the spread of *Map* infections and identify targets for new diagnostics or vaccines

Phase II work plan

- Investigate the interaction between *Map* and host intestinal mucosa
- Investigate *Map* genes associated with ability to survive in host
- Investigate role of mycobacterial lipids in pathogenesis of *Map* infections
- Investigate if genes involved in iron uptake and other iron-regulated genes play a role in *Map* infections

Project 4 - Host Genetics, Immune Response & Vaccine Development

Motivation – Define the events associated with susceptibility to infection with *Map* and the development of immune response in cattle.

Phase II Work plan

- Identify genetic markers for susceptibility to *Map*
- Evaluate the ability of expressed *Map* proteins and mycobacterial lipids to elicit effector T cells with ability to kill infected macrophages
- Determine role of regulatory T cells in immunopathogenesis of paratuberculosis
- Development and evaluation of new generations of vaccines
 - Co-funded by generous support from USDA-APHIS-VS (\$500k)

Project 5 - Education and Extension

Motivation — Provide veterinarians, producers, and other stakeholders with high quality, up-to-date information on JD to foster cost-effective approaches to managing JD risk.

Phase II Work plan

- Complete national survey to determine motivation for & barriers to participation in voluntary JD control programs
- Conduct needs assessment of stakeholder groups
- Design educational programs for stakeholder groups

JDIP Benefits - Researcher

- Facilitate collaboration and cooperation
- Access to and networking with nationally and internationally recognized JD investigators
 - Annual Conference
 - Educational workshops
- Access to research funding on a competitive basis, including funds for exploratory research programs
- Access to state-of-the-art core facilities and services to enhance JD research
 - Access to well characterized biological samples
 - Consulting on research proposals and experimental design

JDIP Benefits – Producer, Vet

- Access to latest information on JD management and control strategies designed and tested by leading JD workers
- Access to high-quality on-line programs, workshops and certification programs for vets and producers
- Opportunity to help identify and prioritize producer needs
- Enhancement of existing tools to improve speed and accuracy of diagnostic tools used in JD programs
- Development of improved diagnostic tools, vaccines and control strategies

Summary

The JDIP program is developing a strong translational pipeline to identify and develop real world solutions that will help producers mitigate losses associated with JD.

Thank You

For more information, please visit
www.jdip.org