Synergizing the RMRCE: With the renewal of the RMRCE, we are initiating a number of activities to foster communication and interactions within the RMRCE. Among these will be a quarterly RMRCE newsletter of which this is the first. With the diverse number of investigators spread over a large geographical region, issues of connectivity and a sense of community are challenged. Thus, as the Administrative Core of the RMRCE completes its distribution of funds and the close-out of the previous funding cycle, efforts will shift to enhancing interactions among RMRCE investigators. We ask that all of you join in this effort and help in the creation of a unified program that provides a valuable scientific resource to infectious diseases research.

New funding and a new focus: Under the renewed RMRCE program, research projects are now directed at therapeutics for infectious diseases. This change in focus has resulted in a reorganization of the RMRCE with research projects clustered under two Integrated Research Foci (IRFs): IRF1 “Bacterial Therapeutics” is directed by Dr. Herbert Schweizer, and IRF2 “Viral Therapeutics” is directed by Dr. John Morrey (see http://www.rmrce.colostate.edu/pages/administrative/org-chart.html for the organizational chart).
News, Highlights and Changes continued

A change has occurred at NIAID: For the first four years of RMRCE funding, Dr. Sue Garges served as our Program Officer and was invaluable in guiding us through various stages of growth. However, Dr. Garges has moved to the National Human Genome Research Institute where she is the Program Director for Sequencing the Human Microbiome. We wish Sue all the best in her new endeavors and thank her for her excellent guidance. At the same time, we welcome our new Program Officer, Dr. Kent Peters. Dr. Peters was previously the Program Officer for Antibacterial Resistance at NIAID and is thus very well suited to assist our programs on infectious diseases therapeutics. Dr. Michael Schaefer will continue to serve as our “backup” Program Officer.

A new look: Every once in a while there is a need ask whether your objectives and mission are properly portrayed through your presentation. When this question was asked of the RMRCE web pages we decided it was time for a make-over. Through the hard work of Lesley Jones the RMRCE now has new web pages. Take a look and provide Lesley with any corrections or suggestions. The new web page format will also facilitate our ability to make updates and share information with RMRCE investigators.

Did you know …

… that compliance with the NIH’s Public Access Policy is a legal requirement and a term and condition of award?

… that the RMRCE Administrative Core is responsible for monitoring RMRCE awards for compliance?

Please remember to acknowledge RMRCE support for your work by referring to grant AI065357. Just as important: make sure that any work attributed to your RMRCE project is part of your approved Specific Aims!

Note the PMCID Update (below) for how long an NIH Manuscript Submission Identification Number (NIHMSID) may be used in lieu of a PubMed Central Identification Number (PMCID) to demonstrate compliance.

** * * * NOTICE * * * **

2009 Annual Reports will be due by January 6, 2010

Instructions & Forms will be sent to investigators

Who has to submit?
Every Project & Core requesting a budget for 2010-2011

Final Reports for Projects ending 04/30/10 will be due at the end of July 2010

* * PMCID Update! *

Effective August 21, 2009, you may now use an NIHMS ID for up to three months after a paper is published. After that, you must use the PMC ID.


8th ASM Biodefense & Emerging Diseases Research Meeting
www.asmbiodefense.org
February 21-24, 2010
Baltimore, MD
This is the major Biodefense/EID meeting of the year, so make sure it’s on your calendar!

2010 National RCE Meeting
Hosted by the Pacific Southwest RCE
www.pswrce.uci.edu
April 11-13, 2010
Las Vegas, NV
[By invitation only]
Funding, Projects and New Additions

On May 1, 2009, the RMRCE was renewed for five years of funding (2009 to 2014) by NIAID. The total five-year award is $38,110,910 (including the ARRA supplement). Through this award a total of 15 Research Projects and 3 Scientific Cores were funded. Since May 1st, four Developmental Projects (DPs), and three Individual Career Development Projects (CDs) were added. In addition, two RCE ARRA projects were recently approved.

Developmental Projects (DPs):

RM DP 001
Dr. Olve Peersen, PI (CSU)
Identification of alphaviral polymerase inhibitors

RM DP 002
Dr. Dean Crick, PI (CSU)
Identification of isopentenyl diphosphate synthesis inhibitors in Burkholderia

RM DP 003
Dr. John Repine, PI (UC-Denver)
Ergothioneine treatment of ARDS following CDC A-C infection

RM DP 004
Dr. Allen Harmsen, PI (MSU)
Development of a therapy to attenuate lung damage in Coxiella infection

RCE ARRA Projects:

Dr. Carmen Menoni, PI (CSU)
Sub-cellular Composition Mapping of Single Bacterium by Extreme Ultraviolet Laser

Dr. Ramesh Akkina, PI (CSU)
Dengue Viral Infection, Immunity and Insect Transmission in Humanized Mice

Individual Career Development Projects (CDs):

RM CD 001
Dr. Torsten Eckstein, PI (CSU)
Defining the Surface Structure of Burkholderia pseudomallei
Mentors: Drs. Herbert Schweizer and Patrick Brennan (CSU)

RM CD 002
Dr. Jerod Skyberg, PI (MSU)
IL-17 Agonist Therapy of Francisella tularensis Infections
Mentor: Dr. David Pascual (MSU)

RM CD 003
Dr. Brett Thibodeaux (CSU)
Use of Viscerotropic Yellow Fever Model to Evaluate Novel Antiviral Therapies
Mentors: Drs. Carol Blair (CSU) and John Roehrig (CDC-DVBID)

Future Funding Opportunities:
We hope to release an RFA for New Opportunities (NO) applications this fall, for funding in 2010-2011. This is an RCE-wide competition (remember that there are 11 RCEs), and so highly innovative, broad-platform, and/or trans-RCE projects are encouraged. Start discussions with potential collaborators early! We will keep you informed through the general RMRCE Listserv and the RMRCE web site at www.rmrce.colostate.edu.
Enhancing Synergy and Scientific Connectivity

In the following sections we will highlight one RMRCE Research Project or Scientific Core, and one RMRCE investigator in each issue. The objective is to stimulate interest in individual RMRCE projects and potential collaborations as well as to highlight the expertise that resides in the RMRCE.

Connecting with Projects:

RM RP 009: Mechanisms of *Burkholderia pseudomallei* Drug Tolerance
Dr. Andres Vazquez-Torres, PI (University of Colorado Denver)
Dr. Martin Voskuil, Co-PI (University of Colorado Denver)

Melioidosis is an endemic disease of South East Asia and Northern Australia caused by the bacterium *Burkholderia pseudomallei*, and it is most commonly observed as a pneumonia or septicemia. Chronic and latent forms of the disease are well noted in the literature, in particular, in U.S. servicemen who had returned from Vietnam, earning it the nickname the “Vietnam time-bomb” because the disease can reactivate after many years.

In addition to chronic or latent disease, a high incidence (6 to 20%) of relapse is observed after antibiotic treatment of acute disease. The prevalence of relapse and the ability of the bacterium to produce chronic infections have led Drs. Vazquez-Torres and Voskuil to hypothesize that drug-tolerant forms of *B. pseudomallei* emerge during an infection, and that tolerance is triggered by the anaerobic environment of abscesses associated with melioidosis and the host’s production of nitric oxide.

Through their RMRCE funding these investigators will study and define the adaptive and metabolic responses triggered by exposure of *B. pseudomallei* to nitrosative stress and anaerobiosis, as well as study how these adaptive responses result in antibacterial tolerance.

The ability to define the genetic and metabolic pathways resulting in drug tolerance will allow for the development of new treatment strategies that either inhibit the emergence of this phenotype or that allow for the development and implementation of drugs to effectively treat chronic and latent infections.

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*Burkholderia pseudomallei*
- Gram-negative, motile, rod shaped, bipolar
- Left photo: colonies on blood agar after 3-5 days
- Right photo: Gram-stained cells
- NIAID Category B Priority Pathogen
- HHS and USDA Select Agent
- The 3D structure of its 2’-O-methyl RNA methyltransferase is the NIAID “Structure of the Month” (Sept 2009)
- Transmission occurs by inhalation of dust, ingestion of contaminated water, and contact with contaminated soil
Enhancing Synergy and Scientific Community (continued)

Meet Your Collaborator:
Dr. Jack Nunberg (University of Montana)

Dr. Jack Nunberg is a Professor and the Director of the Montana Biotechnology Center, at the University of Montana. Although he has been a resident of Missoula, Montana for the past 13 years, his scientific roots began 2,021 miles to the east at the Bronx High School of Science and then Cornell University where he earned Bachelor degrees in Biology (cum laude) and Chemistry.

Following either the sun or the counterculture (his bibliography is a bit vague during this period), Jack moved to Northern California in 1972 where he pursued his Ph.D. in Biophysics under Dr. Robert T. Schimke at Stanford University. His graduate research in the early years of molecular biology and, in particular, his contributions to cDNA cloning, landed him a postdoctoral position in the laboratory of Dr. Stanley Cohen and then a job as a Scientist at Cetus Corporation.

While at Cetus, Jack developed recombinant vaccine antigens, pioneered the use of interleukin-2 as a vaccine adjuvant, and ultimately served as the Senior Scientist in charge of animal health care projects. In 1989, he again switched coasts and moved to Merck where he became the Head of their HIV laboratory and worked on HIV-1 reverse transcriptase inhibitors. This was followed by his second westward migration and his tenure as the Head of the Research Virology Laboratory at Genentech, Inc., where his expertise in HIV and vaccine development were combined. In 1996, after years of swapping-coasts and jumping from one company to another, Jack had an epiphany…find someplace in the middle!! This took him to Missoula and led to the establishment of the Montana Biotechnology Center at the University of Montana.

Jack continued his HIV vaccine research at the University of Montana and expanded his efforts to evaluating the role that the structure of HIV envelope glycoproteins played on host cell interactions. This work was then applied to the study of other viral glycoproteins, including those of hemorrhagic fever arenaviruses. The structural characterization of viral glycoproteins as well as Jack’s previous experience in biotechnology and anti-viral therapeutics has allowed him to develop a very productive RMRCE research project entitled “Arenavirus Entry and Its Inhibition” (RM RP 019).

Outside of his research activities at the University of Montana, Jack is very active in the scientific community where he participates in multiple NIH study sections, is a consultant for biotechnology companies, and has served on national and international scientific panels for vaccine research and emerging infectious diseases. In his spare time, Jack enjoys hiking and backpacking, canoeing, skiing, and eating.
Accomplishments & Recognitions

Herbert Schweizer was invited to present aspects of his RMRCE funded research at the European Melioidosis Network Annual Meeting held on September 11, 2009 at the London School of Hygiene and Tropical Medicine. His presentation, entitled “Characterization of chromosomally-encoded B. pseudomallei antibiotic resistance mechanisms,” included recent results from RM RP 005: Burkholderia pseudomallei Antimicrobial Resistance Mechanisms.

John Morrey was invited to participate in the NIAID/NIH sponsored conference entitled Emerging and Re-emerging Infectious Diseases in Central and Eastern Europe held on September 21-24, 2009 in Sofia, Bulgaria. He gave a presentation about his WNV research funded by RM RP 010: Treatment of Acute West Nile Virus Disease and Neurological Sequelae.

Congratulations to Becky Rivoire and the PDM Core! They are part of the recently funded $979,594, 5-year NIH grant R44AI061940 awarded to Inviragen, Inc., Fort Collins, CO (C. “Harry” Partidos, PI) entitled “Clinical Development of Combination Plague/Smallpox Vaccine.” They will manufacture GMP-quality vaccine seeds and conduct preclinical studies required for FDA approval under the Animal Rule (21 CFR, 314.600) and required to initiate human clinical trials.

Jack Nunberg will represent the RMRCE at an organizational meeting of an RCE-wide network for policy, ethics and legal issues in emerging infections and biodefense research. The meeting, sponsored by SERCEB's Policy, Ethics and Law (PEL) core, will be held on October 14, 2009 in Washington, DC.

Synergy

Synergy (sĭ’n-ər-jē ) [noun]
Term used to describe a situation where different entities cooperate advantageously for a final outcome. Simply defined, it means that the whole is greater than the sum of the individual parts. wikipedia.org

1 + 1 = 3

(Pharmacology) An interaction between drugs where the effects are stronger than their mere sum.

“The way a team plays as a whole determines its success. You may have the greatest bunch of individual stars in the world, but if they don’t play together, the club won’t be worth a dime.”

Babe Ruth
1895-1948
American Baseball Player
RM RP 002 (RMRCE II); RP 1.1 (RMRCE I) – Steven Dow (PI)

RM RP 003 (RMRCE II); RP 2.1 (RMRCE I) – Kenneth Olson (PI), Ann Powers (Co-PI)
Animal Models Core (RMRCE I & II) – Richard Bowen (PI)

RM RP 005 (RMRCE II); RP 1.9, NO 7 (RMRCE I) – Herbert Schweizer (PI)


RM RP 006/007 (RMRCE II); NO 5 (RMRCE I) – Richard Slayden (PI), Peter Tonge (Co-PI)
Animal Models Core (RMRCE I & II) – Richard Bowen (PI)

RM RP 009 (RMRCE II) – Martin Voskuil (Co-PI); RP 1.6 (RMRCE I) – Martin Voskuil (PI)

RM RP 010 (RMRCE II); RP 2.4 (RMRCE I) – John Morrey (PI)

RM RP 016/017 (RMRCE II); RP 2.8 (RMRCE I) – BRIAN GEISS (PI), SUSAN KEENAN (CO-PI)
RM DP 001 (RMRCE II) – OLVE PEERSEN (PI)

RM RP 019 (RMRCE II); RP 2.9 (RMRCE I) – JACK NUNBERG (PI)


RM DP 002 (RMRCE II); RP 1.2 (RMRCE I) – DEAN CRICK (PI)


GENOMICS PROTEOMICS CORE (RMRCE I & II) – RICHARD SLAYDEN (PI)

RP 3.1 AND COXIELLA CULTIVATION CORE (RMRCE I) – MICHAEL MINNICK (PI)

CD 2.3 (RMRCE I) – JEFFREY BENDER (PI), LISA CANNON-ALBRIGHT (MENTOR)


Let us know about your RMRCE-funded publications for the RMRCE web site and this newsletter! Submissions must have a PMCID number, or be a PMC Journal - In Process accepted paper, or have an NIHMSID number.
Ask the Admin Core:

Q: Who is the best person to contact if I have a question about my budget?
A: Very specific budget questions (such as, how much money do I have left?) should be directed to your departmental or institutional grant accountant. Other budget questions may be sent to Ms. Charmaine Matheson (charmaine.matheson@colostate.edu).

Q: May I contact NIAID directly if I have an RCE program question?
A: No. NIAID wants all contact to be through the RMRCE Administrative Core. Please do NOT contact them directly!

Q: Who is the best person to contact if I have any other, non-budget questions?
A: Direct all other questions via e-mail to Dr. Julia Inamine (julia.inamine@colostate.edu).

We welcome any questions, suggestions and contributions. Please submit via e-mail to Julia (julia.inamine@colostate.edu)