VANDERBILT UNIVERSITY

Vanderbilt Environmental Health and Safety

August 5, 2006

Edward H. Hammond, Director
The Sunshine Project
P.O. Box 41987
Austin, TX 78704

Dear Mr. Hammond,

As you requested in your March 15, 2006 fax, please find enclosed approved minutes from all meetings of the Vanderbilt Institutional Biosafety Committee convened between May 1, 2003 and March 15, 2006.

Please note that these minutes are being supplied for the sole use of The Sunshine Project and are not to be transferred to any other party without Vanderbilt's permission.

Redactions have been made only in the following instances:

- We received a specific request for redaction from a private funding source with whom Vanderbilt has a contract restricting the release of proprietary or private information.
- We received no consent for release from a private funding source with whom Vanderbilt has a contract restricting release of proprietary or private information.
- Where specific research locations are listed
- Where personal information, unrelated to IBC function, is listed

Regarding your query on the "Fink Committee" report, Vanderbilt has not yet initiated a formal review of protocols for dual-use of concern potential.

Please let us know if you have any questions regarding this submission.

Sincerely,

LouAnn C. Burnett, MS, CBSP
Assistant Director, VEHS &
Biological Safety Officer

Mark R. Denison, MD
Professor of Pediatrics,
Microbiology & Immunology
Chair, Institutional Biosafety Committee

Robert F. Wheaton, MPH, CIH
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Vanderbilt University Institutional Biosafety Committee

IBC Minutes
May 19, 2003
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Linda Sealy, David Bader, Melanie Swift, James Crowe, Douglas McMahon, Robert Loedding, Greg Hanley, LouAnn Burnett, Cara Sutcliiffe, Robert Coffey and Jerry Rowland (12)

Non-voting members: Christina Jones, Valerie Thayer, Robert Wheaton, and Garnet Jack. (4)

Absent: Charles Stratton and Peter Wright. (2)

Meeting called to order at 2:05 P.M.

The minutes of March 10, 2002 were reviewed. No additional changes were noted. The minutes were approved unanimously on a voice vote.

Announcements/Introductions.
Christina Jones introduced two of the law students (Ramica Sing and Nia Harding) who will be working with her this summer. The students were given a confidentially statement to sign.
LouAnn Burnett informed the committee members that the July 14th IBC meeting will be canceled due to the up coming CSHEMA meeting but may be rescheduled if needed.

UPDATES/REPORT

LouAnn Burnett discussed with the committee BSL3 spaces proposed or existing. LouAnn Burnett indicated that there was a previous meeting with officials from the School of Medicine, Office of Research, Space and Facilities and Plant Services to discuss the status of these spaces and that the main focus for the meeting centered on the ability to get Mark Denison BSL3 space to work with the SARS coronavirus and the quest to get space for persons to work with select agents. From the list of proposed or existing spaces, it was noted that there was only two possible functional BSL3 facilities and that the adequacies of these facilities are not fully known. LouAnn Burnett told the committee that there is going to be a meeting on June 3, 2003 with the Dean of the School of Medicine concerning the establishment and operation of the BSL3 facilities

and that repairs to the facilities be postponed until after the conclusion of the meeting with the dean.
A motion was made to implement by October 1, 2003 guidelines for the local implementation of CDC compliance of certifiable BSL3 working labs and that the BSL3 working group should supply these guidelines to the IBC for approval before the August 11th IBC meeting. The motion was approved unanimously by a voice vote. LouAnn Burnett informed the committee that she would contact the CDC to postpone the up coming visit on June 11, 2003. LouAnn Burnett informed the committee that the Safety and Emergency Response Plans were incomplete and is hoping that it be ready for the next IBC meeting. LouAnn Burnett did give a broad overview of the components of this plan and all that will be required for its successful implementation.

Project Review Updates

There were no projects review updates.

Project Review

P.I: William Mitchell, Pathology.

Title: *SARS genetic Vaccine*

Sponsor: NIH (2004 – 2006)

Summary: This is a project to develop a genetic vaccine against the coronavirus that is responsible for SARS (severe acute respiratory syndrome) and poses a major pending world health problem. The entire genetic sequence of this new virus has been determined allowing this project to be initiated at this time. The development of an animal model is proposed in which efficacy will be assessed.

Comments: The committee recommended the Following: Verification of BSL3 facility to be used is operating within design specification compliant with CDC guidelines, Modification of SOP to include face protection, Modification of SOP to include respiratory protection, Detailed animal exposure procedures agreed upon by both the IBC and Division of Animal Care and DOT/IATA shipping training prior to receipt of infectious substances

Motion: Defer
Total votes: 12
For: 12 **Against** 0 **Abstain** 0.

P.I: Kathryn Edwards, Pediatrics Infectious Diseases.

Title: *A Comparison of Dressing Preparations for Smallpox Vaccination Sites with a Focus upon the Risk of Secondary Transmission of Vaccinia Virus*

Sponsor: *NIH/NIAID/DMID (IRB# 030448))*

Summary: This study will investigate the potential for secondary transmission of vaccinia from smallpox vaccination sites covered by various types of dressings, as well as the effects of each dressing type on the healing of the vaccination.

[Note: The investigator reports that an adjunct investigation to prior clinical trials with smallpox vaccination collected culture specimens from newly vaccinated volunteers to investige the potential for transmission of vaccinia from the vaccination sites. This study was not brought before the IBC.]

Comments: The use of eye protection during vaccine administration and Specimen Handling, for patient contact, standard precautions with eye protection during vaccine administration, confirmation that the laboratory processing the specimens is approved at Biosafety Level 2 (BSL2) for the research specified in the protocol, documentation verifying that the research staff has been informed of the risk and given the opportunity to be vaccinated and all counseling regarding vaccinia vaccination should occur through the Occupational Health Clinic was recommended. All other concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I: Peter Wright, Department of Pediatrics.

Title: *A Worldwide, Phase I, Dose Escalating Study of the Safety, Tolerability, and Immunogenicity of a 3-dose regimen of the MRKAd5 HIV-1 gag Vaccine in Healthy Adults (HVTN 050/Merck 018)*

Sponsor: HVTN/Merck 018 (Ongoing)

Summary: This is an amendment to the previous protocol possessing the same title.

This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this

trial is to establish safety and tolerability of a 3-dose regime of 2 different dosing levels ($1X10^9$ viral particles and $1X10^{10}$ viral particles) of MRKAd5-HIV-1 gag vaccine and to compare the Immunogenicity between the two dose levels. .

Comments: All concerns were adequately answered in the amended proposal submitted.

Motion: Approved, BSL2

Total votes: 12

For: 12 **Against**: 0 **Abstain**: 0.

P.I: Brian Burkey, Department of Otolaryngology.

Title: [redacted]

Sponsor: [redacted]

Adverse Event Reports

Event Date: 10/12/02 Report Date: 1/10/03 [redacted]

The IBC acknowledged receipt of this report and the investigator's assessment, and had no recommendations or changes regarding the assessment.

Motion: Accept
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

Walkthrough: Three labs were presented to the committee with the noted deficiencies. The problem of lab temperature fluctuations, compliance and lab auditing were discussed with the suggestion that these issue be revisited by the committee when a complete data base has been generated and all investigators are informed of the required guidelines.

Meeting adjourned at 3:15PM.

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
June 9, 2003
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Peter Wright, Linda Sealy, Charles Stratton, Melanie Swift, Douglas McMahon, Robert Loedding, Greg Hanley, LouAnn Burnett, Cara Sutcliffe and Jerry Rowland (11)

Non-voting members: Christina Jones, Robert Wheaton, and Garnet Jack. (3)

Absent: David Bader, Valerie Thayer, James Crowe, and Robert Coffey. (4)

Meeting called to order at 2:05 P.M.

The minutes of May 19, 2002 were reviewed. No additional changes were noted. The minutes were approved unanimously on a voice vote.

Announcements/Introductions.
There were no announcements made.

UPDATES/REPORT

LouAnn Burnett informed the committee members of the meeting called by the Dean of the School of Medicine, Steve Gabbe, to discuss preservation of the already existing BSL3 spaces and getting then up to standard with annual verification of facility specifications. There were three members of the IBC that were present at the meeting (Peter Wright, Robert Wheaton and LouAnn Burnett). There was a consensus that the BSL3 spaces be preserved with emphasis on ensuring that these facilities are improved to specifications set forth by the CDC and that these specifications be verified annually. Dr. Gabbe approved a visit by a consulting company to come in and identify the deficiencies that may need to be addressed for proper functioning of the BSL3 spaces. The visit would take place on June 24th and 25th, 2003. LouAnn Burnett indicated that the application for Select Agents that was submitted to the CDC was withdrawn because the facilities that were to be the site of these agents were not at this point in time ready to handle the agents. Peter Wright did suggest that an invitation be sent to Meharry Medical College Biosafety Officer to become a member of Vanderbilt University Institutional Biosafety Committee. LouAnn Burnett and Robert Wheaton indicated that they would be happy to

send out the relevant letters of invitation to the Safety Officer at Meharry Medical College.

Project Review Updates

Dr. Kathryn Edwards submitted a request for reevaluation of the May IBC recommendations for using eye protection during her smallpox vaccine clinical trial. After an in-depth discussion of the methods of inoculation and of current CDC guidelines for smallpox immunization and for biosafety, the committee recommended that while performing the clinical inoculation using standard precautions eye protection would not be required. However, during the specimen collection, handling and processing portions of this trial the biosafety level 2 guidelines be followed as consistent with the laboratory guidelines of the CDC, including the wearing of appropriate eye protection.

Project Review

P.I: Paul Spearman, Department of Pediatrics.

Title: A Probe Study of the Safety, Tolerability, and Immunogenicity of a 1- Dose Regimen of the MRKAd5 HIV-1 Gag Vaccine Versus the ALVAC-HIV (vCP205) Vaccine in Healthy Adults Who Previously Received a 3-Dose Regimen of MRKAd5, Ad5, or Placebo in MERCK V520 Protocols 007 or 012

Sponsor: Merck Research Labs (ongoing)

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to show that subjects who received the MRKAd5 vaccine (1×10^9, 1×10^{10}, 1×10^{11} viral particles per dose) will exhibit a better immunogenicity when given a boosted injection of ALVAC-HIV (vCP205) 1×10^6 than subjects receiving a single boosted injection of MRKAd5 vaccine at either 1×10^9, 1×10^{10}, or 1×10^{11}. The hypothesis behind this trial is that a single dose regimen of the ALVAC-HIV (vCP205) vaccine at 1×10^6 will be generally safe and well tolerated in subjects who have previously received a 3-dose regimen of the Ad5 or the MRKAd5 HIV-1 gag vaccine.

The MRKAd5 and Ad5 viral vector has been approved twice by the IBC in Merck protocols 002 and 007. ALVAC-HIV has not been approved by the IBC for Dr. Spearman's intended use but has been for Peter Wright. The recombinant canarypox virus (ALVAC-HIV) expresses the products of multiple HIV-1 genes as follows: the gag gene expresses the gag p55 protein, the pol gene expresses the p15 protein, a part of the env gene expresses the gp 120 and gp 41glycoprotein.

Comments: All concerns were adequately answered in the amended proposal submitted.

Motion: Approved, BSL2
Total votes: 11
For: 10 **Against** 0 **Abstain** 1.

P.I Paul Spearman, Department of Pediatrics.

Title: AMENDMENT: A Probe Study of the Safety, Tolerability, and Immunogenicity of a 3- Dose Regimen of the MRKAd5 HIV-1 Gag Vaccine in Healthy Adults

Sponsor: Merck Research Labs (ongoing)

Summary: This is a continuation of a previous protocol and has the same title as the previous protocol (IRB# 012) with long term follow-up lasting five years. This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to establish safety and tolerability of a new vaccine against HIV-1, by vaccinating healthy, HIV-negative human subjects with replication-deficient adenovirus with the HIV-1 gag gene inserted. The hypothesis behind this vaccine is that expression of the HIV-1 gag gene will elevate cytotoxic T lymphocyte (CTL) immunity. It is hoped that subjects with this type of immunity may be avoid the deleterious effects of HIV infection.

Comments: All concerns were adequately answered in the amended proposal submitted.

Motion: Approved, BSL2
Total votes: 11
For: 11 **Against**: 0 **Abstain**: 0.

P.I: Robert N. Piana, Department of Cardiology.

Title: [redacted]

Sponsor: [redacted].

Summary: [redacted]

[redacted]

Comments: The Committee recommended eye protection instead of face protection. All concerns were adequately answered in the amended proposal submitted.

Motion: Approved, BSL2

Total votes: 11

For: 11 **Against**: 0 **Abstain**: 0.

Walkthrough: Two labs were presented to the committee with the noted deficiencies.

Meeting adjourned at 3:15PM.

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
August 11, 2003
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Peter Wright, Linda Sealy, Melanie Swift, Douglas McMahon, Robert Loedding, Greg Hanley, LouAnn Burnett, Valerie Thayer, James Crowe, David Bader and Jerry Rowland (12)

Non-voting members: Robert Wheaton, and Garnet Jack. (2)

Absent: Christina Jones, Cara Sutcliffe, Charles Stratton, and Robert Coffey. (4)

Meeting called to order at 2:05 P.M.

The minutes of June 9, 2003 were reviewed. No additional changes were noted. The minutes were approved unanimously on a voice vote.

Announcements/Introductions.
LouAnn Burnett informed the committee that the August 11th meeting would be Peter Wright final meeting as the chair of the IBC. James Crowe has accepted the position as the new chair of the IBC. The committee was also informed that Dr. Richard D'Aquila would be the new committee member to occupy the vacancy created by Dr. Wright's departure. LouAnn Burnett informed the committee that Cara Sutcliffe will be on [redacted] leave through October, 2003. The committee agreed to keep the IBC meetings as has been scheduled in the past (every second Monday of the month).

UPDATES/REPORT

LouAnn Burnett discussed the report that was submitted by Council Rock Consulting (CRC) of the proposed BSL3 spaces. There spaces were [redacted]. The recommendations were noted and a revisit on September 19th, 2003 by CRC for the certification of the [redacted] space was announced. LouAnn Burnett suggested that CRC review and partially validate the BSL3 core policies and procedures and because of this, it was agreed that there be a deferral of the BSL3 core policies and procedures until December for the committee review. LouAnn Burnett discussed briefly an article in the Williamson county AM newspaper that dealt with

smallpox sample collection. The main focus was personal protective equipment and how and when it is supposed to be worn.

Project Review Updates

None to report.

Project Review

P.I Wendell Yarbrough, Department of Cancer Biology.

Title: Tumor Suppressor ARF As a Therapeutic Agent In Oral Malignancies

Sponsor: NIH

Summary: The purpose of this research proposal is to test different novel treatment options for head and neck squamous cell carcinoma (HNSCC) using a model system of human epithelia and HNSCC. Cell lines and mice will be used to test the various options. Adenovirus, adeno-associated virus, and retrovirus expressing various tumor suppressor genes (ARF, p53, p16) will be injected into animals and/or cell lines and tissues to see if this will have an effect on cell growth.

Comments: All concerns were adequately answered in the amended proposal submitted.

Motion: Approved, BSL2/ABLS2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I John Williams, Pediatrics Infectious Diseases.

Title: Determinants of Protective Immunity to Human Metapneumovirus

Sponsor: NIH/NIAID #A56170-01

Summary: The study will investigate the mechanisms of immunity to human metapneumovirus (hMPV) in mice. hMPV is a newly described paramyxovirus that infects most humans by the age of five. [Other paramyxoviruses include measles virus, mumps virus, parainfluenza viruses, respiratory syncytial virus]. It is a major cause of lower respiratory tract infection in children with a spectrum of illness and morbidity similar to that of respiratory syncytial virus (RSV). The goal is to determine which components of the immune system; antibodies or white blood cells mediate protection to hMPV. A mouse model will be created and used by measuring antibody response to hMPV. Cross protective immunity studies against both major groups of hMPV will be

conducted. Explorations of whether primary infection with hMPV induces complete protection against reinfection or only partial protection will also be studied.

Comments: All concerns were adequately answered in the amended proposal submitted.

Motion: Approved, BSL2/ABSL2
Total votes: 11
For: 11 **Against**: 0 **Abstain**: 1.

P.I: Mark Denison, Pediatrics/Microbiology & Immunology

Title: Polymerase Protein in Coronavirus Replication

Sponsor: NIH/NIAID.

Summary: The goal of the research program will be to identify the proteins and proteinase activities of the newly identified SARS associated human coronavirus (CV) and to identify methods for interference with virus reproduction. In addition, we will work to develop an infectious clone of the virus and introduce mutations in the virus to create attenuated viruses as possible vaccine candidates.

The project will involve growing the virus in Vero cells in culture and analyzing virus growth by measuring the number of plaques on a tissue culture monolayer. Inhibitors of the viral proteinase will be used to determine which ones are the most likely to interfere with virus replication in culture.

When working with any cloned virus, mutations will be introduced into the cDNA, which will then be copied into RNA that will then be introduced into cells by electroporation, followed by recovery of virus plaques, and growth and analysis of virus as above.

Comments: After reviewing the protocol with procedures for work, there were numerous minor concerns that were raised. All concerns were recorded and forwarded to investigator for clarification.

Motion: Approved pending clarification of concerns with the committee to review the modifications, BSL2/BSL3

Total: Voice votes: 12

For: 12 **Against**: 0 **Abstain**: 0.

P.I: David Carbone, Oncology.

Title: **AMENDMENT:** A Phase II Randomized Study of GM-CSF Gene-Modified Autologous Tumor Vaccine (CG8123) with and without Low-Dose Cyclosphosphamide in Advanced Non-Small Cell Lung Cancer (THO0285)

Sponsor: Cell Genesys.

Summary: This is an amendment of an already approved human gene transfer trial . This study looks at advanced stage non-small cell lung cancer subjects with a median survival of 2-3 months. The primary objective of this study is to assess the impact of co-administration of immunomodulatory doses of cyclophosphamide on vaccine potency and to boost the immune response. The subjects' own tumor tissue is used to manufacture individual vaccine agent. In similar studies, the primary toxicities experienced were mild flu and local skin reactions. Two study groups (A & B) are used, one with the agent alone and one group combining the agent with cyclophosphamide. This protocol is using a 1 to 1 randomization, with stratification based on prior chemotherapy use, and incorporates quality of life assessments. Study subjects are required to be 18 years or older to enroll, and exclusion criteria includes no previous gene therapy or active autoimmune disease. Cell preparation will fail for 20% of the subjects who will then not be eligible to receive a vaccine. Those subjects will be told about other options, but will continue to be followed.

The amendment consists of several administrative changes and clarifications and also some increased safety guidelines and updated patient communication [redacted]. The trial now also includes 15-year follow-up, as required by FDA for new human gene transfer.

Comments: All concerns were adequately answered in the amended proposal submitted

Motion: Approved with no changes to biosafty level or precautions as previously recommended, BSL2.

Total: votes: 12

For: 12 **Against**: 0 **Abstain**: 0.

Walkthrough: 0

Meeting adjourned at 3:25PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
September 22, 2003
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Linda Sealy, Robert Loedding, Greg Hanley, LouAnn Burnett, James Crowe, Charles Stratton, David Bader and Richard D'Aquilia (9)

Non-voting members: Robert Wheaton, Christina Jones and Garnet Jack. (3)

Absent: Valerie Thayer, Melanie Swift, Douglas McMahon, Cara Sutcliffe, Jerry Rowland and Robert Coffey. (6)

Meeting called to order at 2:00 P.M.

The minutes of August 11th, 2003 were reviewed. No additional changes were noted. The minutes were approved unanimously on a voice vote.

Project Review

P.I David Cortez, Department of Biochemistry

Title: Function of the ATR-ATRIP Complex.

Sponsor: NIH/NCI.

Summary: The purpose of this experiment is to understand how cells preserve genomic integrity. The aim is to define the components of DNA damage response pathways and determine how they work cooperatively to prevent cancer by regulating the cell cycle, promoting DNA repair or initiating apoptosis. ATM and ATR are promoters that function at the apex of these signaling pathways. Research work will focus on the functional domain of ATR kinase, determine how ATRIP (interacting protein) modifies ATR function and determine how phosphorylation of ATRIP promotes checkpoints. To accomplish these goals cell lines lacking the gene for ATR in conjunction with a RNA inhibition system will be used to study these objectives.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2
Total votes: 9
For: 9**Against**: 0 **Abstain**: 0.

P.I Timothy R. Peters, Department of Pediatrics

Title: Mechanisms of Human Metapneumovirus.

Sponsor: Vanderbilt Physician Scientist Development Program.

Summary: The goal of this proposal is to understand how metapneumovirus replicates in infected hosts. The focus will be to identify and characterize interactions between viral and cellular protein to gain a better understanding of viral assembly and trafficking within the host cells. To accomplish this goal the investigator will employ the use of a number of viruses (Metapneumovirus, Respiratory Syncytial Virus (*Paramyxovirus*), Reovirus) and cell lines to mimic and gain incite to the relatively unknown viral replication process. A better understanding of how RNA viruses replicate in infected hosts cells can lead to the development of therapeutic and vaccine strategies to combat this childhood respiratory pathogen.

Comments: The committee concerns centered on the issue of the bisafety cabinet certification and laboratory walkthrough.

Motion After deliberation, the committee decided to have the proposal administratively approved by the Biosafety Officer pending laboratory walkthrough and biosafety cabinet certification, BSL2.

Total votes: 9
For: 9**Against**: 0 **Abstain**: 0

P.I: E. Duco Jansen, Department of Biomedical Engineering

Title: In Vivo Imaging of Transplanted Islets.

Sponsor: Diabetes Research Training Center Pilot and Feasibility Studies

Summary: This study will investigate the ability to access transplanted islets cells by optical imaging. A mouse model will be developed in which islets cells that are infected with replication deficient adenovirus expressing luciferase will be injected into the animals and imaged for luciferase activity. The hope is that this technique can be developed to better understand diabetes in humans leading to improvements in the diagnosis and treatment of diabetes.

Comments: After reviewing the protocol the committee concerns were a lack of information on the nature of the virus (replication deficient), lack of information on the source of human material and facility review.

Motion: After deliberation, the committee decided to have the proposal administratively approved by the Biosafety Officer pending supplied information on source of human materials, documentation of virus inability to replicate and facility review, BSL2/ABSL2.

Total: votes: 9

For: 9**Against**: 0 **Abstain**: 0.

P.I: Wonder Drake, Department of Medicine.

Title: Exploration of M. avium pathogenesis.

Sponsor: Robert Wood Johnson Foundation.

Summary: The purpose of this study is to develop a vaccine that would be effective in providing immunity against *Mycobacterium avium*, which would be advantageous for persons with HIV and lung diseases. The goals is the delete the superoxide dismutase (SOD) gene in the *M. avium* and then replace it with a plasmid that contains a 15% and 25% functional activity of the *M. avium* gene. The hope is that this new version of *M. avium* will grow slower allowing the immune system to recognize it and develop a better immunity towards it. The mutated strain will be introduced into immunodeficient mice at Syracuse University in the lab of Dr. Mike Cynamon.

Comments: All concerns were adequately answered in the proposal submitted

Motion: Approved, BSL2.

Total: votes: 9

For: 9 **Against**: 0 **Abstain**: 0.

P.I: Peter Wright, Pediatrics Infectious Diseases.

Title: A Phase IB Clinical Trial to Evaluate the Safety and Immunogenicity of a Multiclade HIV-1 Plasmid Vaccine, VRC-HIVDNA009-00-VP, Administered at 2 Different Dosing Schedules, in Healthy, HIV-1 Uninfected Adult Participants (HVTN 052).

Sponsor: HVTN.

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to establish safety of the multiclade HIV-1 DNA vaccine VRC-HIVDNA009-00-VP, and to characterize and compare 2 dosing schedules of this vaccine for immunogenicity.

From consent form: "The study vaccine contains a piece of man-made DNA. This means the DNA used to make the vaccine was produced in a laboratory and did not come directly from HIV. Scientists believe that when the vaccine is injected into a muscle, it will tell the body to make small amounts of 4 different proteins normally made by HIV. Scientists will then see if the body makes immune response to these HIV proteins. Immune responses protect your body from infections."

Comments: All concerns were adequately answered in the proposal submitted

Motion: Approved, BSL1/ Standard Precautions during vaccine administration and specimen collection/handling. NIH required consent form elements were also recommended.

Total: votes: 9

For: 9 **Against**: 0 **Abstain**: 0.

P.I: Peter Wright, Pediatrics Infectious Diseases.

Title: A Phase 1 Clinical Trial to Evaluate the Safety and Immunogenicity of a Clade B gag DNA/PLG and env DNA/PLG Microparticles Prime with Clade B Recombinant, Oligomeric gp140/MF59 Adjuvant Boost in Healthy, HIV-1 Uninfected Adult Participants (HVTN 052).

Sponsor: HVTN.

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to establish safety and immunogenicity of a DNA/PLG microparticle prime followed by a recombinant oligomeric glycoprotein boost.

The study is based in the premise that vaccination with plasmid DNA encoding antigenic protein elicits both antibody and cell-mediated immune response and is based on the

assumption that a combination of these responses will be needed for protection against HIV.

Comments: All concerns were adequately answered in the proposal submitted

Motion: Approved, BSL1/ Standard Precautions during vaccine administration and specimen collection/handling. NIH required consent form elements were also recommended.

Total: votes: 9

For: 9 **Against**: 0 **Abstain**: 0.

Announcements/Introductions.
There was a brief introduction by the committee members stating their name and department.

UPDATES/REPORT

Dr. James Crowe discussed with the committee the various issues that the committee has encountered in the past and how the prediction of increased protocol review will impact the committee structure and function. Dr. Crowe suggested that the meetings be shorter and geared towards review of the protocols. Dr. Crowe stated that he would like to utilize the expertise of the committee and by so having individual members review protocols that are associated with their field of discipline. Dr. Crowe indicated that by doing so, this would make the committee more accountable towards their role and responsibility as an IBC member. Dr. Crowe stated that the general summary provided by the biosafety office and the mailing time (a week before the meeting) would remain the same. Dr. Crowe stated that the possibility might arise in which a sub-committee may be established to oversee all select agent issues and that this idea will be discussed at an up coming IBC meeting. Dr. Crowe discussed the role of the IBC in policy-making issues and suggested that all policy issues be addressed in separate meetings. Dr. Crowe mentioned that a checklist would be developed containing relevant issues of concern to that protocol that should be addressed by the IBC. LouAnn Burnett made suggestions as how to address policy issues, committee training on IBC issues and committee education on various topics in research. The committee would be notified on the dates of suggested meeting times for their approval. The committee agreed to have quarterly, an extended meeting to address policy issues. The committee agreed to defer BSL3 update for the next IBC policy meeting scheduled for November 2003.

Project Review Updates
None to report.

Walkthrough: 0
Meeting adjourned at 3:25PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
October 13, 2003
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Melanie Swift, Douglas McMahon, Jerry Rowland, James Crowe, Charles Stratton, Robert Coffey and Richard D'Aquila (8)
Greg Hanley submitted his vote in anticipation of his absence. (1)

Non-voting members: Robert Wheaton, Valerie Thayer, and Garnet Jack. (3)

Absent: Christina Jones, Greg Hanley, Robert Loedding, Linda Sealy, LouAnn Burnett, Cara Sutcliffe, and David Bader. (7)

Meeting called to order at 2:00 P.M.

The minutes of September 22, 2003 were reviewed. No additional changes were noted. The minutes were approved unanimously on a voice vote.

Project Review

P.I.: Ellen Dees, Department of Pediatrics

Title: Function of CMF1 Protein in avian Myogenesis

Sponsor: NIH.

Summary: The aim of this proposal is to identify the process by which cardiac muscle differentiates in an embryo. Specifically, by identification and characterizing novel proteins involved in signaling causing heart muscles from other cells in the embryo to transform from undifferentiated cells to mature muscle cells. Viral vector expressing genes that are implicated in the transformation of undifferentiated cells to muscle cells will be introduced into chick embryo and other cell lines to identify the specific role played in the process.

Comments: The committee concern centered on the fact that data supplied described two separate packaging cell lines (D17.2G and DSN), and there was no supporting data for the packaging cell line (D19) that Dr. Dees proposes to use. The committee recommended that Dr. Dees supply additional information demonstrating that the packaging cell line (D19) is free of competent virus or that she incorporates the use of the DSN (preferably) or the D17.2G packaging cell line instead of the D19.

Motion: Approved pending submission of additional information. BSL2
Total votes: 9
For: 9 **Against**: 0 **Abstain**: 0.

P.I.: Jane Wu, Department of Pediatric Cardiology

Title: Mechanisms of Human Metapneumovirus.

Sponsor: NIH.

Summary: The aim of the research proposal is to investigate the signal that cause white blood cells to migrate to sites of infection allowing the onset of inflammation. The study will focus on a family of signal proteins named slit proteins. Rats will be injected with antibody against a component of the kidney causing glomerulonephritis. Knockout mice for slit protein will be injected with three different bacteria and course of infection studied.

Comments: Concerns centered on the fact that the three bacteria strains were not attenuated, which was in contrast to what Dr. Wu stated and that there needed to be susceptibility test performed on these strains. Another concern was the use of cidex as a disinfectant. The committee recommended that Dr. Wu submit information on the attenuation of the strains and that she include susceptibility test in the revised application to be performed in the clinical microbiology lab at Vanderbilt University. The committee also recommended that the use of cidex be eliminated because of its volatility and toxicity.

Motion Approved pending a final review by Dr. Charles Stratton to ensure appropriate information is received and verified. BSL2/ABSL2.

Total votes: 9
For: 9 **Against**: 0 **Abstain**: 0

Announcements/Introductions.
Dr. Crowe informed the committee that LouAnn Burnett would be absent for the meeting but would be present for the next meeting on 11/10/2003.

UPDATES/REPORT

Dr. James Crowe discussed with the committee what the Biosafety office is trying to accomplish through the walk-through. He stated that by an advanced walk-through it is hoped that the reviewer and the committee would be able to make a more informed decision. Dr. Crowe stated that another goal is to have the labs that have been approved in the past visited so that they can be in compliance and address any issues that they may have. Melanie Swift updated the committee on an accident involving a research assistant who slightly injured himself with liquid nitrogen. Dr Stratton indicated that there should be a way of enforcing a "no eating in the lab" policy to deter research staff from doing this as observed by him in the research areas in close proximity of his office. Dr. Crowe stated that there are plenty of unresolved issues that will be addressed in proceeding meetings, the first being BSL3 core policy followed by the emergency plan. Garnet Jack reminded the committee members about the upcoming educational training class to be held on November 21st, 2003 in Light Hall, Room 407A/B from 2:00pm till 5:00pm.

Project Review Updates

Dr. Crowe discussed briefly the updates on the two protocols that were approved pending additional information received about the viral vectors. These two vectors both had an E1 and E3 deletion rendering them replication incompetent.

Walkthrough: There was a discussion on the walk-through that focused on a distinction between biohazard labels and biosafety level posting out side of lab doors. It was suggested that an additional column be added to differentiate between the two items. The emergency plan was also discussed with Dr. Crowe noting that this would be discussed in the next meeting.

Meeting adjourned at 2:45PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
November 10, 2003
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Sharon Sulkin for Melanie Swift, Douglas McMahon, Jerry Rowland, James Crowe, Charles Stratton, Richard D'Aquila, Greg Hanley, Robert Loedding, Linda Sealy, LouAnn Burnett, Cara Sutcliffe, and David Bader. (13)

Non-voting members: Christina Jones and Garnet Jack. (2)

Absent: Robert: Robert Coffey, Robert Wheaton and Valerie Thayer (3)

Meeting called to order at 2:00 P.M.

The minutes of October 13, 2003 were reviewed. Noted was the incorrect title for Dr. Jane Wu. Also, there was a missing e on Dr. Crowe's name. The minutes were approved unanimously on a voice vote.

Project Review

P.I.: Alissa Weaver, Department of Cancer Biology

Title: (1) Cortactin Assembly and Cancer Metastasis
(2) Cortactin Function in Breast Cancer Metastasis

Sponsor: Vanderbilt Startup Funds/NIH.

Summary: Both projects are the same but seeking different funding sources.
The goal of this project is to understand how certain cell signals referred to as kinases lead to actin assembly which is responsible for cell motility and cancer metastasis. Previous biological studies demonstrated that cortactin, a src kinase substrate and filamentous actin binding protein may regulate such assembly by multiple mechanisms, including stabilization of actin networks and direct activation alone and in concert with N-WASp. Replication deficient retrovirus with genes expressing or inhibiting the

expression of cortactin and WASp will be used to infect mammalian cells to study their role in actin assembly.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2.
Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0.

P.I.: Ann Richmond, Department of Cancer Biology.

Title: (1) The Role of CXC Chemokines in Angiogenesis and Tumorgenesis.
(2) Chemokine Receptor Studies

Sponsor: VAMC Merit Award/NCI.

Summary: Both projects are the same but funded by different sources.

The goal of this project is to understand how cancer cell grows by understanding the signals that lead to cancer formation. To accomplish this goal, replication deficient retrovirus expressing genes of interest will be introduces into a variety of human cell lines and the effects of the genes studied.

Comments: Concerns centered on the use of the term pseudo-retrovirus, which did not correctly describe the virus capabilities for replication, and the manufacturer's warning against the use of the retroviral system with oncogenes.

Motion Approved pending a review of the approval letter by Dr. Linda Sealy and Dr. James Crowe for appropriate wording of concerns. BSL2/ABSL2.

Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0

P.I.: Laura Lee, Department of Developmental Biology.

Title: Cell Cycle Regulation During Drosophila Development

Sponsor: Vanderbilt University Startup Grant.

Summary: The goal of the research proposal is to understand the molecular mechanisms for cell division in the early development of the Drosophila (fruit fly) embryo. To achieve this goal, fruit flies expressing various cell cycle genes will be developed and genes effects on early development of the embryo will be analyzed. Genes will also be expressed in cultured cells to examine their effects on disruption of the cell cycle in the fruit fly embryo.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2.
Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0.

P.I.: Ethan Lee, Department of Developmental Biology.

Title: Reconstitution of Wnt Signaling.

Sponsor: Vanderbilt University Startup Grant.

Summary: The goal of the research proposal is to understand the Wnt signal transduction pathway. To accomplish this goal recombinant DNA for genes in the pathway will be transfected into cultured cells to study their effects on the Wnt signaling. The portion of the study involving embryos will be achieved by injecting mRNA and cDNA into Xenopus laevis (frog) embryos at the one to eight cell stage of development and their effects on early development analyzed.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2.

Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0

P.I.: Terrence S. Dermody/Bryan Youree, Department of Pediatrics

Title: Identification of Orthopoxvirus Receptors

Sponsor: NIH.

Summary: The goal of the project is to identify how rabbitpox virus interacts with cells by investigating the role that cell surface receptors play in allowing the virus to attach to the cell. Identification of antibodies that prevent cell surface binding thereby preventing cell infection is another major focus of this project.

Comments: The committee concern centered on the recognition that all laboratory staff, together with other users of the biosafety cabinet where the rabbitpox virus will be handled should be informed of the risk of exposure to vaccinia and rabbitpox. These persons should be given the opportunity to receive the vaccinia vaccination through the Occupational Health Clinic.

Motion: Approved, BSL2.
Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0.

P.I.: Mary Zutter, Department of Cancer Biology

Title: The α2β1 Integrin: Innate Immunity to Pathogens and Tumors

Sponsor: NIH-NCI

Summary: The study will address the hypothesis that α2β1 integrin expressions are required for innate immune function. Specifically, the study will focus on the mechanisms involved in α2β1 in the immune response to bacteria using *Listeria monocytogenesi*, determine the mechanisms involved in α2β1 integrin mediated immune response to MCMV infection and to determine the role of the α2β1 integrin plays in tumor immunoeditingbacteria and course of infection studied.

Comments: Concerns centered on research staff notification of the risk of exposure to *listeria monocytogenesi* and the use of bleach only to clean the biosafety cabinet.

Motion: Approved, BSL2.
Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0

P.I.: Larry Zwiebel, Department of Biological Science

Title: Examination of Odorant Receptors in Anopheles gambiae

Sponsor: NIH/NIAID.

Summary: The purpose of this research is to characterize a large family of G-protein coupled receptors that bind to odorants cues that activate olfactory signal transduction pathways allowing mosquitoes to sense their chemical environment. The ability to smell such odorants is central to a mosquito's ability to locate and choose human hosts for blood feeding which is critical in establishing the insects overall probability of transmitting pathogens that are responsible for several important human diseases such as malaria which is responsible for over four million deaths per year.

Comments: The committee concern centered on the investigator having the proper shipping permits for shipping his specimens. All other concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2.
Total votes: 13

For: 13 **Against**: 0 **Abstain**: 0.

P.I.: Ann Richmond, Department of Cancer Biology

Title: [redacted] Investigator Initiated Pre-Clinical Research Project.

Sponsor: [redacted]

Summary: The purposes of this study is to understand how two different cytokines are internalized and interact with their common receptor, CXCR4. To accomplish this task, wild type and mutant receptors will be transfected into human breast cancer cells, these cells will then be injected into mice and observation between the cytokines and their receptors in relation to the scope of cancer recorded. Additional studies will look at the migration of tumor cells away from the initial site tumor formation.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2.
Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0

P.I.: Pampee Young, Department of Pathology

Title Role of Endothelial Progenitor Cells in Tumor Vasculature

Sponsor: NIH.

Summary: The goal of the study is to determine the role of endothelial progenitor cells to tumor vascularization. Bone marrow derived endothelial cells will be tracked in a mouse model to tumor sites. Additionally, the biology of human bone marrow and peripheral blood derived endothelial cells at the sites of tumor will be studied.

Comments All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2.
Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0.

P.I.: Douglas S. Kernodle, Department of Medicine/Infectious Diseases

Title: PROGRAM PROJECT: Innate-Adaptive Immune Signaling.

Sponsor: NIH/NIAID.

Summary: Dr. Kernodle and colleagues propose to study the mechanism by which *Mycobacterium tuberculosis* and its vaccine strain (BCG) interfere with immune responses that might eradicate infection. They will also investigate the effect on the host when this inhibitory factor has been reduced.

Comments: After extensive review of the proposal the committee decided to approve work conducted at BSL2 but to defer work at BSL3 until facilities issues are finalized and certified.

Motion: Approved, BSL2/ABSL2.
Defer, BSL3/ABSL3

Total votes: 13
For: 13 **Against**: 0 **Abstain**: 0

Announcements/Introductions.
LouAnn Burnett displayed her award received from the American Biological Association. Dr. Crowe indicated that the biosafety emergency plan would not be discussed but would be placed on the agenda for the next meeting. LouAnn Burnett introduced Sharon Sulkin who sat in for Melanie Swift.

UPDATES/REPORT

Dr. James Crowe and Dr. Greg Haney did indicate that Dr. Ethan Lee title on the agenda was incorrect. There was an extensive review of the Biosafety Level 3 Policies and Procedures. LouAnn Burnett prepared a shortened version of the policy and procedure with level of importance along with the comments and recommendations that were discussed at the meeting. The committee made suggestions that were noted. At the end of the discussion the committee decided to accept the recommendations made with the additional suggestions and that the committee be able to revisit the document to facilitate changes as needed. LouAnn Burnett reminded the committee members about the upcoming educational training class to be held on November 21st, 2003 in Light Hall, Room 407A/B from 2:00pm till 5:00pm.

Project Review Updates
Dr. Crowe discussed briefly the updates on the two protocols that were approved pending additional information received by the biosafety office. Communication with the

investigators and the reviewers were conducted and all appropriate information received and distributed.

Walkthrough: laboratory walk-throughs were noted.

Meeting adjourned at 4:15PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
January 12, 2004
VEHS Training Room
2:00 P.M.

Voting members present: Ben Danzo, Sharon Sulkin and Patricia Kinman for Melanie Swift, Douglas McMahon, James Crowe, Richard D'Aquila, Greg Hanley, Linda Sealy, and LouAnn Burnett. (9)

Non-voting members: Christina Jones, Valerie Thayer and Garnet Jack. (3)

Absent: Robert: Robert Coffey, Jerry Rowland, Charles Stratton, Robert Loedding, Cara Sutcliffe, David Bader and Robert Wheaton (7)

Meeting called to order at 2:05 P.M.

The minutes of November 10, 2003 were reviewed. There no were changes noted. The minutes were approved unanimously on a voice vote.

Project Review

There were no project reviews

UPDATES/REPORT

LouAnn Burnett updated the committee on the status of the BSL3 Policy and Procedure document. She indicated that there were a few comments received from the committee and that the revised procedure was returned to the BSL3 working group for further review. LouAnn Burnett informed the committee about the walk-throughs that have been done, indicating that all labs that have been registered through the IBC have been visited. Walk-throughs will now be focused on labs that have been assigned to BSL1 to assure that research does not require BSL2 containment.. LouAnn Burnett discussed briefly, the convening of a working group implemented by the Chemical Safety Committee to review ways of implementing a university-wide chemical and biological inventory system. LouAnn Burnett suggested that it would be very helpful and beneficial for a member of the IBC to join this workgroup to ensure that the biological aspects of the inventory are well represented.

Training

LouAnn Burnett presented part one of the IBC training for its members covering the history and evolution of the IBC, Vanderbilt university past and present IBC structure and a survey of IBC involving their operation as a committee.

Project Review Updates

There were no project review updates.

Walk-through: Discussed in the Updates/Reports

Meeting adjourned at 4:15PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
February 09, 2004
VEHS Training Room
2:00 P.M.

Voting members present: Sharon Sulkin for Melanie Swift, Jerry Rowland, James Crowe, Charles Stratton, Greg Hanley, Linda Sealy, LouAnn Burnett, and David Bader. (8)

Non-voting members: Christina Jones, Valerie Thayer and Garnet Jack. (3)

Absent: Robert Loedding, Cara Sutcliffe, Douglas McMahon, Richard D'Aquila, Ben Danzo, Robert Coffey and Robert Wheaton (7)
Guests: Carl Gerhard and Kevin Warren.
Meeting called to order at 2:10 P.M.

The minutes of January 12, 2004 were reviewed. Noted was the incorrect placement of Valerie Thayer as a voting member and two spelling errors. The minutes with corrections were approved unanimously on a voice vote.

Announcements/Introductions.
LouAnn Burnett introduced Carl Gerhold and Kevin Warren as part of the VEHS Staff. The committee members also introduced themselves and the department they represented to these guests.

Project Review

P.I.: Neil Osheroff, Department of Biochemistry

Title: (1) Function and Biology of Eukaryotic DNA Topoisomerases.
(2) DNA Lesions as Endogenous Topoisomerase II Poisons

Sponsor: NIH.

Summary: These projects will focus on the enzyme topoisomerase II which removes knots and tangles from the genome by passing a segment of DNA through a double-stranded break that it makes in a separate nucleic acid segment. Beyond its physiological functions, there are a number of anticancer drugs that target this enzyme in clinical use today. The goal of these projects is to examine the effects of topoisomerase II poisons in

cultured human and yeast cells. Work will be carried out to determine whether treatment of cultured cells with a variety of compounds or altering cellular DNA repair pathway requires topoisomerase II mediated DNA repair or recombination. The use of plasmids and adenoviral vector will be employed to express genes of interest to examine the goals of these two projects.

Comments: Concerns centered on a lack of information provided about the adenovirus utilized in these project.

Motion: Defer.
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0.

P.I.: Takaaki Senbonmatsu, Department of Biochemistry.

Title: [redacted]

Sponsor: [redacted]

Summary: [redacted]

Comments: The main concern centered on the deficiencies noted on the review sheet. All other concerns were adequately answered in the proposal submitted.

Motion Approved pending a revisit of the labs to ensure deficiencies are corrected. BSL2.

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I.: L. Jackson Roberts, Department of Clinical Pharmacology.

Title: Oxidant Stress and Oxidized Lipids in Allergic Inflammation.

Sponsor: Sandler program for Asthma Research.

Summary: The purpose of this experiment is to test whether antioxidant therapies (vitamin E supplements) are effective as a treatment for asthma like symptoms induced in mice. To accomplish this goal, *Aspergillus fumigatus* (a fungus) will be administered intranasal to induce asthma-like symptoms. A number of biological and physiological testing methods will be utilized to test the goal of this proposal.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2.
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0.

P.I.: Douglas S. Kernodle, Department of Infectious Diseases.

Title: Epidemiology and Molecular Characteristics of Community Associated Methicillin Resistant *Staphylococcus aureus* in the Healthy Pediatric Population.

Sponsor: NIH/NIAID.

Summary: During the past few years, there has been a marked increase in the occurrence of serious skin infections and pneumonia caused by methicillin-resistant *Staphylococcus aureus* (MRSA) among previously healthy persons in the community, including children. Most MRSA occurs in the hospital where the regular use of antibiotics helps to select for antibiotic-resistant strains. There is evidence that there is a new clone of MRSA referred to as 'community –associated' MRSA (CA-MRSA) that produces lantibiotic making it more resistant and better able to out compete other staphylococci as a flora in the nose and on the skin. Thus, the purpose of this study is to determine the prevalence of CA-MRSA strains as nasal flora in a healthy pediatric population, to see if the lantibiotic genes are functional, and to see whether these strains are capable of killing other staphylococcal strains.

Comments: Concerns centered on the use of 4% chlorhexidine as a handwashing disinfectant and the use of a scrub bush during handwashing. All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2 for PCR with nasal samples, BSL2+ for work involving MW2 or other CA-MRSA, inspection of any new facility prior to the commencement of work, OHC involvement in medical surveillance, and submission to the IBC additional information on any other *E. coli* vectors to be used in the study.

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I.: Peter Wright, Department of Pediatric Infectious Diseases

Title: A Phase I/II Clinical Trial to Evaluate the Safety and Immunogenicity of LIPO-5 Along, ALVAC-HIV (vCP1452) Alone, and ALVAC-HIV Prime/LIPO-5 Boost in Healthy, HIV-1 Uninfected Adult Participants (HVTN 042, Version 1)

Sponsor: HVTN.

Summary: Priming of immune defenses, via the priming of CD8 + CTLs, to virus-infected cells may be an important strategy in developing an effecting HIV vaccine. This study evaluates the use of lipopeptides (LIPO-5) alone and in combination with ALVAC-HIV to increase CD8 + CTL activity.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL1.
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0.

P.I.: Mark S. McClain, Department of Medicine.

Title: Mutagenesis C. perfringens Epsilon Toxin.

Sponsor: Vanderbilt University Discovery Grant Program.

Summary: The study will look at certain mutations within the gene encoding epsilon toxin that may lead to inactivation of the protein toxin. It is postulated that a subset of the inactive epsilon toxin mutants may be able to inhibit the activity of the non-mutated epsilon toxin (dominant-negative mutants). Experimental approaches including recombinant expression of the epsilon toxin in *E. coli,* random mutagenesis of the cloned epsilon toxin gene, and high-throughput analysis of epsilon toxin cytotoxic activity against cultured cells will be used to test the specific aims of this project.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2+ with the adaptation of all biosafety practices as indicated in the summary of research procedures. Also, registration with the CDC as a select agent facility and approved Security Risk Assessment.

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

UPDATES/REPORT

LouAnn Burnett gave a brief update on the [redacted] BSL3 space. LouAnn Burnett indicated that the facility has been inspected and certified, and that Dr. D'Aquila is relocating his lab that is presently in Dr Akins lab to the new space. LouAnn Burnett indicated that Dr. D'Aquila will be submitting all of his materials for work in this space ([redacted]) to the IBC for review utilizing the BioWISE program. LouAnn Burnett informed the committee that the training materials for this lab will have to be reviewed by the committee for approval and that this may be presented in the next IBC meeting. LouAnn Burnett indicated that the next step for the BSL3 core policies will be to present the document to research administration for signatures so that the policies can be in effect, but that this will be somewhat delayed because of the new administrative individual who is not familiar with the BSL3 policies written.

Project Review Updates

None

Walkthrough: laboratory walk-throughs were noted.

Hot Topics: LouAnn Burnett informed the committee about the request made by the Sunshine Project to acquire the two most recent IBC minutes and also requesting the status of Vanderbilt's registration for Select Agents. Christina Jones indicated that because Vanderbilt University receives federal grants, the institution must comply with the request but is under no obligation to respond to the Select Agent question. Christina Jones will review the contracts for the research reflected in the minutes and provide any notice required by those contracts.

Education:

LouAnn Burnett conducted the second part of the annual IBC training entitled "What is Biosafety". The third part to this series will be conducted at the next scheduled IBC meeting.

Meeting adjourned at 4:00PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
March 12, 2004
VEHS Training Room
2:00 P.M.

Voting members present: Melanie Swift, Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Richard D'Aquila, Ben Danzo, Cara Sutcliffe, and David Bader. (10)

Non-voting members: Robert Wheaton, Valerie Thayer and Garnet Jack. (3)

Absent: Christina Jones, Charles Stratton, Robert Coffey and, Jerry Rowland,. (4)
Guests: Carl Gerhold.

Meeting called to order at 2:02 P.M.

The minutes of February 9, 2004 were reviewed. Noted was one misspelled word. The minutes with corrections were approved unanimously on a voice vote.

Announcements/Introductions.
LouAnn Burnett informed the committee that Dr. Coffee had indicated to her that because of his upcoming schedule he will no longer be able to attend the IBC meeting. LouAnn Burnett indicated that this should not be a problem since Dr. Coffee is scheduled to rotate off of the committee this summer. Also, Valerie Thayer is going to be the Occupational Health Clinic representative. Because of her new appointed position she will be replacing Melanie Swift and will also be representing Infection Control. In addition, Ben Danzo announced that he will retire from Vanderbilt effective June 30, 2004.

Project Review

P.I.: Yaun Yi, Department of Medicine

Title: Identifying Metastasis-Suppressor Genes in Prostate Cancer.

Sponsor: DOD.

Summary: The study focuses on the tendency of prostate cancer cells to undergo metastasis. It is hypothesized that metastasis occurs because of a new genetic defect occurring in a small subpopulation of cells. Examination through experimental methods of mouse prostate cancer cells that have undergone metastasis or remained localized will be carried out to examine genes that may have been turned on in the metastasis cells as compared to the non metastasis cells. The ultimate goal is to identify a subset of genes that may prevent metastasis from occurring under normal conditions but have the potential because of genetic defect to cause the cells to undergo metastasis.

Comments: Concerns centered on possible use of ecotropic packaging cell lines for animal work and notification of the various core facilities for proposed work.

Motion: Approved, BSL2/ABSL2
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

Project Review Updates

Dr. Douglas S. Kernodle requested a reconsideration for the requirement to develop an Occupational Health plan involving nasal sampling for appropriate monitoring and reporting in conjunction the Occupational Health Clinic for his project entitled: *Epidemiology and Molecular Characteristics of Community-Associated Methicillin Resistant Staphylococcus aureus in Healthy Pediatric Population.* After an in-depth discussion the committee recommended the following:

- Removal of nasal sampling requirements at this time for work involving non-genetically modified CA- MRSA.
- Prior to genetic manipulation of MRSA, submission of data that can be used to distinguish the identity of a laboratory acquired strain of MRSA versus a community acquired strain of MRSA. The committee will assess the data at that appropriate time and consideration for medical surveillance will be rendered.

All other recommendations were unchanged.

Walkthrough: Laboratory walk-throughs were noted. LouAnn Burnett informed the committee of the progress made in identifying the researchers that have been registered with the IBC at BSL1 but may need to be assigned to a higher BSL posting because of materials that may have added to their research work. Updates of these investigators will be presented to the IBC at the April meeting.

Hot Topics: LouAnn Burnett informed the committee about the information that will be sent to the Sunshine Project and the request made by a sponsor of one of the project listed on the minutes. LouAnn Burnett informed the committee of the initiative announced by the HHS to create the National Science Advisory Board for Biosecurity to review

research that is of concern and potentially should not be published because of the potential misuse of the information for bioterrorism. LouAnn Burnett also discussed briefly the proposed role of the IBC in providing local oversight.

Education:

LouAnn Burnett conducted the third part of the annual IBC training entitled "Key Issues in IBC Review." This concluded the required annual training for the IBC.

Meeting adjourned at 2:55PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
April 12, 2004
VEHS Training Room
2:00 P.M.

Voting members present: Melanie Swift, Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Richard D'Aquila, Ben Danzo, Valerie Thayer, Jerry Rowland, Charles Stratton, and David Bader. (12)

Non-voting members: Christina Jones, Robert Wheaton, and Garnet Jack. (3)

Absent: Cara Sutcliffe. (1)
Guests: Carl Gerhold.

Meeting called to order at 2:02 P.M.

The minutes of April 12, 2004 were reviewed. Noted was the incorrect role that Valerie Thayer will be assuming. Valerie Thayer will serve as one representative from Occupational Health Clinic, along with Melanie Swift. There will be no Infection Control representative, per request by Vicki Brinsko. The minutes with corrections were approved unanimously on a voice vote.

Announcements/Introductions.
Dr. Charles Stratton indicated that Bill Mitchell has received notification of a NIH challenge grant for therapy of SARS to be actuated in September 2004. This project will include some invitro susceptibility testing for the agent. Dr. James Crowe indicated that he attended a meeting initiated by Jeff Balser and that one topic that was discussed, was the role that the institution will play in financial support for BSL3 labs. Dr. Crowe indicated that there will be further discussion on this topic that will involve LouAnn Burnett and possibly two other interested parties.

Project Review

P.I.: Ravi Chari, Department of Hepatobiliary and Liver Transport

Title: Cell Volume Regulated Biology in the Liver.

Sponsor: NIH/NIDDK.

Summary: The study will focus on whether long term delivery of angiopoietin 1 by an adenoviral vector (AdAng1) enhances liver regulation. 5/8 liver mass will be removed from mice and viral vector expressing angiopoietin will be injected. Control animals will receive viral vector expressing β-galactocidase or a soluble Tie2 receptor. Liver regulation will be monitored and data collected.

This protocol has been reviewed in the past. The addition to this protocol is the use of mice. Previously, this work was conducted utilizing cells.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I.: Neil Osheroff, Department of Biochemistry

Title: Function and Biology of Eukaryotic DNA Topoismerases.

Sponsor: NIH.

Summary: These projects will focus on the enzyme topoisomerase II which removes knots and tangles from the genome by passing a segment of DNA through a double-stranded break that it makes in a separate nucleic acid segment. Beyond its physiological functions, there are a number of anticancer drugs that target this enzyme in clinical use today. The goal of these projects is to examine the effects of topoisomerase II poisons in cultured human and yeast cells. Work will be carried out to determine whether treatment of cultured cells with a variety of compounds or altering cellular DNA repair pathway requires topoisomerase II mediated DNA repair or recombination. The use of plasmids and adenoviral vector will be employed to express genes of interest to examine the goals of these two projects.

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Comments: All concerns were adequately answered in the resubmitted proposal.

Motion: Approved, BSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I.: Jennifer Pietenpol, Department of Biochemistry **(Upgraded BSL)**

Title: Function and Biology of Eukaryotic DNA Topoismerases.

Sponsor: NIH/HIEHS.

Summary: This project review was submitted in 2001, and is being reviewed because of the addition of viral vectors to the research work..

Comments: After a careful review of the project summary, the committee decided to defer this project review until a full IBC registration is submitted with the review..

Motion: defer
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I.: David Carbone, Department of Medicine/Hematology and Oncology

Title: **AMENDMENT 3:** A Phase II Randomized Study of GM-CSF Gene-Modified Autologous Tumor Vaccine (CG8123) with and without Low-Dose Cyclosphosphamide in Advanced Non-Small Cell Lung Cancer (THO0285)

Sponsor: Cell Genesys.

Summary: This is an amendment of an already approved human gene transfer trial. This study looks at advanced stage non-small cell lung cancer subjects with a median survival of 2-3 months. The primary objective of this study is to assess the impact of co-administration of immunomodulatory doses of cyclophosphamide on vaccine potency and to boost the immune response. The subjects' own tumor tissue is used to manufacture individual vaccine agent. In similar studies, the primary toxicities experienced were mild flu and local skin reactions. Two study groups (A & B) are used, one with the agent alone and one group combining the agent with cyclophosphamide. This protocol is using a 1 to 1 randomization, with stratification based on prior chemotherapy use, and incorporates quality of life assessments. Study subjects are required to be 18 years or older to enroll, and exclusion criteria includes no previous gene therapy or active autoimmune disease. Cell preparation will fail for 20% of the subjects who will then not be eligible to receive a vaccine. Those subjects will be told about other options, but will continue to be followed

Comments: The amendment provides only changes that are designed to more fully limit risk to the subject – with the exception of the decreased tumor dose allowance. There is no change in risk to healthcare workers, close contacts, or the public.
No change in biosafety level or precautions is recommended.

Motion: Approved, BSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I.: Ravi Chari, Department of Hepatobiliary and Liver Transport

Title: CT 1030: A Phase I/II, Open-Label Study (With a Sequential Dose Escalation Stage Followed by an Expansion of a Selected Dose Cohort), to Evaluate the safety and Anti-Tumor Effects of NV1020, Administered Repeatedly Via Hepatic Artery Infusion Prior to Second-Line Chemotherapy, in Patients With Colorectal Adenocarcinoma Metastatic to the Liver.

Sponsor: MediGene.

Summary: This is a human gene transfer trial to evaluate the safety and anti-tumor effects of NV1020 administered repeatedly via hepatic artery infusion prior to second-line chemotherapy, in patients with colorectal adenocarcinoma metastatic to the liver. NV1020 has been demonstrated to have a cytolytic effect on colorectal carcinoma cells. By administering NV1020 directly into the hepatic artery, it is anticipated that the virus will be distributed throughout the liver, infect hepatocytes and replicate selectively in malignant cells, inducing cytolytic cell death. It is also hypothesized that application of NV1020 prior to chemotherapy may increase susceptibility of tumor cells to cytotoxicity.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I.: Peter Wright, Department of Pediatrics

Title: A Multicenter, Double-Blind, Randomized, Placebo-Controlled Probe Study with an Additional Open-Label Control Arm to Evaluate the Safety and Immunogenicity of a 3-Dose Regimen of the MRKAD5 HIV-1 gag Vaccine in Subjects with Chronic Hepatitis C Virus Infection

Sponsor: Merck and Co. Inc.

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to establish safety and tolerability of a 3-dose prime/boost regime of 2 different dosing levels ($1X10^9$ viral particles and $1X10^{10}$ viral particles) of MRKAd5-HIV-1 gag vaccine in subjects with chronic hepatitis C virus (HCV) infection. Many persons at risk for HIV infection are also at risk for chronic hepatitis. Chronic HCV

infection represents a "worst case" scenario for individuals who have chronic hepatitis – for these reasons HCV infected individuals represent an appropriate population is which to study the hepatic safety profile of candidate HIV vaccines. If the vaccine is safe in subjects with chronic HCV infection, it is unlikely that there would be significant liver toxicity in subjects with other forms of hepatitis.

Comments: The committee concern focused on whether safety needles were being used in this study as it was not indicated in the proposal. All other concerns were adequately answered.

Motion: Approved, BSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

P.I.: Peter Wright, Department of Pediatrics

Title: Evaluation of Two Live Attenuated Parainfluenza Virus Type 3 Vaccines (rHPIV3 – N_B and rB/HPIV3) in Adults, Seropositive 15 to 59 Month Old Children and Seronegative Infants and Children 6 – 36 Months of Age

Sponsor: NIH

Summary: The objective of Dr. Wright's study is to determine the safety, infectivity, and tolerability of two live attenuated parainfluenza virus type 3 vaccines delivered by nasal drops. The candidate vaccines will be tested first in adults, then in seropositive children 15 to 59 months old, and finally, if shown to be safe, in the target population, seronegative infants and children 6 to 36 months of age.
Parainfluenza virus (PIV3) is the second most (after RSV) cause of viral lower respiratory infection severe enough to warrant hospitalization during the first year of life – nearly two-thirds of infants will have been infected – up to 10% of those will demonstrate lower respiratory tract illness. Immunity after primary infection is incomplete and re-infections are not uncommon

Comments: The committee concerns centered on whether sampling/culturing was occurring at Vanderbilt, location of the study and procedures used to determine that subjects were not being enrolled in daycare with pregnant workers. All other concerns were adequately answered in the proposal.

Motion: Approved, BSL2
Total votes: 12
For: 12 **Against**: 0 **Abstain**: 0.

Research Program Upgrades: LouAnn Burnett presented to the committee six (6) research investigators who were approved at BSL1 in the past but have since added human material to their research work requiring them to be upgraded to BSL2. All research investigators will be approved administratively.

Walkthrough: Laboratory walk-throughs were noted.

Meeting adjourned at 2:55PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
May 10, 2004
Room 407A/B Light Hall
2:00 P.M.

Voting members present: Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Ben Danzo, Valerie Thayer, Jerry Rowland, Charles Stratton, and Cara Sutcliffe. (10)

Non-voting members: Garnet Jack. (1)

Absent: Melanie Swift, Richard D'Aquila, Christina Jones, Robert Wheaton, and David Bader (5)

Guests: Carl Gerhold.

Meeting called to order at 2:05 P.M.

The minutes of April 12, 2004 were reviewed. Noted was one incorrect word. The minutes along with the correction were approved unanimously on a voice vote.

Announcements/Introductions.
Dr James Crowe suggested that because of time constrains, the **Policies/Education** part of the meeting be deferred to the next IBC meeting on June 14, 2004. The members agreed to this on a voice vote.

Project Review

P.I.: William P. Hamilton, Department of Civil and Environmental Engineering

Title: Environmental Microorganisms.

Sponsor: NSF.

Summary: The activities of these researchers on the [redacted] focus on the factors affecting bacteria in nature. These researchers investigate the environmental parameters that affect the ability of soil and sediment microbes to utilize organic contaminants as sole carbon and energy sources.

Comments: The discussion focused on the different type of feces used and the potential for infection by pathogens that may be contained in the feces, and also the type of personal protective equipment (lab coats) to be used in the lab. All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2, with a walk-through of facility to be conducted
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I.: Thao P. Dang, Department of Medicine

[redacted]

[redacted]

[redacted]

Comments: concerns centered on whether safety needles were being used and the possibility of the vector/gene combination having the potential for oncogenicity. All concerns were adequately answered in the proposal.

Motion: Approved, BSL2/ABSL2
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I.: Evangeline Easterly, Department of Cell Biology

Title: Role of TGF-bata type II Receptor in Mammary Tumor Cell Progression.

Sponsor: U.S. Army Medical Research and Material Command.

Summary: Breast cancer is the most common cancer in women and the second cause of cancer death in them. In established breast cancer, an excess secretion of transforming growth facter-bata (TGFβ) by tumor cells may promote cancer progression. TGFβ bunds to other receptors such as TGFβ type II receptor (TβRII) to initiate additional signals through the Smad complexes and additional pathways that inhibit cellular proliferation. Some cancers are resistant to TGFβ's anti-proliferative effects and may utilize TGFβ from adjacent cells to enhance proliferation and metastatic progression. It has been shown that loss of signaling through TβRII in human breast cancer cells decreases motility and metastases. The goal of this project is to develop a tumor model in which

TβRII can be conditionally deleted, determine the effects of deletion of TβRII in tumor cells *in vitro* and *in vivo*, and to determine if over-expression of Smad 2/4, Smad 3/4, Alk5-DT, Akt-DD, OR CA/DN forms of MEK1/2 rescues tumor cells from the effects of loss of TβRII. To accomplish these goals mouse mammary tumor cell will be transfected with genes of interest utilizing adenovirus and retrovirus. Following these experiments, mice will be injected with these cells to study the effects *in vivo*.

Comments: The committee concern was centered on the ultimate responsibility of lab safety. After a brief discussion it was agreed upon that the Principal Investigator for the lab should sign off on the IBC application before approval. All other concerns were adequately answered in the proposal.

Motion: Approved, BSL2/ABSL2 with Principal Investigator signature on application.
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I.: Jiyang Cai, Department of Ophthalmology

Title: Role of Mitochondrial Thioredoxin in the Protection Against Oxidation Stress

Sponsor: Vanderbilt Departmental/Internal.

Summary: This study focuses on the role of mitochondrial Thioredoxin (mtTrx) on aging and age related degenerative diseases. Mitochondria produce energy in the form of ATP and controls cell death. These important functions can be affected by oxidative stress induced by an imbalance between the antioxidant capacity and the free radicals that the body is exposed to. Increased levels of antioxidants may protect mitochondria and slow down the process of aging and age-related diseases. By generating specialized types of cells expressing increased levels of mtTrx, studies can de performed to investigate responses to different stimuli that can cause oxidative stress.

Comments: Concerns centered on viral production beyond 48 hours as indicated in application. All other concerns were answered adequately in the application.

Motion: Approved, BSL2
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I.: John A Phillips, Department of Medical Genetics, Pediatrics, and Biochemistry

Title: GH Alternative Splicing: Mechanism and Disease

Sponsor: NIH/NIDDK

Summary: Genes are split into regions referred to as exons and introns. The exon regions code for protein and are joined together by the removal of the introns in a process called splicing. Changes in genes called mutations can cause a gene to function incorrectly which can cause protein deficiencies and disease. Splicing enhancers are specific sequences that help the gene know how to splice out the introns correctly. Silencing RNA (siRNA) is used as a tool to knock out expression of specific genes or degrade the protein product of a specific isoform. The goal of this project is to understand how splicing is regulated and mistakes are avoided. A transgenic mouse model will be developed to study the splicing regulatory protein (SRrp86) by over-expression or expression in tissue where it is not normally detected. A second mouse model will be developed expressing a silencing RNA (siRNA) that will induce degradation of a spliced product from the human growth hormone gene (HG1). One mutation in particular which leads to growth hormone deficiency results from an error in splicing that leads to the loss of exon3 from the GH1 gene and expression of smaller isoform which appears to interfere with the normal protein product. These experiments are designed to test weather we can selectively degrade GH1 RNA transcripts encoding the smaller exon3 skip isoform thereby allowing correctly spliced isoforms to synthesize normal amounts of growth hormone isoform

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2/ABSL2
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I.: Mark S. McClain, Department of Medicine

Title: **AMENDMENT:** Mutagenesis C. perfringens epsilon toxin

Sponsor: Vanderbilt University Discovery Grant Program

Summary: The study will look at certain mutations within the gene encoding epsilon toxin that may lead to inactivation of the protein toxin. It is postulated that a subset of the inactive epsilon toxin mutants may be able to inhibit the activity of the non-mutated epsilon toxin (dominant-negative mutants). Experimental approaches including recombinant expression of the epsilon toxin in *E. coli*, random mutagenesis of the cloned epsilon toxin gene, and high-throughput analysis of epsilon toxin cytotoxic activity against cultured cells will be used to test the specific aims of this project.

AMENDMENT: Dr. McClain proposes to use a genetically inactive mutant to test his methods while waiting for Select Agent registration.

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved, BSL2+
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

FYI: SARS Correspondence

LouAnn Burnett informed the committee of the recent news report carried by Public Radio and the Wall Street Journal about the distribution of the SARS virus to various laboratories in the United States and abroad. This report indicated that the virus distribution should be more tightly regulated and that it should be considered to being placed on the select agent list. LouAnn Burnett indicated that it is possible that this subject will be discussed in the near future by the IBC as it pertains to select agent registration of the university.

Walkthrough: All walk-throughs were noted along with the protocols reviewed.

Meeting adjourned at 3:22PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
June 14, 2004
Room 407A/B Light Hall
2:00 P.M.

Voting members present: Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Ben Danzo, Valerie Thayer, Jerry Rowland, Charles Stratton, and Richard D'Aquila. (10)

Non-voting members: Garnet Jack, and Robert Wheaton. (2)

Absent: Cara Sutcliffe, Melanie Swift, Christina Jones, and David Bader. (4)

Guests: Carl Gerhold.

Meeting called to order at 2:07 P.M.

The minutes of May 10, 2004 were reviewed. Noted were two incorrect words. The minutes along with the correction were approved unanimously on a voice vote.

Announcements/Introductions.
LouAnn Burnett announced that this was the last IBC meeting for Dr. Ben Danzo and that his service was greatly appreciated and he will be missed.

Project Review

P.I.: Terrence Dermody, Department of Microbiology and Immunology

Title: Amendment: 1) Molecular Basis of Reovirus Pathogenesis.
2) Structural Analysis of Reovirus Attachment Mechanism

Sponsor: NIH/NIAIID.

Summary: The goal of this research is to understand the role of the reovirus attachment protein (sigma1) and its specific domains and residues in attachment to receptors, entry into cells, cell death and tropism (targeting of cells). Also, to possibly evaluate the potential use a chimeric adenovirus as a vaccine vector. To accomplish this goal, different constructs associated with the plasmid pL2-Fibtail-T3Dsig1 encoding for an

adenovirus attachment protein, fibers and reovirus sigma1 protein will be inserted into replication deficient adenovirus to study how the mutations affect binding to receptors, entry, and cell death in cultured cells. Mice will also be infected with these constructs containing an additional green fluorescent protein (GFP) to examine which cells are initially infected with these vectors.

Comments: All concerns were adequately answered in the proposal and subsequent correspondence.

Motion: Approved, BSL2/ABSL2.
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I.: Jane Wu, Department of Pediatric Cardiology.

Title: Slit Signaling in Breast Cancer.

Sponsor: NIH.

Summary: The aim of the research proposal is to investigate the role of slit signaling in breast cancer. It has been observed that slit is frequently inactivated in a range of tumors identified. The hypothesis is that slit signaling is important for inhibiting cancer development and metastasis. Experiments will be geared to examine the role of slit signaling in breast cancer cell invasion and migration *in vitro* and in animal models utilizing plasmids and viral vectors that contain the genes that express slit. Understanding how the mechanisms underlying how non invasive tumors can develop into invasive malignant cancers will provide new insight into developing novel approaches for preventing or treating metastatic diseases.

Comments: Concerns centered on the deficiencies noted during the initial walk-through and whether these deficiencies were corrected.

Motion: Approved, BSL2/ABSL2 Pending correction of deficiencies noted in walk-through.
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

Updates/Policies /Education

Emerging Biosafety Issues
LouAnn Burnett informed the committee that the SARS virus may be placed on the select agent list, but no official announcement has been made.

Sunshine Project
Because of the issues raised by both the Sunshine Project and the institutions regarding public requests for IBC minutes, the Office of Biotechnology Activities issued guidelines for the general structure of recording minutes.

NSSBB
The National Science Advisory Board on Biosafety and Biosecurity will be convened in the fall of 2004 to create guidelines for IBC's to use when reviewing research work that may have a dual use function. There has been no official announcement but when this occurs the committee will be informed.

BioWISE
LouAnn Burnett informed the committee that BioWISE should be rolled out in the fall of 2004 initially geared towards project registration followed by laboratory registration. It is hoped that this will capture all of the biological materials used at the institution.

Education
LouAnn Burnett conducted a training session on human gene transfer oversight at Vanderbilt University.

Meeting adjourned at 3:47PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
July 12, 2004
Room 411A/B Light Hall
2:00 P.M.

Voting members present: Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Valerie Thayer, Jerry Rowland, David Bader, Charles Stratton, and Richard D'Aquila. (10)

Non-voting members: Garnet Jack, and Robert Wheaton. (2)

Absent: Cara Sutcliffe, and Christina Jones. (2)

Guests: Carl Gerhold.

Meeting called to order at 2:04 P.M.

The minutes of May 10, 2004 were reviewed. Noted was one incorrect word. The minutes along with the correction were approved unanimously on a voice vote.

Announcements/Introductions.
Dr. James Crowe announced that nominations for new IBC members have been sent out and that responses should be received soon for the up coming IBC year which begins in September, 2004.

Project Review

P.I.: Mary Zutter, Pathology and Cancer Biology.

Title: Diagnostic Markers and Thrombotic/Hemorrhagic Risk in Polycythemia Vera and Essential Thrombocythemia.

Sponsor: DOD

Summary: The specific aim of this study is to investigate the risk of thrombosis utilizing a mouse model with myeloproliferative disorder (MPD) exhibiting genetic defects of platelet glycoproteins and/or coagulation factors, or novel risk factors of thrombosis. To accomplish this, bone marrow from mice with the desired genotype will be collected and

infected with murine stem cell virus (retrovirus) expressing hematopoietic elements. Mice with the same genotype will be recipients of the infected bone marrow. The effects of the expressed gene will be studied to gain a better understanding of this disorder in humans.

Comments: concerns centered on a lack of information about supplier of the vector, packaging cell line to be used, and collaborator of project.

Motion: Defer, further information needed.
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

BSL3 Discussion

P.I.: Dr. Richard D'Aquila

Summary: The focus of this discussion centered on the policies and procedures for room [redacted] BSL3 laboratory. The concerns raised about specific items within the policy were, training materials on proper floor cleaning techniques, cell sorting, training new users, and clarification of duties for each user of the facilities. After a lengthy discussion, it was decided by a voice vote to accept the policies and procedures with concerns to be addressed:

1. Changes identified by LouAnn Burnett prior to committee review are to be addressed.
2. A re-verification procedure is to be developed and presented to the IBC and implemented before the lab begins its second year of operation.
3. LouAnn Burnett will explore working with house keeping staff to provide procedures and perhaps education on house keeping in the BSL3, consistent with usual Vanderbilt practice.
4. A separate tier of training and proficiency for persons operating the flow cytometer must be developed.

Motion: Approved, BSL3 Policies and Procedures.
Total votes: 9
For: 9 **Against**: 0 **Abstain**: 0.

Note: Dr. D'Aquila was present for the discussion but absent for the vote.

Meeting adjourned at 3:25PM

Vanderbilt University
Institutional Biosafety Committee (IBC)

Minutes
August 09, 2004
Room 411A/B Light Hall
2:00 P.M.

Voting members present: Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Valerie Thayer, Jerry Rowland, Cara Sutcliffe, Charles Stratton, and Richard D'Aquila. (10)

Absent: Garnet Jack, Robert Wheaton, David Bader, Carl Gerhold, and Christina Jones. (5)

Meeting called to order at 2:00 P.M.

The minutes of August 09, 2004 were reviewed. The minutes were approved unanimously on a voice vote.

Announcements/Introductions.

Project Review

P.I.: Mary Zutter, Pathology and Cancer Biology.

Title: Diagnostic Markers and Thrombotic/Hemorrhagic Risk in Polycythemia Vera and Essential Thrombocythemia.

Sponsor: DOD

Summary: The specific aim of this study is to investigate the risk of thrombosis utilizing a mouse model with myeloproliferative disorder (MPD) exhibiting genetic defects of platelet glycoproteins and/or coagulation factors, or novel risk factors of thrombosis. To accomplish this, bone marrow from mice with the desired genotype will be collected and infected with murine stem cell virus (retrovirus) expressing hematopoietic elements. Mice with the same genotype will be recipients of the infected bone marrow. The effects

of the expressed gene will be studied to gain a better understanding of this disorder in humans.

Comments: concerns centered on whether the packaging cell line was amphotropic or ecotropic. If the packaging cell line is amphotropic, research staff need to be aware that the vector can infect their cells.

Motion: Approved, pending clarification on the packaging cell line.
Total votes: 10
For: 10 **Against:** 0 **Abstain:** 0.

P.I.: Kathryn Edwards, Pediatrics.

Title: [redacted]

Sponsor: [redacted]

Summary: [redacted]

Comments: The committee had a detailed discussion regarding the status of staff in charge of autoclaving waste from this study. The committee recommended that waste be autoclaved as close to the point of generation as possible and that staff who handle the waste be offered [redacted] vaccination. All other concerns were adequately answered in proposal submitted by Dr. Edwards and the sponsor of the trial concerning safety issues.

Motion: Approved.
Total votes: 10
For: 10 **Against:** 0 **Abstain:** 0.

<u>Policies /Education Discussion</u>

New Members/ Meeting Schedule
LouAnn Burnett informed the committee that all IBC appointments were confirmed and are expected to present at the September meeting. The meeting time will remain the same (the 2nd Monday of each month at 2pm to 3pm; with quarterly extensions to 4pm for policy and education (Nov, Feb, May, Aug)).

Public Meeting

LouAnn Burnett discussed with the committee the draft memo submitted by Christina Jones addressing the issue of open IBC meetings. The committee discussed the option of making the meetings closed. LouAnn will have further discussions with Legal Counsel and will bring a draft policy to the IBC for our November policy meeting.

Biosafety Manual vs. Fact Sheets.

The committee discussed whether the format of a biosafety manual or fact sheets was most appropriate to communicate good biosafety practices. After a lengthy discussion, it was decided to use fact sheets with general information supplemented with an area for lab-specific information. The compilation of these relevant fact sheets will comprise the biosafety plan for each investigator's research program. All fact sheets will be available on the web.

BioWISE

LouAnn Burnett reported that BioWISE is ready to be used as the sole means of registration of projects with the IBC as of September 1, 2004.

Meeting adjourned at 3:25PM

Vanderbilt University
Institutional Biosafety Committee (IBC)

Minutes
September 13, 2004
Room 437 Light Hall
2:00 P.M.

Voting members present: Robert Loedding, James Crowe, Greg Hanley, Linda Sealy, LouAnn Burnett, Valerie Thayer, Jerry Rowland, Cara Sutcliffe, Charles Stratton, Mark Denison, Timothy Cover, and Douglas McMahon. (12)

Non-voting members: Garnet Jack. (1)

Absent: Robert Wheaton, Richard D'Aquila, and Christina Jones. (3)

Meeting called to order at 2:00 P.M.

The minutes of August 13, 2004 were reviewed. The minutes were approved unanimously on a voice vote.

Announcements/Introductions.
LouAnn Burnett informed the committee that the launching of BioWISE was postponed because of an upgrade that could be added to the program for easier use by faculty and staff using the system. The committee members introduced themselves and the department in which they represent. LouAnn Burnett informed the committee about the NIH symposium that would take place on September 22, 2004 7:30am through 12:30pm central time, and the topics to be discussed. The conference room in the Peabody Library would be the meeting place to view the webcast.

Project Review

P.I.: Sanjoy K. Das, Pediatrics.

Title: 1) Environmental Toxins and Gene Expression.
2) Aspects of uterine Cell Cycle Regulation in Implantation.

Sponsor: NIEHS/NICHD/NIH

Summary: The objective of the research projects is to study the relationship between gene specific modulation using gene therapy versus uterine specific proliferation and/or differentiation primarily during stromal cell decidualization or using estrogen hormone treatment. Replication deficient adenovirus containing the genes of interest will be injected into mice via tail vein injection, and transfected into mice uterine stromal cells to analyze there effects on the system.

Comments: concerns centered lack of information on genes being used in the project and whether any of the genes had oncogenic potential.

Motion: Approved, pending clarification of the nature of the genes being used in the project.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Carl Johnson, Biological Science.

Title: Molecular/Genetics Analysis of Biological Clock in Cells

Sponsor: NIMH.

Summary: The objective of this study is to monitor the activity of per-1 promoter in fibroblast cells to evaluate whether this promoter exhibits any daily rhythm of activity. In order to accomplish this goal, lentivirus containing genes for the expression of per-1 construct and luciferase for easy tracking will be generated and transfected into the cell.

Comments: All concerns were adequately answered in application submitted.

Motion: Approved.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Andrzej M. Krezel, Biological Science.

Title Cell Contact and Acidity induced Novel Transcription Regulator in H pylori.

Sponsor: NIH/NCI.

Summary: The objective of the study is to investigate how *H. pylori* alters cell growth and death, and predisposes infected individuals to develop stomach cancer. An altered

strain of the bacteria lacking the gene that expresses the protein HP022 that is associated with adherence to gastric cells will be utilized in this study. Mice will be infected with wild type and mutant strains of H. pylori to elucidate the role of HP0222 in colonization and cancer formation. Stomach of the animals will also be harvested postmortem and analyzed for information leading to the objectives of the study. Because the pattern of colonization in mice is similar to humans, the results may help in identifying pathways in the development of the disease allowing for an effective form of treatment to be developed.

Comments: Concerns centered on whether lab personnel had been informed of the possible risk of infection and the availability of the Occupational Health Clinic (OHC) for counseling.

Motion: Approved.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Kevin Niswender, Medicine.

Title: Lipid and Insulin Activity in the Brain; Role of Obesity.

Sponsor: NIH.

Summary: Obesity is epidemic in the U.S. and world wide. The regulation of body weight is achieved by the hormones insulin and leptin through an endocrine feed back loop. There hormones are secreted into the blood stream in direct proportion to body fat stores. These hormones interact with neurons in the brain that causes a number of physiological processes, including food intake and energy expenditure that ultimately maintain body weight. The specific aims of this proposal is to identify the neurons in which P13K signaling is required, to determine if impaired P13K signaling accounts for insulin and leptin resistance, and to determine if gene therapy approach to increase P13K will prevent diet induced obesity. It is hoped that the findings will lead to the development of molecular targets for drug development.

Comments: Concerns centered on procedures that may generate aerosols and containment procedures to minimize aerosol production.

Motion: Approved.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Anna Spangnoli, Pediatrics Endocrinology.

Title: [redacted]

Sponsor: [redacted]

[redacted]

Comments: Concerns centered on lack of information on lentivirus and type of packaging cell line used in these experiments.

Motion: Defer.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Jordan Berlin, Hematology/Oncology.

Title: [redacted]

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Sponsor: [redacted]

Summary: This Phase III clinical trial [redacted]

Comments: Concerns centered on the logistics of conducting the trial in a patient care area serving immunocompromised patients.

Motion: Approved, pending submission of facility-specific information.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Peter Wright, Pediatric Infectious Diseases.

Title: [redacted]

Sponsor: [redacted].

Summary: This study will evaluated the safety of a vaccine [redacted]

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Kathryn Edwards, Pediatric Infectious Diseases.

Title: [redacted]

Sponsor: [redacted]

Summary In light of the need for improved influenza vaccination strategies for young children, the medical need for influenza prevention in this group, [redacted]

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Approved.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

P.I.: Peter Wright, Pediatric Infectious Diseases.

Title: A Phase I Clinical Trial to Evaluate the Safety of a Multiclade Recombinant Adenoviral Vector HIV-1 Vaccine Administered to Healthy, HIV-1 Uninfected Adult Participants Who Received DNA Plasmid Vaccine or Placebo in the HVTN 052 Clinical Trial

Sponsor: NIH Division of AIDS.

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to evaluate the safety and tolerability of two or three doses of 4.0 mg of an HIV-1 DNA vaccine (from HVTN 052) followed by 1 X 10^{10} viral particle units (vpu) of a recombinant adenoviral vector vaccine boost (VRC- HIVADV014-00-VP).

Comments: All concerns were adequately answered in the proposal submitted.

Motion: Defer.
Total votes: 12
For: 12 **Against:** 0 **Abstain:** 0.

Meeting adjourned at 3:45PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
October 11, 2004
VEHS Training Room
2:00 P.M.

Voting members present: Douglas McMahon, Valerie Thayer, Linda Sealy, LouAnn Burnett, James Crowe, Charles Stratton, Timothy Cover and Richard D'Aquila (8)

Non-voting members: Garnet Jack. (1)

Absent: Robert Wheaton, Christina Jones, Robert Loedding, Greg Hanley, Cara Sutcliffe, Mark Denison and Jerry Rowland (7)

Meeting called to order at 2:05 P.M.

The minutes of September 11th, 2004 were reviewed. Minor changes were noted by Dr. James Crowe. The minutes were approved unanimously on a voice vote.

Project Review

P.I Anna Spangnoli, Department of Pediatrics Endocrinology (Previously deferred)

Title: [redacted]

Sponsor: [redacted]

Summary: [redacted]

Comments: Concerns centered on whether the viral vector used in the study had a self-inactivating LTR region, procedures for minimizing aerosol production, the use of 100% bleach for decontamination and lab personnel awareness of OHC for counseling.

Motion: Approved, BSL2/ABSL2, with clarification of concerns
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0.

P.I Friedrich Schuening, Department of Medicine/Hematology & Oncology

Title: Evaluation of FVIII Encoding HIV-1 Vectors in Dogs.

Sponsor: NIH.

Summary: The purpose of this study is to investigate whether the introduction of human clotting factor VIII utilizing a HIV-1 vector based system in dogs can provide therapeutic levels of FVIII production in the animals. Plasmids containing genes of interest along with the vector system will be utilized to generate transfectants that will be introduced to the dogs intravenously. Blood and organ parts will be collected from the animals and various analytical procedures will be used to identity the level of expression of FVIII in the animals.

Comments: The concern of the committee was whether lab personnel were informed of the availability of OHC for counseling.

Motion Approved BSL2/ABSL2, with language in the approval letter to address the committee's concern.

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I: Paul Spearman, Department of Medicine/Pediatric infectious Diseases

Title: AMENDMENT: A Phase I Dose-Ranging Study of the Safety, Tolerability, and Immunogenicity of the MRKAd5 gag/pol/nef Vaccine (MRKAd5 Hiv-1 gag/pol/nef) in a Prime-Boost Regimen in Healthy Adults.

Sponsor: Merck Research Laboratories

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). This protocol represents the first introduction of a multi-valent prophylactic vaccine by Merck Research Laboratories. This study will investigate the tolerability and immunogenicity of a

trivalent vaccine versus placebo. Equal amounts of MRKAd5 HIV-1 gag, MRKAd5 HIV-1 pol, and MRKAd5 HIV-1 nef will comprise the vaccine.

AMENDMENT: This amendment adds 42 subjects in an additional stage (IVb) of the trial – this stage will include a 2-dose regimen of MRKAD5HIV-1 gag/pol/nef at $3x10^{10}$ vp. Previous doses of $3x10^{10}$ vp have been administered in a 3-dose regimen.

Comments: All concerns were adequately answered in the proposal.

Motion: BSL2

Total: votes: 8

For: 8**Against**: 0 **Abstain**: 0.

P.I: Peter Wright, Department of Medicine/Pediatric infectious Diseases.

Title: A Phase I Study of the Safety and Immunogenicity of Tick-Borne Langat/Dengue 4 Chimera Virus (LGT(TP21)/DEN4), a Live Attenuated Vaccine for Tick-Borne Encephalitis

Sponsor: NIH/NIAID.

Summary: This is a human vaccine trial designed to determine safety and immunogenicity of the LGT(TP21)/DEN4 vaccine.

Comments: Concerns centered on consent form issues, inactivation procedures of investigational pharmacy, site of titration of virus, and verification of BSL2 facility.

Motion: Approved, BSL2 with clarification of committee concerns..

Total: votes: 8

For: 8 **Against**: 0 **Abstain**: 0.

Policies/Education

LouAnn Burnett informed the committee of the final report produced by the Sunshine Project. Based on the Sunshine Project's criteria for transparency, Vanderbilt University was ranked as "Needs improvement-Average". LouAnn Burnett will keep the committee posted on any updates regarding the report.

Meeting adjourned at 3:06PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
November 08, 2004
VEHS Training Room
2:00 P.M.

Voting members present: Douglas McMahon, LouAnn Burnett, James Crowe, Timothy Cover, Robert Loedding, Greg Hanley, Cara Sutcliffe, Mark Denison, and Jerry Rowland (9)

Non-voting members: Garnet Jack, Robert Wheaton. (2)

Absent: Charles Stratton, Valerie Thayer, Linda Sealy, Christina Jones and Richard D'Aquila (5)

Guest: Carl Gerhold.

Meeting called to order at 2:12 P.M.

The minutes of September 11th 2004 were reviewed. No corrections were noted. The minutes were approved unanimously on a voice vote.

Announcements

LouAnn Burnett informed the committee that Christina Jones will no longer be working at Vanderbilt University but may be contracted to continue serving on the IBC.

Project Review

P.I Agnes Fogo, Department of Pathology

Title: Resolution of Glomerulosclerosis

Sponsor: NIH

Summary: The objective of this study is to determine whether angiopoetin-1 and angiopoetin-2 has any effect on vasculogenesis in the regression of glomerulosclerosis. Adenovirus containing genes that express angiopoetin-1 and angiopoetin-2 will be

injected (i.v.) into mice. The upregulation of the proteins will be analyzed to identify their effects on vasculogenesis that should have a positive effect on glomerulosclerosis.

Comments: Concerns centered on whether the investigator had relevant information on the viral deletions to render the virus replication deficient and the transfer of virus between laboratory within the university

Motion: Approved, BSL2/ABSL2, with clarification of concerns
Total votes: 9
For: 9 **Against**: 0 **Abstain**: 0.

P.I Michael L. Freeman, Department of Radiation Oncology

Title: Repression of ARC-Mediated Gene Expression.

Sponsor: pending

Summary: Radiation therapy is a major modality used in the treatment of cancer. However, up to 20% of patients irradiated in the chest or neck develop radiation induced pneumonitis and fibrosis. The objective of this study is to determine whether over-expression of TGF-β1 in the lungs of mice can have a negative effect similar to irradiation causing induced pneumonitis and fibrosis. Replication deficient adenovirus expressing the gene for TGF-β1 will be administered to mice intranasally at a concentration of 5×10^8 PFU. Mice will be sacrificed at 3,6,24, 72, and 96 hrs, lungs will be analyzed for the presence of tumor induced pneumonitis and fibrosis. It is hoped that study findings will help reduce the incidence of radiation damage to the lungs of cancer patients.

Comments: The concerns of the committee were whether the investigator had informed the collaborative institution IBC of transfer of research material to its Facility for this project and whether lab personnel had completed training in shipping infectious substances and diagnostic specimen.

Motion Approved BSL2/ABSL2, with language in the approval letter to address the committee's concerns on transfer of research material and shipping guidelines.

Total votes: 9
For: 9**Against**: 0 **Abstain**: 0

P.I: Pampee P. Young, Department of Pathology

Title: EPC's in Vasculogenesis.

Sponsor: Vanderbilt Departmental Grant.

Summary: The objective of this study is to determine whether VEGF and VEGF receptor 1 interaction in progenitor cells (EPC's) plays a role in chemotaxis to PIGF and VEGF. EPC's will be produced that express a higher level of VEGF receptor 1 to study their effect on migration and proliferation *in vitro*.

Comments: All concerns were adequately answered in the proposal.

Motion: BSL2

Total: votes: 9

For: 9 **Against**: 0 **Abstain**: 0.

Policies/Education

Bob Wheaton addressed the committee on the Environmental Health & Safety Management System policy that is being adopted throughout the university in response to the EPA statement on 'Aiming for Excellence' to encourage institutions to improve compliance, pollution prevention and other measures of environmental performance. The commitment statement and the guiding principles developed by the institution were reviewed along with a chart identifying responsible parties for each area of concern within the university.

LouAnn Burnett informed the committee that there was still some work being done to refine the use of BioWISE and should be completed for possible launching in January 2005.

Meeting adjourned at 3:37PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
December 13, 2004
Conference Call
2:00 P.M.

Voting members present: Douglas McMahon, LouAnn Burnett, James Crowe, Timothy Cover, Greg Hanley, Cara Sutcliffe, Mark Denison, Valerie Thayer, Linda Sealy, and Jerry Rowland (10)

Non-voting members: Garnet Jack (1)

Absent: Robert Loedding, Charles Stratton, and Richard D'Aquila (5)

Meeting called to order at 2:12 P.M.

The Conference Call began at 2:00pm with an introduction of IBC members present and recorded by LouAnn Burnett and Garnet Jack. James Crowe Began the review of the protocol at 2:05pm.

Announcements
No announcements made.

Project Review

P.I Peter Mohler, Department of Pathology

Title: Role of Ankyrin-G in Voltage-Gated Na Channel 1.5 (Na V1.5) Targeting to Excitable Membrane in Heart

Sponsor: American Heart Association

Summary: The rhythmic beating of the heart requires the influx and outflux of small charged molecules across the membrane of specialized cells of the heart called cardiomyocytes. This movement is facilitated by small pores in the membrane known as ion channels or transporters. The inability of mislocalization of these ion channels may lead to abnormal function or arrhythmia and even death. Ankyrin is the protein produced by the cardiomyocytes that are responsible for the delivery and stability of the ion channels. The goal of this project is to identify the mechanism involved in the targeting

and stability of the ion channels and transporters in cultures cells. To accomplish this goal, replication deficient lentivirus containing wild type and mutant sodium channel cDNA will be introduced into cultured cardiomyocytes. Protein production along with channel formation and stability will be studied.

Comments: All concerns were adequately answered in the proposal.

Motion: Approved, BSL2 **(Voice Vote)**
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

Meeting adjourned at 2:15PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
January 24, 2005
VEHS Training Room
2:00 P.M.

Voting members present: Douglas McMahon, LouAnn Burnett, James Crowe, Charles Stratton, Valerie Thayer, Linda Sealy, Greg Hanley and Mark Denison (8)

Non-voting members: Garnet Jack, Robert Wheaton. (2)

Absent: Cara Sutcliffe, Jerry Rowland, Timothy Cover, Robert Loedding and Richard D'Aquila (5)

Meeting called to order at 2:10 P.M.

The minutes of November 08th 2004 and December 13th 2004 were reviewed. No corrections were noted. The committee requested that a method for tracking follow-up issues be amended to the minutes for each meeting. LouAnn Burnett agreed to implement this by the march 2005 meeting minutes. The minutes were approved unanimously on a voice vote.

Announcements
No Announcements

Project Review

P.I Vivien Casagrende, Cell and Developmental Biology

Title: Visual System Organization and Development

Sponsor: NIH

Summary: The purpose of this research study is to investigate how visual information is conveyed from the lateral geniculate nucleus (LGN) through three distinct parallel pathways, the large cell (M), the small cell (P) and the very small cell (k) to the visual cortex (V1) and whether these signals are combined or utilized independently to generate output to the retina allowing us to see. In order to trace these pathways, a generated replication deficient SAD-B19 rabies virus conjugated with a green fluorescent protein

marker will be utilized allowing for the labeling of the cells needed to study. Special emphasis will be placed on the K pathway because less in known about its function.

Comments: Concerns centered on whether the investigator and staff needed to be vaccinated for proposed work and ensuring that deficiencies noted be addressed. After the committee discussion, it was agreed that mandatory vaccination would not be necessary and if needed, vaccination will be at the cost of the investigator. Also, it was noted that the laboratory deficiencies be corrected before an approval letter is released.

Motion: Approved, BSL2/ABSL2, with recommendation noted in the comments.
Total votes: 8
For: 8**Against**: 0 **Abstain**: 0.

P.I Luc Van Kaer, Microbiology and Immunology

Title: Functional Genomics of inflammation: Project 3: T-Lymphocyte-Based Functional Genomics of Inflammation (1)

Sponsor: NIH

Summary The objective of this study is to identify genes that are important for the activation of an inflammatory response to infection. This study centers on the T-lymphocyte and its contribution to the inflammatory response. To accomplish the goals of this project, genetically modified mice lacking different components of the inflammation process will be generated. These mice will be infected with influenza virus, lymphocytic choriomeningitis virus and *Listeria monocytogenes* bacteria. Animals will be observed for signs and symptoms caused by these organisms, following which the animals will be sacrificed and samples analyzed to gain a better understanding of the mechanisms involved so that better indicators can be developed to aid in combating these infections.

Comments: The concerns of the committee were whether the investigator had a surveillance plan for identifying and dealing with respiratory illness and G.I. illness, how infectious are animals infected with HIN/A/PR/8/34 to humans, are agents being used one at a time, whether all work with LCV be conducted in the animal BSL3 facility for aerosol containment, and whether there was an appropriate counseling plan in place for staff. All laboratory deficiencies must be corrected before an approval letter is released.

Motion Approved BSL2/ABSL2, with concerns to be addressed with P.I.

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I Luc Van Kaer, Microbiology and Immunology

Title: Functional Genomics of inflammation: Project 3: T-Lymphocyte-Based Functional Genomics of Inflammation (2)

Sponsor: NIH

Summary The objective of this study is to identify genes that are important for the activation of an inflammatory response to infection. This study centers on the T-lymphocyte and its contribution to the inflammatory response. To accomplish the goals of this project, genetically modified mice lacking different components of the inflammation process will be generated. Cells will be isolated form these animals and challenged with vaccinia virus constructs containing full length and mini genes of ovalbumin and influenza virus nucleoprotein. This study will directly correlate with protocol 1 involving the use of the genetically modified mice. All laboratory deficiencies must be corrected before an approval letter is released.

Comments: All concerns were adequately answered in submitted protocol.

Motion Approved BSL2.

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I: Sergio Fazio/Yan Ru Su, Medicine and Pathology

Title: Macrophage Expression of apoA-1 and Atherosclerosis

Sponsor: NIH/NHLBI

Summary: Atherosclerosis is the build up of fatty deposits in the artery walls. It is the common cause of heart attacks and strokes and the leading cause of death in the United States. A well known risk factor for coronary heart disease (CHD) are elevated levels of low-density lipoprotein (LDL) which deposits as fatty plaques in the arteries and low levels of high-density lipoprotein (HDL) which acts as a transporter in removing cholesterol to the liver. Interventions against atherosclerosis attempts to prevent plaque formation in the blood vessels or to shrink and stabilize the already formed plaque. To this end, the goals of this research project focuses on developing a new cell-based treatment to deliver high-density lipoprotein in the vessel wall through progenitor cells. To accomplish this goal progenitor cells will be harvested form mice grown and transfected with replication deficient lentivirus that expresses the gene for apolipoprotein A-1 which is the major component of HDL. Following this, the cells will be reintroduced to the animals through retro-orbital venus plexus injection and their effects studied.

Comments: All concerns were adequately answered in the proposal.

Motion: BSL2/ABSL2

Total: votes: 8

For: 8 **Against**: 0 **Abstain**: 0.

P.I: Mark Anderson, Cardiology and Clinical Medicine

Title: Calmodulin Kinase II and Early Afterdepolarizations

Sponsor: NIH

Summary: The L-type calcium channel (LTCC) plays a critical role during the cardiac action potential and during cardiac cell contraction. Understanding the regulation of LTCC is important to human health because LTCC drives contraction, triggers arrhythmia-initiating early depolarization and active calcium dependant transcription pathways Protein Kinase A (PKA) phosphorylates serine 1928 on the LTCC C-terminus to enhance the calcium current. Data has shown that the multifunctional calcium and calmodulin dependant protein kinase II (CaMKII) also increases calcium and both CaMKII and PKA increase calcium by inducing LTCC in a high activity gating mode. Because of this finding the aims of this study are designed to (1) determine the molecular basis and cellular consequences of TLCC regulation by CaMKII, (2) identify the critical CaMKII phosphorylation binding site on TLCC and test the functional consequences of CaMKII phosporylation of TLCC, and (3) to measure the effects of β-adrenergic stimulation when TLCC is functionally unresponsive to CaMKII. To accomplish these goals, primary cultured cardiomyocytes from mice and rats will be grown and transfected with replication deficient lentivirus containing genes of interest to elucidate the goals of this project.

Comments: The concern of the committee was whether the P.I. knew if the LTR was deleted or not based on his description of the packaging plasmid

Motion: BSL2/ABSL2 with clarification of plasmid safety features.

Total: votes: 8

For: 8 **Against**: 0 **Abstain**: 0.

Meeting adjourned at 3:20PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
February 14, 2005
412 Light Hall
2:00 P.M.

Voting members present: Douglas McMahon, LouAnn Burnett, Charles Stratton, Valerie Thayer, Greg Hanley, Cara Sutcliffe, Jerry Rowland, Robert Loedding, Richard D'Aquila and Mark Denison (10)

Non-voting members: Garnet Jack. (1)

Absent: James Crowe, Timothy Cover, Robert Wheaton, and Linda Sealy (4)

Meeting called to order at 2:05 P.M.

The minutes of January 10th 2005was reviewed. Noted was the incorrect month and location listed on the minutes. The minutes were approved unanimously on a voice vote.

Announcements

LouAnn Burnett informed the committee that Dr. James Crowe would not be present at the meeting and that Dr. Charles Stratton would preside as acting Chair in the absence of Dr. Crowe. Dr. Mark Denison introduced his assistant Sadie Coberley who will be assisting him in the establishing and overseeing the daily operations of his BSL3 laboratory under construction.

Project Review

P.I Susan Kasper, Urologic Surgery

Title: Stathmin: A 'Relay Protein' in the Development of Prostate Cancer and a Potential Target for Anti-Cancer Therapy.

Sponsor: DOD

Summary: There are many factors that are involved in the promotion of prostate cancer growth, invasion and metastasis. Thus far, the understanding of how this occurs is limited. The lab has identified a protein called ststmin in human prostate cancer biopsy and in the LPB mouse model for prostate cancer. Clinical studies comparing androgen-

dependant and androgen independent prostate samples have identified increased levels of stathmin. Because of this finding, our research objective aims to answer the following questions: How do the levels of stathmin expression regulate prostate cancer development? Which signaling pathway is activated through stathmin, and can stathmin be blocked by taxol or erbitux anticancer treatment. To accomplish these goals, pLenti/V5 lentiviral vector will be used to generate cell lines that express this protein along with mouse models to investigate our specific aims.

Comments: The committee recommended that the Occupational Health Statement be included in the approval letter. All other concerns were adequately addressed in the submitted protocol.

Motion: Approved, BSL2/ABSL2
Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0.

P.I Earle Burgess, Medicine/Hematology and Oncology

Title: Regulation of p63 in Prostate Epithelium

Sponsor: DOD

Summary This project aims to identify proteins that interact with p63 in prostate epithelial cells. Various human prostate immortalized and malignant cell lines will be generated. These cells will be harvested and lysed to isolate p63. The Isolate will be tagged for easy tracking and identification. This will be introduced into established cell lines through the use of plasmids, lentivirus and retrovirus transfection. Associated proteins will be isolated and identified.

Comments: The committee recommended that the Occupational Health Statement be included in the approval letter. All other concerns were adequately addressed in the submitted protocol.

Motion Approved BSL2

Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0

P.I George Hill, Microbiology and Immunology

Title: Characterization of a New Class of Compounds that Inhibit the Trypanosome Alternative Oxidase.

Sponsor: Vanderbilt University

Summary Sleeping sickness is a fatal disease caused by unicellular parasites known as trypanosomes. Transmission to man and animals is through bites of the tsetse fly. The parasite adapts to the host environment and is able to evade the immune response and very few drugs are able to treat the infections. The life cycle is very complex and alternates between the salivary glands of the fly and the blood and lymph fluid of mammals. In mammals the parasite respiration is completely dependant on an enzyme not found in mammals known as trypanosome alternative oxidase (TAO). Thus, the goal of this project is to test the effectiveness of new drugs developed to act specifically on this enzyme in model systems using mice and rats. Parasites will be grown and mitochondria isolated for the testing of the effectiveness of the drugs on the enzyme. Mice and rats will be infected with the parasite for testing of the drugs in animals. It is hoped that these experiment will yield valuable information for the effective treatment of this disease.

Comments: Concerns centered on whether the infected animals would be housed separately and whether infected males would be housed in single cages. The investigator will be asked to address these questions and to provide supporting documentation indicating that the agent is not prohibited or restricted by law or by the U.S. Department of Agriculture regulations or administrative policies before the release of the approval letter.

Motion Approved BSL2/ABSL2

Total votes: 10
For: 10 **Against**: 0 **Abstain**: 0

Policies/Education

LouAnn Burnett discussed the incident that occurred at Boston University and the implication that it may present to the boisafety community, along with challenges in practices and procedures that the IBC may be faced to confront in the future.

LouAnn Burnett discussed with the committee the issue of establishing a policy for transfer of biological material to and from Vanderbilt University. After some discussion is was agreed that a subcommittee be established to address the issues associated the transfer agreement. Subcommittee members will include Rich D'Aquila, Chuck Stratton, and LouAnn Burnett. LouAnn will contact Legal Counsel for a clarification of the scope of the policy that was recommended prior to convening the subcommittee.

LouAnn Burnett revisited the Office of Biotechnology Activities workshop presentation on Safety Considerations in Recombinant DNA Research with Pathogenic Virus. Dr. Deborah Wilson's presentation, *Update on the Revision to the Influenza Section of Biosafety in Microbiological and Biomedical Laboratories (4th ed.)*, was reviewed and comments mentioned by the committee with regards to the importance for Vanderbilt University.

Meeting adjourned at 3:30PM

IBC Meeting Follow-Up List

Date	Investigator	Follow-up needed	Responsible party	Resolution	Date Resolved
1/9/05	V. Casagrande	Installation of eyewash, Biohazard labels on equipment, First aid kit	P.I.	Deficiencies corrected	2/18/05
1/9/05	L. Van Kaer	No lab coats, Recapping of needles, Biohazard labels on equipment	P.I.	Deficiencies corrected	2/14/05
1/9/05	S. Fazio	Non functional biosafety cabinet, Open doors while working, Recapping needles, Biohazard labels on equipment,	P.I.	Deficiencies corrected	2/15/05
2/14/05	G. Hill	First aid kit, Biohazard labels on equipment Animal housing issue, CDC restriction on organism	P.I.	Animal housing and parasite restriction issues have been resolved. All other deficiencies have been corrected	2/23/05

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
March 14, 2005
412 Light Hall
2:00 P.M.

Voting members present: Douglas McMahon, LouAnn Burnett, Charles Stratton, Timothy Cover, Linda Sealy, Cara Sutcliffe, and Jerry Rowland. (7)

Non-voting members: Garnet Jack and Menah Pratt. (2)

Absent: James Crowe, Robert Loedding, Richard D'Aquila, Mark Denison Valerie Thayer, Greg Hanley, and Robert Wheaton, (7)

Meeting called to order at 2:13 P.M.

The minutes of February 14th 2005 was reviewed. No changes were noted. The minutes were approved unanimously on a voice vote.

Announcements

Although Dr. Crowe could not attend the meeting, he did send in his vote sheets for the protocols reviewed along with corresponding questions and comments.

LouAnn Burnett introduced Menah Pratt, University Compliance Officer and informed the committee that she will be fulfilling the advisory role of Christina Jones who is no longer at Vanderbilt.

LouAnn Burnett indicated to the committee that for the May 9th 2005 IBC meeting she would like for the committee for the first part of the meeting to take a field trip to Mark Denison's newly constructed BSL3 lab so that committee members can become familiar with the operations of this lab.

Project Review

P.I Timothy Blackwell, Medicine

Title: Molecular Regulation of Lung Inflammation by NF-kB.

Sponsor: NIH

Summary: The objective of this study is to understand the molecular mechanisms that lead to lung inflammation and injury. This investigation is important is important because lung injury and inflammation lead to increased disease and death in a verity of human diseases, including bacterial pneumonia, chronic bronchitis, cystic fibrosis, and the adult respiratory distress syndrome. To accomplish this goal, mouse will be exposed to *Pseudomonas aeruginosa.* Specific cell types will be examined to identify molecules that regulate the development of lung inflammation. It is hoped that a better understanding of the process that regulates these events in the lungs will hopefully lead to better ways to prevent injury to the lung while maintaining the ability to fight inflammation.

Comments: Concerns centered on a lack of information about the organism not presented to the research staff. All other concerns were adequately answered.

Motion: Approved, BSL2/ABSL2 with statement in approval letter addressing information about the organism and the dissemination of this information to the research staff.
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0.

P.I Jeff Franklin, Cell and Developmental Biology

Title: The Epithelial Regulatory Potential of Genes Associated with both Colon Embryonic Development and Colon Cancer.

Sponsor: NCI

Summary The overall purpose of this experiment is to access the potential role of colon cancer genes to determine how they function in abnormal colon cancer cell growth. To accomplish the goals of the project, genes that may play a role in tumor suppression or tumor promotion will be transfected into embryonic intestine to analyze expression changes at different developmental stages in the colon. In addition, this step will be performed in clonogenic primary stem cells to generate expression profiles. Further studies are geared to test the role of these genes in controlling cell growth and differentiation in tissue culture and explant cultures. 213 human genes will be analyzed for function in this part of the study.

Comments: All concerns were adequately answered in the protocol submitted.

Motion Approved BSL2/ABSL1`
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I John Pope, Urologic Surgery/Pediatrics

Title: Mechanisms of Bladder Fibrosis.

Sponsor: NIH

Summary The study will focus on how to prevent scaring (fibrosis) of the bladder by preventing blockage of the flow of urine through the urethra. The renin angiotensin system (RAS) is predominantly involved in blood pressure control as well as one of the mediators of tissue fibrotic response. RAS causes an up regulation of transforming growth factor beta (TGF-beta) which has been shown in previous experiments to be involved in tissue scaring. Dr. Pope plans to use lentivirus systems (LZRS/PHNX and pLENTI-system) to over express TGF-beta in rats and mice cells, following which these cells will be implanted into the renal capsule of the animals to observe the effects of the genes of interest.

Comments All concerns were adequately answered in the protocol submitted.

Motion Approved BSL2/ABSL2

Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

P.I Peter Wright, Pediatrics

Title: A Phase I Dose-Escalation Clinical Trial to Evaluate the Safety and Immunogenicity of a Multiclade, Multivalent Recombinant Adenoviral Vector HIV-1 Vaccine Administered to Healthy, HIV-1 Uninfected Adult Participants Who Have Low Titers of pre-existing Ad5 neutralizing antibodies (HVTN 054)

Sponsor: NIH

Summary This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to evaluate the safety and tolerability of a single dose delivered at each of two escalating dose (10^{10} and 10^{11} PU) of a recombinant adenoviral vector vaccine (VRC-HIVADV014-00-VP).

Limited data suggest that pre-existing immunity to adenovirus type 5 (Ad5) may attenuate the immune response to an Ad5 vector vaccine. Although such attenuation may exist in mice, little clinical data are available on the correlation between antibody titer and the magnitude of vaccine response.

Comments All concerns were adequately answered in the protocol submitted.

Motion Approved BSL2
Total votes: 8
For: 8 **Against**: 0 **Abstain**: 0

Meeting adjourned at 3:43PM

Vanderbilt University Institutional Biosafety Committee

IBC Minutes
April 25, 2005
Conference Call
2:00 P.M.

Voting members present: Charles Stratton, LouAnn Burnett, James Crowe, Timothy Cover, Cara Sutcliffe, Valerie Thayer, Linda Sealy, Jerry Rowland and Richard D'Aquila (9)

Non-voting members: Garnet Jack (1)

Absent: Douglas McMahon, Greg Hanley, Mark Denison, Menah Pratt, Robert Wheaton, and Robert Loedding, (6)

Meeting called to order at 2:00 P.M.

The Conference Call began at 2:05pm with an introduction of IBC members present and recorded by LouAnn Burnett and Garnet Jack. James Crowe made an introduction of the protocols for review with Linda Sealy reviewing the first protocol and James Crowe reviewing the second protocol.

Project Review

P.I Douglas McMahon, Biological Science

Title: Molecular Physiology of Circadian Pacemaking

Sponsor: NIH/NIMH.

Summary: The specific aim of this proposal is to understand the mechanisms involved in the control of rhythmic daily expression of circadian clock genes in the brain and other tissues. The daily biological clock is controlled by the transcription/translation autoregulatory network of clock genes and this forms the molecular basis for the biological clock. The experimental goal is to perform real time gene expression imaging with the use of replication deficient lentivirus that contains the construct *Period1* (a clock gene) along with green fluorescent protein (GFP) as a marker for *Period1* activity in cell lines and primary tissue cultures. The use of lentivirus in this procedure is favored

because of the difficulty experienced using traditional transfecting methods into the cell lines and the animal tissues used.

Comments: All concerns were adequately answered in the proposal.

Motion: Approved, BSL2 **(Voice Vote)**
Total votes: 9
For: 8 **Against**: 0 **Abstain**: 1.

P.I Paul Spearman, Pediatric Infectious Disease

Title: A Phase 1 Dose Ranging Study of the Safety, Tolerability, and Immunogenicity of a 3 Dose Regimen of the MRKAd5 HIV-1 Trigene and the MRKAd6 HIV-1 Trigene Vaccines Alone and in Combination in healthy Adults.

Sponsor: Merck

Summary: This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to establish safety and tolerability of a 3-dose regimen of 2 different dosing levels ($1X10^9$ viral particles and $1X10^{10}$ viral particles) of MRKAd5+6-HIV-1 trigene vaccine and to evaluate immunogenicity of the same regimen. These product have not been used in human subjects previously

Comments: All concerns were adequately answered in the proposal along with recommendations made by the HGTAG.

Motion: Approved, BSL2 **(Voice Vote)**
Total votes: 9
For: 9 **Against**: 0 **Abstain**: 0.

Announcements/Other Items

LouAnn Burnett explained to the committee about the Emergency Response to Situations Involving Biological Materials and what we were trying to accomplishing by having such a plan available to research staff. LouAnn Burnett requested that the committee members review the Draft and forward any comments to Garnet Jack for modification of the draft if necessary. LouAnn Burnett informed the committee about the upcoming May IBC meeting which will be conducted in room S-3407 Medical Center North (MCN) and about the proposed laboratory walk-through of Dr Mark Denison's BSL3 laboratory. It was indicated that Dr. Denison is scheduled to make a presentation prior to the walk-through.

Meeting adjourned at 2:28PM

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

Monday, June 13, 2005

2 TO 3PM
407 A/B LIGHT HALL
VANDERBILT UNIVERSITY

ATTENDEES:
Voting members present:, LouAnn Burnett, James Crowe, Timothy Cover, Mark Denison, Robert Loedding, Charles Stratton, Cara Sutcliffe, and Richard D'Aquila, (8)
Non-voting members:
Absent: Douglas McMahon, Greg Hanley, Menah Pratt, Valerie Thayer, Linda Sealy, Robert Wheaton, and Jerry Rowland (7)
Meeting called to order at 2:00 P.M.

- CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS
- PROTOCOL REVIEWS
  - **Heidi Hamm, Department of Pharmacology**
    - ***Protein Production Utilizing Lentivirus***

Granting Agency: Vanderbilt University Developmental Grant
Grant Period: 2005 - 2006

Brief Description	The goal of this project is to utilize replication deficient lentivirus containing genes of interest for the transfection of human embryonic kidney cells (HEK293) for the over expression of desired proteins. Crystallography studies will be conducted to identify the physical structure of the proteins in question.
Hosts	Prokaryotic: None Human: HEK293, (Dr Tina Inverson, Vanderbilt University) Other eukaryotic: None
Vectors	Plasmid: pMD.G, pCMV-vprRTIN, pCMV-gag-pro, pCMVLV, pTet-O-LV (Dr. [redacted]ohn Kappes, UAB) Viral: Self inactivating replication deficient lentivirus (Kappes, UAB)
D/RNA	Human: - adenosine receptors 1and 2, muscarinic receptors 1and 4; Cow: - synthetic rhodopsin; Norway Rat: - glucogon-like peptide 1.
Infectious Substances	None
Animals	None
Reason for Review	Creation of recombinant DNA constructs; Use of human materials; Use or Replication deficient lentivirus
Recommended BSL	BSL2

Walk-through	Conducted on 3/20/2003 Deficiencies noted:- open doors, non functional eye wash, no lab coats, biohazard labels recapping needles, no first aid kit, and no emergency plan All deficiencies were corrected on subsequent revisit on 4/25/03
IBC Action	Deferred on June 13, 2005 for more information on the packaging system for the lentivirus. See attached email from Jim Crowe to Heidi Hamm.
PI Response	Dr. Hamm has submitted a revised application (attached) indicating that they will produce their vector using the Invitrogen ViraPower Bsd Lentiviral Support Kit. The lentiviral vector will remain the same, but the packaging system will change
Revised Recommendation	BSL2
IBC Discussion	Deferred on June 13, 2005 for more information on the packaging system for the lentivirus.
IBC Vote	Deferred to July IBC meeting

- **Chuan-Ming Hao, Department of Medicine/Nephrology**
  - ***Renal Medullary COX2 in Blood Pressure Regulation***

Granting Agency: NIH.
Grant Period: 2005 - 2010

Brief Description	The specific aim of this experiment is to understand the mechanism by which COX2 is regulated by high salt intake and the process by which it regulates the physiological mechanism of maintaining body fluid homeostasis and normal blood pressure. In order to accomplish this goal, transgenic mice will be generated lacking the COX2 or modified so that the Cre enzyme renders it ineffective. A replication deficient adenovirus will be used carrying the gene for the expression of Cre enzyme which will be infused in the kidney. The hope is that the results will aid in the development of new therapies that will target novel pathways of this system.
Hosts	Prokaryotic: None Human: HEK293 (ATCC) Other eukaryotic: None
Vectors	Plasmid: None Viral: AdCre Replication Deficient Adenovirus (E1 Deletion) **(Gene Transfer Vector Core, the University of Iowa)**
D/RNA	**The gene that encodes a protein called Cre-recombinase. This protein mediates site-specific recombination between 34 bp sequences present in P1 bacteriophage referred as loxP, which stand for Locus of crossover (x) in P1.**
Infectious Substances	None
Animals	Mice. (Recombinant replication deficient adenovirus will be infused into renal medulla to assess the effects COX2 and blood pressure regulation)
Reason for Review	Creation of recombinant DNA constructs; insertion of constructs into whole animals, Use or Replication deficient adenovirus
Recommended BSL	BSL2/ABSL2, **plus use of a face shield (not just protective eyewear) during manipulation of adenovirus outside of the Biosafety Cabinet; use of a Biosafety Cabinet during administration of adenovirus to animals;**
Walk-through	To be set up. Bench work at VA; animal work at VU

IBC Discussion	Face shield must be worn during manipulation of adenovirus outside of the Biosafety Cabinet. Biosafety cabinet must be used during administration of adenovirus to animals.
IBC Vote	For: 8; Against: 0

- **Jacek Hawiger**
  - ***Intracellular Anthrax Toxin Traps and Signaling Inhibitors***

Granting Agency: Departmental Discovery Fund
Grant Period:

Brief Description	Experiments described in this proposal will employ subcutaneous infection of mice with spore preparations of *Bacillus anthracis* strain Sterne, an attenuated vaccine strain lacking the pXO2 virulence plasmid (non-select agent), to induce an inflammatory response. Mice will be treated with cell-penetrating peptides or proteins to assess their ability to attenuate the effects of *B. anthracis* infection. In addition to monitoring clinical signs, we will collect blood at intervals and harvest organs upon euthanasia to measure cytokine and chemokine production, apoptosis in tissues, and other biochemical markers of inflammation.
Hosts	Prokaryotic: Eukaryotic: Human:
Vectors	Plasmid: Viral:
D/RNA	
Infectious Substances	***Bacillus anthracis* strain Sterne (see description in application)**
Animals	Mice will be injected subcutaneously with spores from *B. anthracis* strain Sterne
Reason for Review	Use of human and animal pathogen
Recommended BSL	BSL2/ABSL2
IBC Discussion	Approval recommended with following stipulations: Confirmation/verification of Stern strain derivation
IBC Vote	For: 8; Against: 0

- **H. Earl Ruley, Department of Microbiology and Immunology**
  - ***Development and Use of Retrovirus Gene Trap Vectors***

Granting Agency: DOD
Grant Period: Not provided

Brief Description	The mammalian genome projects provide the DNA sequences of nearly all genes, but the functions of most genes are unknown. We use gene trap retrovirus vectors to disrupt cellular genes in order to infer their function based on the behavior of cells and animals lacking the genes. The gene trap vector carries an antibiotic resistance gene that is expressed only when the virus inserts into a cellular gene. Thus, after exposure to the entrapment vector, the progeny of individual cells that survive in media containing the antibiotic contain a single cellular gene that has been disrupted by the gene trap vector. Some versions of the vector contain β-galactosidase or green fluorescent protein genes that provide a simple way to monitor the expression of the disrupted cellular gene. Some projects use the vectors to identify genes that, when disrupted, give rise to altered cells that can be selected from cell populations. For example, disruption of genes required for sensitivity to tamoxifen (a drug used to treat breast cancer) will produce cells that survive in the presence of the drug. The identification of genes disrupted in tamoxifen resistant cells is an important problem since the same genes may also be responsible for the development of resistant tumors in patients treated with tamoxifen. In other projects, the vector is used to disrupt genes in mouse embryonic stem cells and the mutations are characterized by sequencing segments of DNA next to the vector. The stem cells are then used to make mice containing mutations in genes of interest. We are particularly interested in genes that may be important in inflammation and cancer.
Hosts	Prokaryotic: *E.coli* DH5α Human: MCF7 human breast cancer cells. Other Eukaryotic: Phoenix Eco and Phoenix Ampho retrovirus packaging cells lines. Target cells include mouse embryonic stem cells, mouse NIH3T3 cells
Vectors	Plasmid: pBluescript Viral: Derived from pBabe or similar replication-deficient Moloney Murine Leukemia Viruses (MLV).
D/RNA	**The vectors contain segments of a number of genes: (1) Promoters—mouse phosphoglycerol kinase, human RNA polymerase II, herpes Simplex Virus thymidine kinase; (2) reporter genes—*E. coli LacZ* firefly green fluorescent protein (3) selectable marker genes—HSV thymidine kinase; (4) other sequences—RNA destabilization sequence from human GM-CSF, splice acceptor site (intron2/exon3) from the human *Bc12* gene, splice donor site (exon8/intron8) from the mouse *Hprt* gene; ECMV internal ribosome entry site, polyadenylation signal from bovine growth hormone gene and recombinant sequences for the Cre DNA site-specific recombinase.**
Infectious Substances	Replication defective vector based on Moloney Leukemia Virus.
Animals	Mice. Animals will not be directly exposed to recombinant DNA constructs or infectious agents. However, embryonic stem cells containing stably integrated gene trap vectors will be used to make chimeric mice and the offspring of the mice may inherit genes disrupted by the entrapment vector.

Reason for Review	Creation of recombinant DNA constructs. Use of retroviral vectors. Use of human materials.
Recommended BSL	BSL2/ABSL1
Walkthrough	
IBC Discussion	Approval recommended with following stipulations: Quarterly checks for competent virus
IBC Vote	For: 8; Against: 0

- **Peter Wright, Medicine/Pediatric Infectious Disease**
  - ***Phase I Study of the Safety and Immunogenicity of West Nile/Dengue-4 3'Δ30 Chimeric Virus Vaccine (WN/DEN4-3'Δ30), a Live Attenuated Vaccine for West Nile Encephalitis***

Sponsor: NIH NIAID

Brief Description	**This is a human vaccine trial designed to determine safety and immunogenicity of the WN/DEN-43´Δ30 chimeric vaccine virus by:** **☐ Determining the frequency and severity of vaccine related AEs for each dose graded by severity.** **☐ Determine the amount of WN neutralizing antibody induced by the vaccine at study day 42 (these studies will be performed at the CIR laboratories using the WN/DEN4-3´Δ30 virus as the antigen in the neutralization assay.)**
Hosts	**56 (2 groups of 28) healthy male and non-pregnant female volunteers 18 to 50 years of age with no history of dengue or West Nile virus infection**
Vaccine	**West Nile (ME)/DEN4-3´Δ30 (referred to as WN/DEN4-3´Δ30)is a live virus vaccine produced using recombinant DNA technology. The preM and E proteins of the live attenuated DEN-4 vaccine candidate rDEN4Δ30 have been replaced by those of the wild-type West Nile virus NY99-35262. The C protein and all non-structural proteins are those of the rDEN4Δ30 vaccine virus. The vaccine virus is supplied in flame-sealed 2 mL cryules containing 0.5 mL of vaccine virus at a titer of approximately 3.1 x 105 PFU/mL.** **The WN/DEN4-3´Δ30 virus vaccine candidate will be administered subcutaneously in a placebo controlled study at a dose of 103 or 105 PFU to a group of 28 volunteers in each dose cohort, in an outpatient setting. The use of an outpatient protocol is appropriate since viremia was not detectable in rhesus monkeys and since the WN/DEN4-3´Δ30 chimera was poorly infectious for both *Aedes aegypti* and *Culex* mosquitoes.** **The level of viremia and immunogenicity in the volunteers will be determined. Serum samples will be tested for antibodies to West Nile virus (a BSL3 virus) at the BSL3 laboratory in [redacted] at NIH (only non-coded specimens will be assayed). The longevity of the response will be assessed by an examination of the level of antibody at six months after infection.** **Subjects will be asked to record their temperature three times each day for study days 0 to 19.** **After vaccine is received, a sample will be tested for titer and stability per SOP by the Investigational Drug Pharmacy. The Investigational Drug Pharmacy will also prepare the proper dose.** **There is no anticipated release of vaccine from the subjects after administration.**
Reason for Review	**Use of attenuated microorganisms for vaccination.**
HGTAG Review	**This is a study representing a grey area in gene transfer. There is no expression system being administered but the product was genetically modified. At this time, HGTAG has not been asked to provide consultation.**

Recommended BSL/Precautions	**Vaccine Handling and Administration: BSL2; safety needles, eye protection contingent upon receipt of pharmacy protocols.** **Patient Contact: Standard Precautions during vaccine administration and specimen collection/handling** **Occupational Health Issues: Report any unexplained fever. Report any exposures.**
IBC Discussion	**Approval recommended with following stipulations: Contingent upon pharmacy protocols.**
IBC Vote	**For: 8; Against: 0**

- **Peter Wright, Medicine/Pediatric Infectious Disease**
  - ***A Phase I Clinical Trial to Evaluate the Safety and Immunogenicity of an HIV-1 gag DNA Vaccine with or without IL-12 DNA Adjuvant, Boosted with Homologous Plasmids or with HIV CTL Multiepitope Peptide Vaccine/RC529-SE Plus GM-CSF, in Healthy, HIV-1 Uninfected Adult Participants (HVTN 060)***

Brief Description	From the Consent Form: "You are being asked to take part in this research study because you are a healthy adult who has expressed interest in joining this study that will test experimental vaccines against HIV, the virus that causes AIDS. Vaccines are given to prevent infection or fight disease. This study is testing 2 experimental vaccines against HIV. This study is also testing 3 experimental adjuvants. An adjuvant is a substance that helps the body respond to a vaccine. We are testing the vaccines and adjuvants to see if they are safe (cause any side effects) to give to people and well tolerated. We are also testing to see how your immune system responds to them. The immune system protects your body against infection."
Hosts	Healthy non-HIV infected humans
Vaccine	Please see the descriptions for these plasmid-based vaccines on page 10 of the protocol summary. These agents are not infectious. The primary risk from the agents is allergy to components of the vaccine or side effects related to the production of IL-12 after the DNA-based IL-12 adjuvant is administered. Subjects will be observed for any ill effects 25 to 45 minutes after vaccination and then monitored for other reactions 3 days after the vaccination The study agents are provided in different formulations and are administered in a variety of combinations. The Vanderbilt Investigational Pharmacy will receive and store the vaccine and will prepare syringes for vaccination. The vaccine is administered in [redacted] by study personnel. Study agents will be administered via intramuscular injection in the deltoid muscle. Please see the schema on page 7 of the protocol summary for a table describing the different combinations of agents to be used. No release of agent is anticipated. No special housekeeping or disposal mechanisms are recommended.
Reason for Review	Use of plasmids for delivery of genetic material intended to induce an immune response.
HGTAG Review	The HGTAG is reviewing this study electronically. The HGTAG discussion summary is provided. Any comments from the HGTAG will be provided to the IBC for their consideration.

Recommended BSL/Precautions	Vaccine Handling: BSL1 **contingent on review of pharmacy procedures** Patient Contact and Specimen Handling: Standard Precautions Study personnel should be aware that the side effects of an accidental exposure to study agents could be similar to those described for the subjects of the study. Personnel who are allergic to study agent components should not administer those agents.
IBC Discussion	No additional issues
IBC Vote	For: 8; Against: 0

Mary Zutter, Department of Pathology and Cancer Biology
Unexpected Roles for the α2β1 Integrin
Granting Agency: NIH
Grant Period: 2005 - 2010

Brief Description	The **α2β1 integrin is a collagen/laminin receptor expressed on platelets, endothelial cells, fibroblasts, epithelial cells, and subsets of leukocytes. To define the role of the α2β1 integrin in vivo, we created a genetically engineered mouse in which the expression of the α2β1 was completely eliminated. Mice deficient in the α2β1 integrin are viable and fertile and develop normally.**
Hosts	Prokaryotic: DH5α **chemically-competent *E.coli*; Invitrogen. Chemically competent BL21 (DE3)pLyS (Invitrogen) for protein expression.** Human: human embryonic kidney cells, HEK293FT, Invitrogen. Other Eukaryotic: Primary immortalized endothelial cells and primary mast cells from mice.
Vectors	Plasmid: pBS.human **α2β1 integrin (Stratagene), subcloning vector. Will only be used for subcloning. pGEX6p1- α2β1 integrin (Pharmacia) will be used for protein expression in BL21 cells.** Viral: pLenti6-V5; Invitrogen; replication incompetent, pLP1, pLP2, pLP/VSVG (Invitrogen, viral packaging vectors).
D/RNA	All cDNAs are derived from *Homo sapiens*, **α2β1 and α1β1 integrin genes. These constructs will be used to assess the downstream signaling pathways of α2β1 /α1β1 integrin cytoplasmic domains in cultured endothelial cells and mast cells.**
Infectious Substances	*Lentiviridae* (Lentivirus) replication -incompetent.
Animals	None.
Reason for Review	Creation of recombinant DNA constructs. Use of lentiviral vector. Use of human materials.
Recommended BSL	BSL2
Walk-through	
IBC Discussion	No additional issues
IBC Vote	For: 7; Against: 0

❖ **ADJOURNMENT**

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
AGENDA

Monday, July 11, 2005

2 TO 3PM
407 A/B LIGHT HALL
VANDERBILT UNIVERSITY

ATTENDEES:
Voting members present:, LouAnn Burnett, James Crowe, Timothy Cover, Mark Denison, Robert Loedding, Jerry Rowland, Linda Sealy, Charles Stratton, Cara Sutcliffe, and Richard D'Aquila, (10)
Non-voting members: Robert Wheaton
Absent: Douglas McMahon, Greg Hanley, Menah Pratt, Valerie Thayer (4))
Meeting called to order at 2:00 P.M.

- CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS
- *Review/Approval of Minutes of june 13, 2005 (TO BE DISTRIBUTED AT MEETING)*
  - *MINUTES APPROVED ON VOICE VOTE*
- PROTOCOL REVIEWS
  - **Jian-Xiong Chen, Pathology**
    - ***Angiopoietins/Tie-2 and Diabetic Impaired Myocardial Angiogenesis***

Granting Agency: American Heart Association
Grant Period: 07/01/05 – 06/30/07

Brief Description	**In diabetic patients, heart angiogenesis (forming a new vessel from preexisting vessel) and coronary new vessels formation in response to hypoxia are impaired and may contribute to high morbidity and mortality in diabetic patients. So far little is known about the mechanism(s) of impaired new vessel formation in diabetic heart. Our proposed studies will elucidate important and novel mechanisms underlying hyperglycemia-induced impairment of heart angiogenesis.**
Hosts	**Prokaryotic: N/A** **Human: HEK293** **Other Eukaryotic: N/A**
Vectors	**Plasmid: N/A** **Viral: Adenovirus vectors E1, E3 deletions (Nucleic Acids Res, 1995, 23 (19); 3817)**
D/RNA	**Angiopoietin-1 and Angiopoietin-2, mutant Akt (provided by Dr. Daryl K Granner at Vanderbilt University)**
Infectious Agents	**None**
Animals	**Intravenous tail vein injection**
Reason for Review	**Use of replication-deficient adenovirus. Use of human materials.**

Recommended BSL	**BSL2/ABSL2.**
Walk-through	
IBC Discussion	**Approval recommended with following stipulations: Confirm Dr. Meyrick's oversight**
IBC Vote	**For: 9; Against: 0**

- **Dennis Hallahan, Department of Radiation Oncology**
  - ***Nanotechnology Applications to Cancer Metastasis/TARGETED DRUG DELIVERY TO BRAIN METASTASES***

Granting Agency: NIH.
Grant Period: Dec. 2005 – Dec. 2010

Brief Description	The overall goal of this proposed research is to develop tumor targeted drug delivery systems that are intended for clinical use and to monitor the biodistribution and kinetics of the scFv antibody-conjugates. The targeted drug delivery is achieved by the use of antibodies that bind selectively to tumor antigens. Following radiation, tumor blood vessels express many receptors and these can serve as targets for drug delivery. We will load Ad.Egr-TNF into the optimal immunonanoparticles and measure the amount of therapeutic gene expression within tumor and each organ. The Ad.Egr-TNF vector can serve as a marker for gene expression and will allow us to assess the biological function of therapeutic genes targeted by use of nanoparticle vectors.
Hosts	Prokaryotic: None Human: HEK293 cells (ATCC); Human cell lines: D54, MDA-MB-231, MCF-7 (ATCC) Other eukaryotic: None
Vectors	Plasmid: None Viral: Adenovirus containing the gene encoding for tumor necrosis factor (Ad.Egr-TNF)
D/RNA	Human tumor necrosis factor
Infectious Substances	None
Animals	Mice. (Animals will be injected with Ad.Egr-TNF conjugates with immunonanoparticles)
Reason for Review	Use of replication-deficient adenovirus. Use of human materials.
Recommended BSL	BSL2/ABSL2
Walk-through	
IBC Discussion	Approval recommended with following stipulations: Pending Lab Walkthrough
IBC Vote	For: 9; Against: 0

- **Heidi Hamm, Department of Pharmacology**
  - ***Protein Production Utilizing Lentivirus***

Granting Agency: Vanderbilt University Developmental Grant
Grant Period: 2005 - 2006

Brief Description	The goal of this project is to utilize replication deficient lentivirus containing genes of interest for the transfection of human embryonic kidney cells (HEK293) for the over expression of desired proteins. Crystallography studies will be conducted to identify the physical structure of the proteins in question.
Hosts	Prokaryotic: None Human: HEK293, (Dr Tina Inverson, Vanderbilt University) Other eukaryotic: None
Vectors	Plasmid: pMD.G, pCMV-vprRTIN, pCMV-gag-pro, pCMVLV, pTet-O-LV (Dr. John Kappes, UAB) Viral: Self inactivating replication deficient lentivirus (Kappes, UAB)
D/RNA	Human: - adenosine receptors 1and 2, muscarinic receptors 1and 4; Cow: - synthetic rhodopsin; Norway Rat: - glucogon-like peptide 1.
Infectious Substances	None
Animals	None
Reason for Review	Creation of recombinant DNA constructs; Use of human materials; Use or Replication deficient lentivirus
Recommended BSL	BSL2
Walk-through	Conducted on 3/20/2003 Deficiencies noted:- open doors, non functional eye wash, no lab coats, biohazard labels recapping needles, no first aid kit, and no emergency plan All deficiencies were corrected on subsequent revisit on 4/25/03
IBC Action	Deferred on June 13, 2005 for more information on the packaging system for the lentivirus. See attached email from Jim Crowe to Heidi Hamm.
PI Response	Dr. Hamm has submitted a revised application (attached) indicating that they will produce their vector using the Invitrogen ViraPower Bsd Lentiviral Support Kit. The lentiviral vector will remain the same, but the packaging system will change
Revised Recommendation	BSL2
IBC Discussion	**The risk of spreading a vector lentivirus to others following an occupational exposure (e.g., a needlestick or a non-intact skin or mucous membrane exposure) to any lentiviral vector may theoretically be higher for those who are infected with HIV (at the time of a lentivirus vector-inoculating accidental exposure or at a later time). Theoretically, the recombinant lentivirus vector could be mobilized and be transmitted to others in the same manner that HIV-1 is transmitted, if HIV is also present in the body (see Logan, A.C., *et al., J. Virol.* 78: 8421-8436). If a laboratory worker participating in a lentivirus vector research project may have a risk of HIV exposure, it is an option to consider HIV screening at Occupational Health Clinic, 640 Medical Arts Building, 6-0955**
IBC Vote	For: 10; Against: 0

- **Erik Skaar/Sebastian Joyce, Microbiology and Immunology**
  - ***Molecular Basis of CD1d1 and Natural T Cell Function***

Granting Agency: NIAID/NIH
Grant Period: April 1, 2003 – March 31, 2007

Brief Description	Understanding how the immune system fights against infectious agents such as viruses, bacteria and parasites is key to rational design of vaccines. The focus of this project is to understand how mice fight infections by the bacterium that causes Lyme disease in humans. Current evidence indicates that dendritic cells and NKT cells, the key players of the innate (those that respond immediately to foreign invasion) immune system, play a critical role in the process. Because these key innate immune system cells are conserved in mouse and man, the lessons learned from this project have the potential to yield insights into how the humans fight infectious with the bacterium that causes Lyme disease. To accomplish the goals of this project, will entail in vitro and in vivo experimentation. In vitro experiments will entail isolation and characterization of the antigen(s) recognized by the innate immune cells mentioned above. Current evidence indicates that one type of antigen recognized by the mouse innate immune system might be a lipid(s) that is located in the cell wall of Lyme bacterium. Therefore, we will establish large in vitro batch cultures (~3-5 litres) of Lyme bacteria for large-scale lipid isolation and analyses. Once the required quantities are cultivated, we will dissolve the cell pellet in acetone and dry under vacuum. This procedure will inactivate and kill the bacteria prior to lipid isolation and characterization. In vivo experiments will entail inoculation of normal and genetically engineered laboratory mice that are deficient in various components of the immune system under the skin with 10-50 thousand Lyme bacteria. One-to-four weeks later, we will perform specific experiments that assess the roles of different components of the immune system. Additionally, we will obtain blood and urinary bladder from uninfected and infected mice to determine the amount of bacteria in them in relation to the number of bacteria used for the original infection. If an immune cell is essential to clear the bacterial infection, then the selective loss of that component will result in outgrowth of the bacteria. If not essential, then selective loss of that component will not alter bacterial clearance and the rate at which clearance occurs.
Infectious Substances	***Borrelia burgdorferi* strain B31 (ATCC). *B.burgdorferi* is transmitted to humans through the bite of an infected tick. In a laboratory situation, accidental injection of the organism into the blood stream is the only potential route of infection. Although aerosols generated during laboratory conditions may contain infectious organisms, there have been no descriptions of human to human transmission, nor have there been any reports of laboratory infection with *B.burgdorferi*.**
Animals	Mice. (Intradermal inoculation of 1-5x10^4 Borrelia bacteria per mice)
Reason for Review	Use of human pathogen
Recommended BSL	BSL2/ABSL2
Walk-through	May 26, 2005 – No deficiencies
IBC Discussion	Approval recommended with following stipulations: Approved with clarification that genes are not being moved between two pathogenic strains.
IBC Vote	Defer until investigator addresses potential risk of aerosol For deferral: 10; Against: 0

- **Michael Rock, Pediatrics**
  - ***Cell-Mediated Immune Responses to Influenza A/H5N1 Vaccine***

Sponsor: NIH NIAID

Brief Description	These studies will use an attenuated influenza strain, rg A/Vietman/1203/2004 x A/PR/9/34, to evaluate antibody and cellular immune responses induced by vaccine candidates against A/H5N1 influenza.
Infectious Agent	Influenza strain - rg A/Vietman/1203/2004 x A/PR/9/34 Please see attached data.
Reason for Review	Use of attenuated human and animal pathogen.
Recommended BSL/Precautions	BSL2 facilities/BSL3 practices for growing virus stocks BSL2 containment of inactivated virus or materials exposed to virus (pending proof of inactivation) Extreme care should be taken to isolate this influenza strain from any other strain. This can be accomplished by using separate facilities and/or by doing a complete decontamination of any equipment used for any other influenza strain.
IBC Discussion	Request PI addresses the following by August meeting: 1. Please provide an outline of the training plan for preparing personnel in the different locations to work with this agent. 2. Please make arrangements to offer the inactivated influenza vaccine to those working with this agent. 3. Please consider (and comment on) requiring the wearing of surgical masks during work with live virus to prevent the potential contamination of the experimental virus with a currently circulating flu virus that might have infected a worker. 4. Please clarify the location of the microneutralization assays. The Committee is concerned that live virus will be used in these assays and that the attenuated virus could resort with other influenza viruses currently used experimentally in the laboratory indicated. 5. Please consider (and comment on) storing the live virus stocks in a secure freezer.
IBC Vote	Defer. For deferral: 10; Against: 0

- **Peter Wright, Pediatric Infectious Disease**
  - ***Phase II clinical trial to evaluate the safety and immunogenicity of a multiclad HIV-1 DNA plasmid vaccine, VRC-HIVDNA016-00-VP, followed by a multiclade recombinant adenoviral vector HIV-1 vaccine boost, VRC-HIVADV014-00-VP, in HIV-1 uninfected adult participants***

Sponsor: NIH Division of AIDS

Brief Description	This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to evaluate the safety and tolerability of three doses of an HIV-1 DNA vaccine followed by one dose of an adenoviral vector vaccine.
Hosts	Healthy non-HIV infected adults. Participants will receive the DNA vaccine or placebo at Days 0, 28, and 56, followed adenoviral vector vaccination or placebo at Day 168 . The vaccination will be administered by intramuscular injection.
Vaccine	VRC- HIVADV014-00-VP: This recombinant adenoviral vector product is a replication-deficient, combination vaccine containing four recombinant serotype 5 adenoviral vectors. These vectors contain gene sequences that code for Clade B HIV-1 Gag and Pol as well as Clade A, Clade B, and Clade C Env protein. The World Health Organization UNAIDS HIV Vaccine Advisory Committee has recommended that candidate HIV vaccines be designed based upon the strains prevalent in the country in which trials are to be conducted. The combination of genes used represents the viral subtypes responsible for about 90% of new HIV infections in the world. VRC-HIVDNA016-00-VP: Comprised of six closed circular plasmid DNA macromolecules that, separately, code for Clade B HIV-1 Gag, Pol, Nef, and Clade A, B, and C Env proteins. Subjects will be asked to record their temperature and other side effects on a symptom log for at least 3 days after vaccination. If participants develop cold, flu, or conjunctivitis within 4 weeks of the vaccine, their throat or eye will be swabbed to see if they have adenovirus possibly related to the experimental vaccine. The vaccine is shipped to the investigator in one-dose vials. The adenovirus based vaccine will be administered by intramuscular injection by needle and syringe. The DNA vaccine will be administered using the Biojector Needle-Free Injection Management system. There is no anticipated release of vaccine from the subjects after administration.
Reason for Review	Human vaccine/human gene transfer trial using recombinant DNA and viral vectors for the purposes of expression. Please note that NIH Recombinant DNA Advisory Committee review is not necessary as this trial is designed to elicit immune response (*NIH Guidelines*, Appendix M-VIII). These products have been previously reviewed and approved by the IBC for HVTN 057, HVTN 052, and HVTN 054 in September 2003, September 2004, and March 2005.
HGTAG Review	HGTAG was provided the review materials and the opportunity to comment on the products previously. No comments were generated from HGTAG review.
Recommended BSL/Precautions	DNA Vaccine Handling/Administration: BSL1 Adenoviral Vaccine Handling/Administration: BSL2 Patient Contact: Standard Precautions during vaccine administration and specimen collection/handling Study personnel should be aware that accidental exposure to this vaccine may result in a positive HIV test and should be provided with the same information on these risks that are available to the subjects in the consent form.
IBC Discussion	No additional comments
IBC Vote	For: 9; Against: 0

- **ADJOURNMENT**

Next Meeting: **August TBA**

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

September 12, 2005

2 TO 3 PM
407 C/D LIGHT HALL
VANDERBILT UNIVERSITY

- **VOTING MEMBERS PRESENT:** Rich D'Aquila (acting chair); Mark Denison, Susan Kasper, Tim Peters, Derya Unutmaz, David Wright, Larry Zwiebel, LouAnn Burnett, Cara Sutcliffe, Charles Stratton, Valerie Thayer, Jerry Rowland (quorum = 8 voting members)

  NON-VOTING MEMBERS PRESENT: Maria Garner, Bob Wheaton

  ABSENT: Tim Cover, Bob Loedding

  GUESTS: Sadie Coberley

- **CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS**
- PROTOCOL REVIEWS
  - Mark Denison, Biosafety Level 3 Laboratory
    - LouAnn Burnett provided a brief review of what constitutes Biosafety Level 3 containment and of the emergency response and illness/exposure plans established for Dr. Denison's laboratory
    - The committee discussed several issues centering around emergency response and security. In particular, the committee was concerned that there be a list of persons to be contacted in case of an emergency where an immediate response is necessary and that there be a sufficient pool of persons able to monitor work in the BSL3 in case of absences by Drs. Denison or Coberley. The method of securing the lab was discussed. The appropriateness of persons with pre-existing medical conditions working in the lab was discussed. A timeline for laboratory work was reviewed.
    - The committee received a motion and a second to allow Dr. Denison to begin tissue culture work at Biosafety Level 2 in the laboratory. The motion carried (11 votes FOR; 0 votes AGAINST, 1 vote ABSTAIN (Dr. Denison)).
- **ADJOURNMENT**

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

October 4, 2005

10:45AM
CONFERENCE CALL

- **VOTING MEMBERS PRESENT:** Rich D'Aquila (acting chair); Mark Denison, Susan Kasper, Tim Peters, Derya Unutmaz, David Wright, Larry Zwiebel, LouAnn Burnett, Cara Sutcliffe (quorum = 8 voting members)

  NON-VOTING MEMBERS PRESENT: NONE

  ABSENT: Tim Cover, Bob Loedding, Charles Stratton, Valerie Thayer, Jerry Rowland, Bob Wheaton

- **CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS**

- PROTOCOL REVIEWS

  - Mark Denison, Biosafety Level 3 Laboratory
    - LouAnn Burnett reviewed the development and structure of the BSL3 Core Policies and Procedures document.
    - The committee began discussion on the IBC response prepared by Sadie Coberley and LouAnn Burnett.
      - A discussion about the possibility of multiple pathogens being used in this laboratory was discussed. This laboratory was developed for use with the SARS-associated coronavirus only. All BSL3 labs at Vanderbilt are currently only approved for single pathogens. A motion was made (Peters) and seconded (Unutmaz) to convene the Biosafety Level 3 Working Group to consider 1) development of a policy on review of requests for uses of multiple pathogens in Biosafety Level 3 laboratories and 2) to consider necessary revisions to the Core Policies and Procedures document. The CPP revisions do not need to be considered until the CDC/NIH publication of the 5th edition of the *Biosafety in Microbiological and Biomedical Laboratories* handbook expected in early 2006. This motion carried by a voice vote (9 FOR; 0 AGAINST; 0 ABSTAIN)
      - Additional comments were accepted towards the IBC response letter. One committee members asked about the use of animals in this protocol. The use of animals is likely in the future but is not addressed by any of these SOPs at this time. Another question was whether safety drills would occur. Safety drills will be regularly scheduled for this laboratory. Two committee members commented

that more explicit termination of authorized user status should be developed in the CPP. This will be addressed in the CPP update in early 2006. Another member requested information regarding the status of emergency power and keycard access.

- After discussion and resolution of the issues above, a motion was made and seconded to allow Dr. Denison to move forward with BSL3 work in the facility, pending satisfactory resolution of outstanding facility issues as determined by LouAnn Burnett. There will be a regular update of BSL3 activities at monthly IBC meetings. The motion carried (8 FOR; 0 AGAINST; 1 ABSTAIN (Denison))

❖ **ADJOURNMENT**

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

October 10, 2005

2 TO 3 PM

407 C/D LIGHT HALL

VANDERBILT UNIVERSITY

- **ATTENDANCE**
  - **VOTING MEMBERS (Quorum = 8 voting members)**

☐ Mark Denison, Chair	☒ Larry Zwiebel
☒ Timothy Cover	☒ LouAnn Burnett
☒ Richard D'Aquila	☒ Cara Sutcliffe
☐ Susan Kasper	☒ Charles Stratton
☒ Timothy Peters	☐ Valerie Thayer
☒ Derya Unutmaz	☒ Robert Loedding
☐ David Wright	☒ Jerry Rowland

  - **NON-VOTING MEMBERS**

☒ Maria Garner	☒ Robert Wheaton
☐ John Manning	☐ Kimberly DiGiandomenico

  - **GUESTS**

- **CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS**
  - The meeting was called to order at 2:05pm.

- **APPROVAL OF MINUTES FROM SEPTEMBER 12, 2005 MEETING & OCTOBER 4, 2005 CONFERENCE CALL MEETING**
  - The minutes of the September 12, 2005 and October 4, 2005 meetings were accepted as written.

❖ PROTOCOL REVIEWS

➢ **John S. Penn, Ophthalmology**

▪ ***Molecular Basis of Retinal Angiogenesis***

Brief Description	Endothelial progenitor cells (EPCs) have been observed to target areas where blood vessel formation (angiogenesis) is occurring in retinal disease. Dr. enn proposes to determine how these cells find their target and control gene expression and growth. EPCs will be transfected with viral vectors coding for both angiogenic growth factors (VEGF) and anti-angiogenic factors. These cells will be injected into rats prone to retinopathy.
Hosts	Prokaryotic: Transforming One Shot Stbl3 Competent E. coli, Invitrogen Human: 293FT Cell Line, Invitrogen Other eukaryotic: Bone-marrow derived endothelial progenitor cells isolated from adult female Sprague-Dawley rats.
Vectors	Plasmid: pENTR 5'-UbCp, pLp1, pLP2, pLP/VSVG - Invitrogen Viral: pLenti6/R4R2/V5-DEST, pLenti/UbC/V5-GW/lacZ - Invitrogen Other:
D/RNA	Angiostatic & anti-angiogenic factors from rat
Infectious Substances	None
Animals	Constructs will be transfected into rat EPCs and then injected into newborn rat pups
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify: lentivirus) ☒ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☐ Other:
Recommended BSL	BSL2/ABSL2; all manipulations should be performed in a biological safety cabinet (BSC) with extra sharps precautions and attention to procedures where mucous membrane or non-intact skin exposure could occur
Walk-through	To be scheduled; review of appropriate disinfectant and use of safety sharps to be highlighted
IBC Discussion	Committee discussion focused on what precautions are necessary in the use of lentiviral vectors with growth factor inserts. The Committee felt that the extra precautions recommended were adequate to address the additional concerns.
IBC Action	Approved as recommended above: 10 FOR, 0 AGAINST, 0 ABSTENTIONS

➢ Carl G. Hellerqvist, Biochemistry

[redacted]

Brief Description	[redacted]
Hosts	Prokaryotic: Human: [redacted] Other eukaryotic:
Vectors	Plasmid: [redacted] Viral: Other:
D/RNA	[redacted]
Infectious Substances	[redacted]
Animals	[redacted]
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☐ Use of replication deficient viral vector (specify:) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of microorganism pathogenic for: humans, particularly neonates and elderly ☐ Other:
Recommended BSL	BSL2/ABSL2; use of safe sharps; manipulation of excised [redacted] in biological safety cabinet or other containment device Other questions: 1. What are recombinant DNA constructs used for? 2. What is the relative virulence of the organism [redacted]? 3. What is the nature of the toxin? What practices are appropriate for handling the toxin?
Walk-through	To be scheduled
IBC Discussion	Committee discussion focused on the lack of information in the initial registration and the lack of response by the investigator to preliminary questions. The Committee also requested that a determination of whether this protocol represented a conflict of interest be made prior to IBC approval.
IBC Action	Deferred until Question # 2, above is adequately addressed by the investigator. To be reviewed at next convened IBC meeting. 10 FOR, 0 AGAINST, 0 ABSTENTIONS

➢ Dana Brantley-Sieders, Rheumatology

- ***The role of EphA2 receptor signaling in host-tumor interactions***

Brief Description	This study aims to investigate the chemical signals used by tumors to induce angiogenesis (new blood vessel growth). The objective is to determine the molecular mechanism(s) how ephrin-A1, a chemical signal produced by malignant tumor cells and the receptor, EphA2 communicate to promote blood vessel recruitment. Dr. Brantley-Sieders will increase or decrease ephrin-A1 expression in tumor cell lines in culture and examine the impact on the ability of these cells to induce angiogenesis and metastasize in cell culture and in whole animal models.
Hosts	Prokaryotic: E. coli DH5-alpha (Vanderbilt DNA and Reagent Core) Human: Other eukaryotic: Mouse mammary adenocarcinoma cell lines 4T1 (ATCC) and 67NR (Wayne St. Univ.); mouse pulmonary microvascular endothelial cells (Jin Chen, Vanderbilt)
Vectors	Plasmid: Viral: pRetroSuper replication-deficient retroviral vector; pAd-Easy Adenovirus Vector (Qbiogene); LZRS replication-deficient retroviral vector (Reynolds Lab, Vanderbilt) Other:
D/RNA	siRNA oligonucleotides for mouse ephrin-A1 gene to downregulate expression of murine ephrin-A1 in mouse mammary adenocarcinoma cell lines; human ephrin-A1 cDNA to upregulate expression of ephrin-A1 in mouse mammary adenocarcinoma cell lines
Infectious Substances	none
Animals	Cells transduced with viruses in culture will be introduced into animals.
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify: retrovirus; adenovirus) ☒ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☐ Other:
Recommended BSL	BSL2/ABSL1; extra precautions with sharps Questions: Are the retroviruses ecotropic? Are HEK293 cells used?
Walk-through	Chen lab - last walkthrough - 2/4/2003; a updated walkthrough will be scheduled
IBC Discussion	IBC discussion focused on whether Dr. Brantley-Sieders was using ecotropic systems for this research.
IBC Action	Approved as recommended above with the additional stipulation that ecotropic retroviral systems must be used. Any use of ampotrophic systems must be justified in writing and brought back to the committee. 10 FOR; 0 AGAINST; 0 ABSTENTIONS

➢ Roger J. Colbran, Molecular Physiology & Biophysics

- ***Mechanisms of CaMKII Signal Transduction***

Brief Description	We will use the lentiviral transduction system to investigate calcium signaling in cardiac myocytes (heart muscle cells) and neurons. We will culture cells from the hearts and brains of rats and genetically altered mice, then introduce novel proteins into the cells by viral transduction. Transduced cells will be characterized biochemically, immunohistochemically, and electrophysiologically. Specifically, we are studying the role of calcium/calmodulin-dependent protein kinase II (CaMKII) in regulating voltage-dependent calcium channels and glutamate receptors. The lentiviral system allows the proteins to be introduced into a high percentage of the cultured cells, thus increasing the efficiency of the studies.
Hosts	Prokaryotic: E. coli DH5alpha Human: HEK293FT; COS cells Other eukaryotic: rat cardiac myocytes, mouse cortical neurons
Vectors	Plasmid: pLenti; pCDNA3.1; pME18s; pCMv4 Viral: plp-1; plp2, and plp-vsv6, Invitrogen Other:
D/RNA	mouse: CaMKIIN (CaMKIIN inhibitor protein); CaMKIIalpha (protein kinase) rat: LTCC beta2A (beta 2A subu. of L-type Ca chan); NR2B (2B subu. of NMDA glutamate recptr) human: GluR1 (subunit of AMPA glutamate receptor)
Infectious Substances	lentiviral expression system
Animals	none
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:lentivirus) ☐ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☐ Other:
Recommended BSL	BSL2
Walk-through	to be scheduled
IBC Discussion	The committee had no discussion beyond the details of the protocol provided above.
IBC Action	Approved as recommended above. 10 FOR; 0 AGAINST; 0 ABSTENTIONS

➢ Danny Winder, Molecular Physiology & Biophysics

- ***Regulation of Synaptic Transmission in BNST by Alcohol***

Brief Description	We propose to use the lentiviral transduction system to examine the role of specific forms of glutamate receptor in stress-induced relapse of alcohol addiction. We have shown that alcohol affects the strength of connections between neurons (synaptic plasticity) in regions of the brain associated with stress-effects on addictive behavior (the bed nucleus of the stria terminalis). We will inject lentivirus carrying a DNA-altering enzyme into the brains of genetically-altered mice that will prevent production of a specific type of glutamate receptor. Thus, we will study the role of this receptor in alcohol addiction and neuronal function. The DNA-altering enzyme (Cre recombinase) can only affect our special genetically-altered mice, and would have no effect on an unaltered animal or human.
Hosts	Prokaryotic: E. coli DH5alpha Human: HEK293FT; COS cells Other eukaryotic: rat cortical neurons, mouse cortical neurons
Vectors	Plasmid: pLenti Viral: plp-1; plp2, and plp-vsv6, Invitrogen Other:
D/RNA	Lambda bacteriophage: Cre recombinanse rat: NR2B (2B subu. of NMDA glutamate receptor)
Infectious Substances	lentiviral expression system
Animals	Stereotaxic injection of viral particles into brain
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:lentivirus) ☐ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☐ Other:
Recommended BSL	BSL2/ABSL2: use of safety needles for injection into animals; injection of animals under biological safety cabinet
Walk-through	to be scheduled
IBC Discussion	The committee had no discussion beyond the details of the protocol provided above.
IBC Action	Approved as recommended above. 10 FOR; 0 AGAINST; 0 ABSTENTIONS

- **Laurence Zwiebel, Biological Sciences**
  - **Disruption of Malaria Transmission by Chemical Manipulation of Anopheline Olfactory Responses**

Brief Description	The objective of this research is to identify chemicals that can be used to interfere with the blood seeking behavior of mosquitos. To achieve this goal mosquito odorant receptors are produced in cell culture, where thousands of chemicals can rapidly be tested for their potential to stimulate or inhibit these receptors. Chemicals with such potential will then be tested if they are useful to lure mosquitoes into traps or as repellants
Hosts	Prokaryotic: E.coli K12 (DH5-alpha) Human: Human embryonic kidney cells, 293H and AAV-293; human fibrosarcoma AAV-HT1080 Other eukaryotic:
Vectors	Plasmid: see list on application Viral: Adeno-associated virus serotype 2 (AAV2), Stratagene, replication-deficient. Infects a broad range of mammalian cells, AAV-2 is a naturally defective virus, requiring provision of several factors in trans for productive infection and has not been associated with any human disease. In the AAV Helper-Free System, the AAV-2 ITR sequences and rep/cap genes are present on separate plasmids that lack homology, preventing production of recombinant wild-type virus. Other:
D/RNA	Anopheles gambiae ss G#, AgOR1-AgOR 79, 79 odorant receptor encoding genes, functional characterization of An. gambiae odorant receptors in HEK293 cells
Infectious Substances	AAV vector (see above)
Animals	none
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify: adeno-associated virus) ☐ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☒ Other: Use of human materials
Recommended BSL	BSL2
Walk-through	10/10/2003; update to be scheduled
IBC Discussion	The committee had no discussion beyond the details of the protocol provided above.
IBC Action	Approved as recommended above. 9 FOR; 0 AGAINST; 1 ABSTENTIONS (Dr. Zwiebel)

- BSL3 UPDATE: **No updates on BSL3 facilities were offered.**
- ADJOURNMENT - The meeting was adjourned at 2:55pm.

IBC Meeting Follow-Up List

Date	Investigator	Follow-up needed	Responsible party	Resolution	Date Resolved
10-10-05	Hellerqvist	Determine nature/method of increased virulence of organism	Burnett	Justification email provided by Dr. Hellerqvist to IBC for 11-14-05 meeting	To be reviewed at 11-14-05 IBC meeting
10-10-05	Hellerqvist	Determine whether conflict of interest exists	Garner Burnett	M. Garner referred L. Burnett to SOM Faculty Office; S. Ontiveros indicated that Dr. Hellerqvist's interests in this area have been reviewed by the COI committee and found acceptable	To be reviewed at 11-14-05 IBC meeting
10-10-05	Brantley-Sieders	Determine if ectotropic retroviral system is used	Burnett	Email from Dr. Brantley-Sieders indicating that they will use only ecotropic retroviral systems.	11-10-05

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

November 14, 2005

2 TO 4 PM
407 C/D LIGHT HALL
VANDERBILT UNIVERSITY

- **ATTENDANCE**
  - **VOTING MEMBERS (Quorum = 8 voting members)**

☒ Mark Denison, Chair
☐ Timothy Cover
☐ Richard D'Aquila (regrets)
☒ Susan Kasper
☒ Timothy Peters
☒ Derya Unutmaz
☒ David Wright
☒ Larry Zwiebel (arrived 2:33pm)
☒ LouAnn Burnett
☒ Cara Sutcliffe
☐ Charles Stratton
☐ Valerie Thayer (regrets)
☒ Robert Loedding
☒ Jerry Rowland

- **NON-VOTING MEMBERS**

☐ Maria Garner (regrets)
☐ John Manning
☒ Robert Wheaton
☒ Kimberly DiGiandomenico

GUESTS:

John McCauley - Risk Management

- CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS
  - **The meeting was called to order at 2:08 p.m.**
- APPROVAL OF MINUTES FROM OCTOBER 10, 2005 MEETING
- The minutes were accepted as written (Mark Denison-motion/Timothy Peters 2nd) (For: (9) Against: (0) Abstain: (1 - late arrival))
- PROTOCOL REVIEWS
  - **Carl G. Hellerqvist, Biochemistry (previously deferred)**

[redacted]

Brief Description	[redacted]
Hosts	Prokaryotic: Human: [redacted] Other eukaryotic:
Vectors	Plasmid: [redacted] Viral: Other:
D/RNA	[redacted]
Infectious Substances	[redacted]
Animals	[redacted]
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☐ Use of replication deficient viral vector (specify:) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of microorganism pathogenic for: humans, particularly neonates and elderly ☐ Other:
Recommended BSL	BSL2/ABSL2; use of safe sharps; manipulation of excised [redacted] in biological safety cabinet or other containment device Other questions: 1. What are recombinant DNA constructs used for? ANSWERED IN APPLICATION 2. What is the relative virulence of the organism [redacted]? 3. What is the nature of the toxin? What practices are appropriate for handling the toxin?
Walk-through	To be scheduled

IBC Action	10/10/03: Protocol deferred pending response from investigator and determination of appropriate conflict of interest review
Investigator Response	Dr. Hellerqvist provided an email to the committee responding to the questions of virulence of the microorganism. Conflict of interest issues were addressed with the SOM Faculty Office.
IBC Discussion	The committee agreed that the additional information provided by the investigator was sufficient to address their initial concerns. They also noted that there could be a risk to immunocompromised individuals and pregnant women and agreed that this should be indicated in the approval letter.
IBC Action	Approved as recommended above For: (9) Against: (0) Abstain: (1) (late arrival)

- **David W. Haas M.D, Infectious Diseases/AIDS Clinical Trials Center**
  - [redacted]

Brief Description	[redacted]
Human Subjects	[redacted]
Vaccine Description	[redacted]
Expected Concerns for Healthcare Workers or Community	[redacted]
Reason for Review	☐ Creation of recombinant DNA constructs; ☐ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☐ Use of replication deficient viral vector (specify:) ☐ Insertion of potential oncogene, growth factor, etc. ☒ Use of microorganism pathogenic for humans ☒ Other: use of pathogen in humans

Recommendation	[redacted]: Biosafety Level 2 containment Patient Contact: Standard Precautions
IBC Discussion	The committee discussion focused on what extra precautions are necessary with the use of the [redacted]. They felt that the extra precautions recommended were adequate to address their concerns
IBC Action	Approved as recommended above For: (10) Against: (0)

- **Peter Wright, Pediatrics**
  - ***A Phase I Clinical Trial to Evaluate immune response kinetics and safety of two different primes, adenoviral vector vaccine (VRC HIVADV014-00-VP) and DNA Plasmid, VRC-HIVDNA009-00-VP, each followed by an Adenoviral Vector boost, in healthy HIV-1 Uninfected Adult Participants (HVTN 068)***

Brief Description	This is a human vaccine trial that also meets the criteria for human gene transfer (deliberate transfer of recombinant DNA into humans). The primary objective of this trial is to evaluate the safety and tolerability of one dose of an adenoviral vector vaccine prime or two doses of an HIV-1 DNA vaccine each followed by one dose of an adenoviral vector vaccine. The kinetics and magnitude of the HIV-specific CD4+ and CD8+ T-cell responses will also be evaluated.
Hosts	Healthy non-HIV infected adults (18-50 years old) with pre-existing Ad5 neutralizing antibody titers of <1:12. About 20 participants will be enrolled at Vanderbilt (66 nationally). Group 1 participants will receive the DNA vaccine or placebo at Days 0 and 28 followed adenoviral vector vaccination or placebo at Day 168. Group 2 participants will receive the adenoviral vaccine or placebo at Day 0 followed adenoviral vector vaccination or placebo at Day 168.
Vaccine	VRC- HIVADV014-00-VP: This recombinant adenoviral vector product is a replication-deficient, combination vaccine containing four recombinant serotype 5 adenoviral vectors. These vectors contain gene sequences that code for Clade B HIV-1 Gag and Pol as well as Clade A, Clade B, and Clade C Env protein. The World Health Organization UNAIDS HIV Vaccine Advisory Committee has recommended that candidate HIV vaccines be designed based upon the strains prevalent in the country in which trials are to be conducted. The combination of genes used represents the viral subtypes responsible for about 90% of new HIV infections in the world. VRC-HIVDNA009-00-VP: Comprised of four closed circular plasmid DNA macromolecules that, separately, code for Clade B HIV-1 Gag, Pol, Nef (plasmid 1) and Clade A, B, and C Env proteins (plasmids 2, 3, & 4). Subjects will be asked to record their temperature and other side effects on a symptom log for at least 3 days after vaccination The vaccine is shipped to the investigator in one-dose vials. The adenovirus based vaccine will be administered by intramuscular injection by needle and syringe. The DNA vaccine will be administered using the Biojector Needle-Free Injection Management system. There is no anticipated release of vaccine from the subjects after administration.
Reason for Review	Human vaccine/human gene transfer trial using recombinant DNA and viral vectors for the purposes of expression. Please note that NIH Recombinant DNA Advisory Committee review is not necessary as this trial is designed to elicit immune response (*NIH Guidelines*, Appendix M-VIII). These products have been previously reviewed and approved by the IBC for HVTN 057, HVTN 052, HVTN 054, and HVTN 204 in September 2003, September 2004, March 2005, and July 2005.

HGTAG Review	HGTAG was provided the review materials and the opportunity to comment on the products previously. No comments were generated from HGTAG review.
Recommended BSL/Precautions	DNA Vaccine Handling/Administration: BSL1 Adenoviral Vaccine Handling/Administration: BSL2 Patient Contact: Standard Precautions during vaccine administration and specimen collection/handling Study personnel should be aware that accidental exposure to this vaccine may result in a positive HIV test and should be provided with the same information on these risks that are available to the subjects in the consent form.
IBC Discussion	The committee expressed some concern with experimental design and use of the Nef plasmid. However, they felt that the extra precautions recommended were adequate to address their concerns.
IBC Action	Approved as recommended above For: (10) Against: (0)

❖ BSL3 UPDATE

Since the previous meeting, Sadie Coberley resigned from her position as laboratory coordinator for Mark Denison. For now, Dr. Denison is holding the position until a new laboratory coordinator is found. The lab is moving forward with BSL2 experiments. In December/January, upon presentation from Dr. Denison, the IBC will determine which viable SARS experiments can be performed.

❖ POLICIES

- **Discussion of Vanderbilt Coverage for compliance issues for Investigators - John McCauley, Risk Management**

The conviction of Dr. Thomas Butler has sparked concern among many research institutions as to what a researcher's legal coverage would be if he/she were ever brought under investigation. On the medical side of Vanderbilt University, the primary investigators (PIs) are provided this information at their faculty orientation; whereas outside the medical center they are not. The discussion focused on making these resources more well-known to incoming, non-medical faculty and staff and also on what role IBC would play if such an issue would arise. The committee concluded that if a PI under investigation was acting in good faith and according to his/her approved protocols, IBC does provide some assistance since it reviews all experimental protocols according to Vanderbilt EHS policy and CDC/NIH research guidelines. The committee also felt that more information needs to be presented at a new-faculty orientation, so a PI would know who to contact first if ever brought under investigation.

❖ ADJOURNMENT

The meeting was adjourned at 3:46 p.m.

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

January 9, 2006

2 TO 3 PM
350 LIGHT HALL
VANDERBILT UNIVERSITY

- **ATTENDANCE**
  - **VOTING MEMBERS (Quorum = 8 voting members)**

☒ Mark Denison, Chair
☒ Timothy Cover
☒ Richard D'Aquila
☒ Susan Kasper
☒ Timothy Peters
☒ Derya Unutmaz
☐ David Wright
☒ Larry Zwiebel
☒ LouAnn Burnett
☐ Cara Sutcliffe
☒ Charles Stratton
☐ Valerie Thayer
☒ Robert Loedding
☒ Jerry Rowland

- **NON-VOTING MEMBERS**

☒ Maria Garner
☐ John Manning
☒ Robert Wheaton
☒ Kimberly DiGiandomenico

GUESTS:

none

- CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS
  - **The meeting was called to order at 2:08 p.m.**
- APPROVAL OF MINUTES FROM NOVEMBER 14, 2005 MEETING
- The minutes were accepted as written (For: (11) Against: (0))
- PROTOCOL REVIEWS
  - **Eugenia Gurevich, Pharmacology**
  - ***Dopamine Receptor Trafficking in Parkinson's Disease***

Brief Description	Parkinson's disease (PD) is caused by a degeneration of dopaminergic neurons. Dopamine replacement therapy with L-DOPA and DA agonists is effective in treating PD, however long-term use often results in motor complications. This project aims to study the role arrestins and G-protein-coupled receptor kinases (GRKs) play in Parkinson's disease and L-DOPA therapeutic side effects. The first objective is to study the role of arrestins and GRKs in desensitization of dopamine receptors. Secondly, the toxin, 6-hydroxydopamine, will be used in an animal model of PD to destroy dopamine-producing cells in the brain and then evaluate the effects of L-DOPA and other antiparkinsonian drugs. Lastly, the amount of GRKs will be examined to determine if an increase could change the behavior of dopamine receptors in Parkinsonian animals. This will be done by injecting replication-incompetent lentiviral constructs into the brain of the animals to induce production of GRKs and then determining if the viruses could prevent changes known to occur in the brain of Parkinsonian animals or if the viral constructs could prevent side effects induced by antiparkinsonian drugs.
Hosts	Prokaryotic: Human: HEK293 Other eukaryotic:
Vectors	Plasmid: Viral: self-inactivating replication-incompetent lentivirus; pLenti6/V5-DEST, Invitrogen Other:
D/RNA	G protein-coupled receptor kinase 2; rat GRK2, rat GRKct (truncated GRK2), rat GRK2 miRNA
Infectious Substances	lentiviral expression system
Animals	Sprague-Dawley rats
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:lentivirus) ☐ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☒ Other: use of human materials
Recommended BSL	BSL2/ABSL2 - plus procedures specified by investigator in revised application
Walk-through	01/06/06

IBC Discussion	**The committee stressed extra sharps precautions as well as emphasized that the risk of spreading a vector lentivirus to others following an occupational exposure to any lentiviral vector may theoretically be higher for those who are infected with HIV.**
IBC Action	**Approved with emphasis on issues discussed above** **For: (11) Against: (0)**

- **Utpal Dave, Medicine**
- ***BioWISE application #2718***
  - ***Studying genes that cause leukemia and lymphoma in mice***

Brief Description	Dr. Dave is studying the genes that cause leukemia and lymphoma in mice. Candidate genes are tested for their ability to cause cancer by cloning them into retroviruses and then transducing hematopoietic stem cells in vitro. These stem cells are then put back into mice and the animals are monitored for disease. Human cells are also transduced but they are left in culture for in vitro assays.
Hosts	Prokaryotic:E.coli (DH10B) Human: (Cell lines) CD34 positive HSC, Phoenix-Eco cells, HEK293T, Pheonix-Ampho cells, GP+E86, PA317 Other eukaryotic: (virus) Retroviridiae Moloney MLV
Vectors	Plasmid: phRL series, pSPORT1, pT7T3-Pac, pCL-Eco, pCL-Ampho, pCL-10A1, pCR2.1, pGEMTEasy, pBluescript, pCDNA3.1, pGEM series Viral: Retroviridiae pMSCV, Retroviridiae pLSXN Moloney, Retroviridiae pQCXIH, Retro. MoMLV, Retro. MFGs-IL2RG, Retro. MSCV-GFP, Retro. pCLSNX, Retro. pCLNCX, Retro. pCLNdx, Retro. pCLNRX, Retro. pCL-MFG-LacZ Other:
D/RNA	LMO2, IL2RG, PRDM16, SSDP2, IRS2, TAL1, EVI27, EVI1, MEF2C (all derived from humans or mice) gp70, 4070A Env, 10A1 Env (all derived from Retroviridiae)
Animals	mice
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:retrovirus/lentivirus) ☒ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☒ Other: Use of human materials
Recommended BSL	BSL2/ABSL2 *with clarification on the following: quantities of microorganisms produced; into what vectors oncogenes are being inserted; strain of E.coli being used; shedding of materials in mice/for how long and if any extra risks involved with a bite/scratch from infected/exposed animal; safe sharps practices.*
Walk-through	01/05/06

IBC Discussion	The committee requested more information about: -The specific viral vectors that Dr. Dave had listed in his BioWISE application (for example: where are the Copeland, Bodine Dunbar, etc. laboratories located? How were the viral vectors confirmed replication-deficient?). -What inserts will be placed into these viral vectors? -What are the commercial/institutional sources of your human cell lines (ex. ATCC, another colleague)? They also stressed the use of safe sharps precautions and that the risk of spreading a vector lentivirus to others following an occupational exposure to any lentiviral vector may theoretically be higher for those who are infected with HIV
IBC Action	Approved pending response to the questions listed above (see attached follow-up list) For: (11) Against: (0)

➢ Heather Ball, Biochemistry

- *Maintenance of Genome Stability and Breast Cancer: Molecular Analysis of DNA Damage Activated Kinases - DOD*

Brief Description	The goal of this research is to understand the mechanism by which ATR kinase becomes activated after cells are exposed to DNA damage. The investigator plans to generate a specific lesion to the DNA, by translating previous findings from the mammalian cell system to that of *Saccharymyces cerevisiea*, and then use chromatin immunoprecipitation to determine whether the ATRIP homolog, Lcd1 (mutated to prevent interaction with RPA) is still recruited to the location of DNA lesions. In addition, to determine if localization of ATR to DNA lesion is required for ATR signaling, the investigator aims to immobilize ATR in the nucleus by implementing three different methods: 1. tethering to the membrane; 2. tethering to a histone; and 3. disrupting ATR-ATRIP binding. Then the ability of these immobile ATR proteins to activate a checkpoint response will be assessed. Lastly, the investigator proposes to identify the stoichiometry of the ATR-ATRIP complex to identify the proper type of ATRIP oligomerization. To further elucidate the role of oligomerization in the function of the ATR-ATRIP complex , the ATR oligomerization will be disrupted to assess the role of ATR oligomeriztion in ATR-ATRIP checkpoint signaling.
Hosts	Prokaryotic: E.coli Human: HeLa, U20S, HEK293 Other eukaryotic: Saccharomyces cerevisiae
Vectors	Plasmid: pCKNA3.1 (Invitrogen) Viral: Other:
D/RNA	ATRIP (from humans; using for protein expression) and DDC2 (From yeast; using for protein expression)
Reason for Review	☒ Creation of recombinant DNA constructs; ☐ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☐ Use of replication deficient viral vector (specify:) ☐ Insertion of potential oncogene, growth factor, etc. ☐ Use of microorganism pathogenic for ☐ Other:
Recommended BSL	BLS2 (due to viral vectors also being used in the laboratory)
Walk-through	01/11/06
IBC Discussion	LouAnn Burnett explained that this project was applicable to administrative review and approval and therefore, did not need further discussion by IBC unless otherwise requested.
IBC Action	Received administrative approval; no further action by IBC

❖ BSL3 UPDATE

Since the previous meeting, Dr. Denison went to Chapel Hill for a one-week BSL3 training session. Also, as a result of the construction being done near the BSL3 lab, all of the HEPA filters needed to be checked to assure that they do not require replacement.

❖ OTHER

- Much discussion centered around Dr. Dave's BioWISE application, as this was the first that has been seen by IBC. One suggestion offered to enhance the application included a "genetic library" section. In addition, the committee was reminded that BioWISE is still a 'work in progress'. Currently, the initial application is received and reviewed. Then, if more specific information is needed, it is requested. It was suggested that each committee member complete a BioWISE application to gain a better understanding of the system and to set an example for other researchers.
- LouAnn Burnett was selected to be part of the National Academies Committee on A New University-Government Partnership on Science and Security. Her first meeting was slated for January 12-13, 2006 in Washington, DC.
- One of the IBC members suggested that a lentiviral fact sheet may be helpful to the committee when reviewing protocols that used lentiviral vectors.
- A draft document for who to contact in case of a major compliance investigation is planned for distribution at the February IBC meeting.

❖ ADJOURNMENT

- The meeting was adjourned at 3:07 pm.

01-09-06 IBC Meeting

FOLLOW-UP LIST

Date	Investigator	Follow-up needed	Responsible party	Resolution	Date Resolved
01-09-06	Dave	More specific detail on the viral vectors listed in BioWISE application needed (origin, replication-deficient verification) What inserts are being placed into these viral vectors? What are the commercial/institutional sources of the human cell lines (ex. ATCC, another colleague)?	K. DiGiandomenico	Justification email provided by Dr. Dave to LouAnn Burnett	Reviewed on 01-18-06 and approved as being sufficient

VANDERBILT INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)
MINUTES

February 13, 2006

2 TO 4 PM

350 LIGHT HALL

VANDERBILT UNIVERSITY

- ATTENDANCE
  - **VOTING MEMBERS (Quorum = 8 voting members)**

☒ Mark Denison, Chair
☐ Timothy Cover (regrets)
☐ Richard D'Aquila (regrets)
☒ Susan Kasper
☒ Timothy Peters
☒ Derya Unutmaz (left at 3:07pm)
☒ David Wright (conflict with Williams – arrived ~2:15pm)
☒ Larry Zwiebel
☒ LouAnn Burnett
☒ Cara Sutcliffe
☒ Charles Stratton
☒ Valerie Thayer
☒ Robert Loedding
☐ Jerry Rowland (regrets)

  - NON-VOTING MEMBERS

☒ Maria Garner
☐ John Manning (regrets)
☒ Robert Wheaton
☒ Kimberly DiGiandomenico

GUESTS:

none

- **CALL TO ORDER/INTRODUCTIONS/ANNOUNCEMENTS**
  The meeting was called to order at 2:05 p.m.
- **APPROVAL OF MINUTES FROM JANUARY 9, 2006 MEETING**
  The minutes were accepted as written.
  For: (10) Against: (0) Abstain: (1 – late arrival)
- **PROTOCOL REVIEWS**

John Williams, Pediatrics
[redacted]
Candidate DNA and Protein Vaccines for H5 Influenza in a Mouse Model
Reviewed by: Charles Stratton

Brief Description	The recent emergence of H5 avian influenza has sparked efforts to develop pandemic preparedness plans. Previous vaccine trials for H5N1 influenza were unsuccessful in stimulating an efficient immune response in humans. Dr. Williams has developed novel methods for making recombinant virus proteins that are likely to provide good immune responses. His lab, in collaboration with Dr. Michael Rock, plans to test the ability of these vaccines to generate an immune response and provide protection against influenza in a mouse model.
Hosts	Prokaryotic: E.coli (DH5α) Human: 293 cells (protein production) Other eukaryotic: Mouse lymphocytes, MDCK cells (growth and plaque titration of virus)
Vectors	Plasmid: pcDNA3.1, pcDNA3.1- *myc*HIS (Invitrogen)
D/RNA	Hemagglutinin gene derived from strain pHW1203; a Vietnam strain of H5N1 influenza. Polybasic cleavage site has been deleted (this construct was used to generate the attenuated vaccine strain)
Infectious Agents	Orthomyxoviridae, Influenza A (rg A/Vietnam/1203/2004 x A/PR/8/34)
Animals	Mice
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of microorganism pathogenic for animals, humans (wild-type) ☒ Use of human cell lines
Recommended BSL	[redacted]: BSL2 : BLS2+): ABSL3
Walk-through	01/11/06 - deficiencies noted: fabric chair in tissue culture room; 'no food/drink' labels needed; no written emergency plan; no biohazard stickers
IBC discussion	The committee was concerned that the nucleic acids being inserting from the H5N1 might be able to encode an infectious form of the virulent H5N1 (or that it theoretically could occur). Dr. Williams was contacted via email and sufficient documentation was provided to demonstrate that not even a theoretical chance existed that this could occur.
IBC action	Approved as recommended above plus recommendation for workers to receive flu shot and wear surgical masks. For: (11) Against: (0)

Chris Willey, Radiation Oncology

[redacted]

Reviewed by: Susan Kasper

Brief Description	[redacted]
Hosts	[redacted]
Vectors	[redacted]
D/RNA	[redacted]
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Use of replication deficient viral vector (specify:retrovirus, adenovirus) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2
Walk-through	02/08/06 - Proper use of disinfectants are being used
IBC Discussion	The committee did not express any additional concerns that were not addressed during the preliminary application review.
IBC Action	Approved as recommended above For: (11) Against: (0)

Todd Miller, Medicine

The role of AIB1 genomic signaling in HER2-mediated tamoxifen resistance - DOD

Reviewed by: Timothy Peters

Brief Description	Dr. Miller aims to discover new drug targets and diagnostic tools for use in tamoxifen-resistant cancers while providing comprehensive information regarding hormonal regulation of cell activity. He plans to use genomic DNA tiled microarrays as a tool to comprehensively scan the human genome for AIB1 trasncription factor-bound DNA. He will then study the global transcriptional regulatory function of AIB1 and determine its role in tamoxifen resistance.
Hosts	Prokaryotic: E.coli (DH5a) Human: MCF-7 cells (ATCC)

Vectors	Plasmid: pcDNA3.1+ (Invitrogen) Viral: pBMN -I-GFP (Stanford); pBMN-HER2-I-GFP (Vanderbilt) - MMLV-based retroviral vectors (amphotropic)
D/RNA	human HER2 oncogene inserted into viral vector to make stable cell lines
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Use of replication deficient viral vector (specify:MMLV-based retroviral vector) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2
Walk-through	02/08/06
IBC Discussion	The viral vector from the Nolan Lab at Stanford was deemed safe by the committee. They questioned why a research fellow was listed as the primary investigator; LouAnn indicated that this is how DoD grants are filed. The committee suggested that a list of previously approved viral vectors should be supplied to them prior to application reviews.
IBC Action	Approved as recommended above For: (11) Against: (0)

Lynn Matrisian, Cancer Biology
[redacted]

Microenvironmental Influences on Breast Cancer Metastasis to Lung - DOD

Brief Description	Dr. Matrisian seeks to understand how proteases are involved in breast cancer metastasis to the lung. To accomplish this, a novel co-culture system will be used that consists of fluorescently labeled breast cancer cells from mice and unlabeled mouse lung cells that are placed in an artificial matrix. These co-cultures will then be studied using a variety of methods to determine which proteases may be involved in causing breast cancer.
Hosts	Prokaryotic: *E.coli* (DH5α) Other eukaryotic: Murine polyoma virus middle T breast cancer cells
Vectors	Viral: retrovirus - pMSVC puro (Clontech) - amphotropic
D/RNA	GFP (green fluorescent protein)
Animals	mice
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Use of replication deficient viral vector (specify:retrovirus - pMSVC puro) ☒ Insertion of potential oncogene, growth factor, etc.
Recommended BSL	BLS2 / ABSL2
Walk-through	02/16/06
IBC Discussion	The committee agreed on the safety of the retroviral vector proposed and inquired about the signature sheet from the PI.
IBC Action	Approved as recommended above For: (11) Against: (0)

Reviewed by: Mark Denison

Barbara Fingleton, Cancer Biology
[redacted]

Fas ligand, friend or foe in breast cancer - DOD

Reviewed by: Derya Unutmaz

Brief Description	Fas ligand is a protein found on breast cancer cells. Dr. Fingleton will study if this protein helps breast tumors develop or if it is needed for chemotherapeutic drugs to effectively work. She will use siRNA to silence this protein in a mouse cancer cell line and then orthotopically inject mice with tumor cells that have or lack the Fas ligand. She will then compare growth of mammary tumors and their response to chemotherapeutic drugs.
Hosts	Prokaryotic:E.coli (DH5α) - for cloning Human: 293HEK (ATCC) - for viral packaging Other eukaryotic: PyVT R221A (murine mammary tumor line isolated in-house) - for expression
Vectors	Plasmid: pPACK packaging plasmid (System BioSciences) Viral: pFIV-H1/U6-puro siRNA (System BioSciences) FIV-based lentiviral vector
D/RNA	siRNA to target *Mus musculus Tnfsf6* (Fas ligand) gene
Animals	wild-type FVB mice

Reason for Review	☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:FIV-based lentiviral vector) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2 / ABSL2 Address in walk-through: sharps precautions IBC discussion: affirmative use of safety needles with animals?
Walk-through	02/16/06 – The lab manager has researched the use of safety needles and concluded that they are not appropriate for experiments being performed. Documentation can be requested if required.
IBC Discussion	This is the first FIV-viral vector that the committee has reviewed, and they felt it was safe to use. Some questions did arise about the use of siRNA/shRNA and its safety. Dr. Unutmaz explained that siRNA does not change the pathogenicity of a product and therefore is appropriate to use as a research tool. LouAnn asked the committee if safety needles for all animal work needed to be implemented. After some discussion, they concluded that more 'hard data' was needed for an affirmative decision.
IBC Action	Approved as recommended above For: (11) Against: (0)

Shimian Qu, Medicine
Genome-wide in vivo Screening for Candidate Tumor Metastasis Suppressor Genes, DOD
Reviewed by: Derya Unutmaz

Brief Description	Dr. Qu is proposing to identify breast cancer metastasis suppressor genes or their regulators by a genome-wide in vivo genetic screening with an siRNA library. To do this, Dr. Qu will generate localized tumors in the absence of metastasis in primary human mammary epithelial cells (HMECs). The HMECs will then be infected with retroviruses derived from the human 50k GeneNet Lentiviral siRNA library. The infected cells will be selected by puromycin; puromycin-resistant cells will be resuspended and orthotopically injected into ingunial mammary glands of athymic nude mice. The metastatic dissemination will be carefully evaluated from dissected organs and individual metastatic nodules will be dissected and preserved for later use. The genomic DNA from these nodules will be amplified to obtain the siRNA and then sequenced. Finally, the individual metastatic suppressor candidate gene will be validated by a gene-specific siRNA knockdown experiment.
Hosts	Human: Primary human mammary epithelial cells (HMECs), Cambrex Bio Science Walkersville, Inc.
Vectors	Viral: pFIV Expression and Cloning lentiviral vector - System Biosciences
D/RNA	siRNA library comprised of a redundant set of siRNA for each known human gene
Infectious Substances	lentivirus - can infect mammalian cells
Animals	athymic nude mice

Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:lentivirus) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2 / ABSL2 - confirmation of safe sharps
Walk-through	02/10/06 *Address during walk-through*: positive confirmation of purchase of safety syringes/sharps and the disinfectants being used
IBC Discussion	This was another FIV-based vector system which the committee determined was safe to use. However, in regards to safe sharps, they did feel that the proposed experiments required use of safe sharps and therefore, requested written confirmation of the purchase of safety syringes/sharps. Kim also requested positive confirmation for the BSC certification, since it had not been certified since 2003.
IBC Action	Approved as recommended above, with stipulations on safe sharps use and BSC certification For: (11) Against: (0)

Sarki Abdulkadir, Pathology
Modeling Prostate Cancer by Conditional Gene Targeting, DOD
Reviewed by: Richard D'Aquila

Brief Description	Dr. Abdulkadir will infect mouse prostate cells with lentivirus expressing genes of interest and then will implant them under the kidney capsule of a mouse. He will evaluate if normal prostate cells or prostate cancer is regenerated.
Hosts	Prokaryotic:E. coli-K12 Human: 293FT cell lines Other eukaryotic: mouse prostate cells
Vectors	Viral: lentiviral vectors; Invitrogen; replication-deficient
D/RNA	Human Egr-1, human Myc
Animals	upon IBC and IACUC approval - SCID mice
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of replication deficient viral vector (specify:lentivirus) ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2/ABSL2 with education on appropriate waste disposal and disinfection during walk-through
Walk-through	To be scheduled
IBC Discussion	The lentiviral vector is the 'preferred viral vector' by the IBC. Other than the education recommended during the walk-through, no other concerns arose.
IBC Action	Approved as recommended above For: (11) Against: (0)

❖ PROTOCOLS RECEIVING ADMINISTRATIVE REVIEW/ IBC NOTIFICATION

LouAnn Burnett explained that these projects were applicable to administrative review and approval and therefore, did not need further discussion by IBC unless otherwise requested. All received administrative approval; no further action by IBC.

Zhixiong Xu, Hematology/Oncology

[redacted]

Regulation of LMO4 Oncoprotein Stability in Breast Carcinogenesis - DOD

Brief Description	Dr. Xu hypothesizes that increased expression of the SSBP2 gene increases LMO4 and LDB1 protein abundance, stimulates cellular proliferation and/or inhibits differentiation, and promotes/accelerates breast tumorigenesis. He plans to study the contribution of SSBP2 to LMO4 and LDB1 protein abundance in breast epithelial cells and to determine the role of this regulation in mammary morphogenesis and oncogenesis.
Hosts	Human: MDA-MB-231 (human breast cancer cell line) MCF10A (human breast epithelial cell line) Other eukaryotic: CHO (Chinese hamster ovary cell line)
Vectors	Plasmid: pEFIRES-P (S.Hobbs - Institute of Cancer Research, London UK)
D/RNA	SSBP2, LDB1, RNF12, LMO4 siRNA targeted to SSBP2, LDB1, RNF12 (Ambion)
Animals	nude mice
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2 / ABSL2
Walk-through	To be scheduled - Address during walk-through: disinfectants being used, waste disposal, safe sharps use

Chuanzhong Ye , Medicine

Dimerization of Her2/neu and its alternative splicing in breast cancer: a mechanism of Herceptin resistance? - *DOD*

Brief Description	Herceptin is widely used among breast cancer (BC) patients; however, some patients do not respond to its treatment. Dr. Ye belives that HER-sp plays a critical role in Herceptin desensitization by modulating cellular localization of HER2 and HER2 overexpressing BC cells. He has proposed to investigate the formation and distribution of HER2/HER-sp heterodimerization by bimolecular fluorescence complementation in living breast cells. He also hopes to gain insight into the molecular mechanisms underlying the HER-sp on response to Herceptin treatment, signaling and apoptosis in HER2 overexpressing BC cell lines.
Hosts	Human: Breast cancer cell line: MDA-MB-231 (ATCC)

Vectors	Plasmid: pSVL (Pharmacia) pcDNA3.1 and pEYFP (Invitrogen) pTRE2hyg (BD Biosciences)
D/RNA	HER2 cDNA and HER2-sp (cloned from BC tissue by RT-PCR)
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of potential oncogene, growth factor, etc. ☒ Use of human cell lines
Recommended BSL	BSL2; pending sharps use and proper decontamination methods
Walk-through	To be scheduled

Min Chang , Ophthalmology
[redacted]

The novel adhesion molecule Bves and corneal healing

Brief Description	Dr. Chang aims to determine the role of the junction protein, blood vessel epicardial substance - or Bves, in corneal wound healing. He will employ constructs of Bves with different portions of the protein deleted in order to determine the portions that are critical to the regulation of corneal wound healing. To test this, the constructs, as well as reporter proteins, will be administered both *in vitro* and *in vivo* via iontophoresis.
Hosts	Prokaryotic:INV*aF* E.coli (Invitrogen) Human: SV40 immortalized human corneal epithelial cells Other eukaryotic: primary adult male Balb/c mouse corneal epithelial cells
Vectors	Plasmid: PCR 2.1-CMV vector from Invitrogen
D/RNA	full-length chick-Bves with a FLAG epitope, truncation and deletion mutants and GFP will be ligated to PCR 2.1 CMV-vector
Animals	mice
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Insertion of rDNA constructs, microbes, or cell lines into whole animals, ☒ Use of human cell lines
Recommended BSL	BSL2 / ABSL2
Walk-through	To be scheduled

Walter Chazin, Biochemistry
[redacted]
n/a, DOD

Brief Description	Accumulation of the cell signaling protein β-catenin can lead to various types of cancer. The goal of this project is to determine the mechanism of β–catenin degradation. To accomplish this, each protein will be produced and the three dimensional architecture of the complex will be determined by electron microscopy.
Hosts	Prokaryotic:*E.coli* (Bl21(DE3), DH10Bac and Rosetta competent cells - Invitrogen Other eukaryotic: Insect cells: Sf-9, Sf-21 and Hy-5 - Invitrogen
Vectors	Plasmid: pFastBac, pET vectors and pET-Duet - Invitrogen Viral: Bacmid - Invitrogen (Bac-to-Bac Baculovirus Expression System)
D/RNA	Human: β-catenin, Skp1, ubiquitin Mouse: transducin beta-like 1, Siah-1, Siah-interacting protein, E2 rabbit: E1 All of the proteins are a part of a multi-subunit complex that regulates cell signaling molecule β-catenin through degradation.
Reason for Review	☒ Creation of recombinant DNA constructs; ☒ Use of replication deficient viral vector (specify:Baculovirus) ☒ Insertion of potential oncogene, growth factor, etc.
Recommended BSL	BSL1
Walk-through	n/a

- BSL3 UPDATE

  Denison BSL3: **During a generator test for emergency power back-up, it was discovered that normal ventilation continued and supply air operated in excess of the exhaust, making the laboratory positive in just a few seconds. This would never happen if the lab actually lost power, but because the generators are tested each month, this could be a frequent occurrence unless the lab is removed from the normal power grid prior to the test.**

- POLICIES

  LouAnn Burnett gave a brief PowerPoint presentation pertaining to 'Crises Compliance," which was acquired from an in-service Medical Center meeting that Bob Wheaton attended. This was a follow-up to the last quarterly meeting policy discussion about the conviction of Thomas Butler. One question that arose in discussion was what to do if someone shows up and starts asking questions about compliance or wants to look around a lab. Legal services indicate that a PI should first ask for some form of identification and then inform the individual that according to University policy, legal services must be contacted before any further action is taken. General consensus of the IBC was that one specific phone number should be used for these purposes – whether it is campus police or a switchboard operator who directs the call to the appropriate individuals in legal services or risk management.

- OTHER

  LouAnn Burnett attended the National Academies Science & Security Committee meeting. The meeting was largely geared around policy issues, one of which was export controls. This

encompasses issues from international collaborations and foreign graduate students to email and conversations with colleagues. In March, she will be attending the NIH Recombinant DNA Advisory Committee (RAC) meeting in Bethesda, MD. Lentiviral vectors are one topic of discussion slated for this meeting.

- ADJOURNMENT

  The meeting was adjourned at 3:47 pm.