

**NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES**

FEBRUARY 21, 2012

CALL TO ORDER / ANNOUNCEMENTS

The NCI-Frederick Institutional Biosafety Committee was convened at 12:05 p.m. in Building 549 Executive Board Room with the following members in attendance:

Voting (Quorum = 8)

- | | |
|---|---|
| <input checked="" type="checkbox"/> Michael Baseler | <input checked="" type="checkbox"/> Sarah Hooper |
| <input checked="" type="checkbox"/> Theresa Bell | <input checked="" type="checkbox"/> Serguei Kozlov |
| <input checked="" type="checkbox"/> Rev. David Betzner | <input checked="" type="checkbox"/> Dan McVicar (Chair) |
| <input checked="" type="checkbox"/> Stephen Creekmore | <input checked="" type="checkbox"/> Randall Morin |
| <input checked="" type="checkbox"/> Bruce Crise | <input type="checkbox"/> Shalini Oberdoerffer (regrets) |
| <input checked="" type="checkbox"/> Eric Freed | <input type="checkbox"/> Raja Sriperumbudur (regrets) |
| <input checked="" type="checkbox"/> Melinda Hollingshead (left at 2:00pm) | <input type="checkbox"/> Lucien Winegar (regrets) |
| <input checked="" type="checkbox"/> Stephen Hughes | |

Non-Voting

- Walter Hubert
 Kim DiGiandomenico

Other

Capt. Darrell Laroche; contracting officer's technical representative for EHS
Margaret Slaughter; OHS Senior Occupational Health Nurse
Debra Schubardt; Nurse Practitioner Student (University of Cincinnati)

APPROVAL OF MINUTES FROM JANUARY 17, 2012 MEETING

The minutes from the January 17, 2012 meeting were approved as written.
A motion and second were made. (For: 11; Against: 0; Abstain: 0)

ACCIDENT REVIEWS – No accidents to report

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

David Salomon 12-09: Tumor growth and metastasis assessment This group will investigate an experimental mouse model of breast cancer metastasis to the lungs and assess potential therapeutic targets for inhibition of tumorigenesis and/or lung metastasis. They are investigating the relationship between Cripto-1 protein and Wnt signaling pathway and will use a lentiviral vector to transfect Cripto-1 gene into the target cells. The committee requested the following prior to release of approval: 1. Can the PI wait one week post-transduction before injecting the transduced cells into mice? If not, please explain why. 2. If for scientific reasons the PI cannot wait one week, please explain how the cells will be injected into animals to ensure (lab or LASP) staff conducting these procedures are aware of the increased potential for infectious lentivirus to be contained within the cell suspension (in the event of autoinoculation). Are animals restrained (physically or chemically)? How are injections done (one needle

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for multiple injections or one needle/injection)? Etc. 3. The PI must provide a signed employee roster (lab and LASP staff) <http://home.ncifcrf.gov/ehs/ibc/docs/addendum1.dot> and PI signature sheet prior to release of approval. Dan McVicar motioned to conditionally approve the registry pending responses to the questions noted above. Bruce Crise seconded the motion. For: 11; Against: 0; Abstain: 0

Alfred Singer 12-20: *Breeding and Maintenance of mice* Breeding only protocol-Notification to committee

RENEWALS

Jairaj Acharya 12-06 (06-03 and 06-16): *Transport studies in mouse embryonic fibroblasts (MEFs) using Vesicular Stomatitis Virus G Protein A and Functional Analysis of Enzymes of Sphingolipid Metabolism* The study objectives of this IBC renewal are as follows:

- 1) Conduct functional analysis of enzymes of sphingolipid metabolism and correlate their activity to signaling events (e.g., cell division, differentiation and death) linked to the sphingolipid metabolic pathway. The lab does this by generating mutations in the genes of sphingolipid metabolic pathway in the mouse and *Drosophila*.
- 2) The objective of the study is to infect MEFs (Mouse embryonic fibroblasts) with the vesicular stomatitis virus (VSV) orsay, (Indiana strain) and VSV tso45 orsay, (Indian strain) and compare the synthesis, maturation, transport and secretion of its cell surface envelope protein (G protein) using immunofluorescence and western blot analysis.
- 3) Identify genes that interact with sphingolipid metabolizing enzymes using shRNAs that will be introduced into MEFs and mouse embryonic stem cells using replication defective lentiviral vectors.
- 4) Study the role of sphingolipid metabolizing enzymes in human cancer cell lines.
- 5) Infect MEFs with the VSV orsay, (Indiana strain) and VSV tso45 Orsay, (Indian strain) and compare the synthesis, maturation, transport and secretion of its cell surface envelope protein (G protein) using immunofluorescence and western blot analysis.

The lead reviewers had much interaction with the investigator and the paperwork is still unclear as to how viral systems will be segregated, how the VSV will be propagated and how lab staff are trained on the hazards involved with the research. It was also noted that this laboratory has had reportable accidents in the past six-years. Dan McVicar moved to defer the registry to the March IBC meeting while he and Steve Hughes worked with the PI to address the concerns of the committee. Bruce Crise seconded the motion. For: 11; Against: 0; Abstain: 0

Anatoli Malyguine 12-12 (P310101MBA02): *Immunological monitoring NIH clinical trials and basic research support* The Laboratory of Cell-Mediated Immunity, Clinical Services Program, within the Applied/Developmental Research Support Directorate, serves as a contract laboratory for immunological monitoring and assay development. The laboratory's mission is to develop, validate and run immunological assays for NCI investigators and the greater NIH community. LCMI has several assays to evaluate adaptive immunity, including cellular proliferation, ELISPOT assays, 51Cr-Release assay, and a flow cytometric-based cytotoxicity assay. Several pre-review questions were still outstanding as of the meeting date; however, the lead reviewers felt that once these clarifications were received, they will address all outstanding concerns they have with the described research. Dan McVicar motioned to defer approval to lead reviewers once the clarifications have been received. Melinda Hollingshead seconded the motion. For: 11; Against: 0; Abstain: 0

Giorgio Trinchieri 12-14 (07-70): *Toxoplasma gondii and the innate response* This proposal involves propagation of the ME49 *Toxoplasma gondii* cysts in mice as a renewable source for infecting experimental animals and involves the injection of ME-49 cysts, RH or TS-4 forms of *T. gondii* into mice. These animals will be euthanized and tissues harvested for examination of cell subsets and function

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during acute phase of infection and other infected animals will be observed long term through a chronic infection for survival. The mice to be used are knockout or mutated lines. The lead reviewers were concerned that the SOP lacked specific information regarding safe handling practices when working with *T. gondii* or specific information for how to inactivate the cysts once experiments were completed. As of the meeting date, the additional information lead reviewers had requested was not received. Dan McVicar moved to defer approval to lead reviewers pending responses to the pre-review questions and training of new lab staff/animal facility staff. For: 11; Against: 0; Abstain: 0

Andy Hurwitz 12-15 (08-38): *Modulating T Cell Activation in the Anti-Tumor and Autoimmune Responses*
The goal of this laboratory is to understand how the immune system can be used to generate immunity to cancer and to understand how immunity to self-antigens (autoimmunity) can be used to elicit tumor immunity. They use several approaches to elicit immunity to melanoma and prostate cancer antigens. In another set of studies, they are testing whether chronic inflammation of the prostate predisposes mice to the development of prostate cancer. The only clarification the committee requested was regarding a cell line that had been previously transduced with a retroviral vector. The committee wanted clarification if an MLV-based retroviral vector was used to make the cell line and if so, they requested the inclusion of a statement regarding potential recombination and mobilization if the cells are injected back into mice. Serguei Kozlov motioned to approve the registry pending the aforementioned clarification. Steve Creekmore seconded the motion. For: 11; Against: 0; Abstain: 0

Eric Freed 12-16 (P150304EFA): *Replication of HIV-1 and Other Retroviruses* The overall goal of the lab, the Virus-Cell Interaction Section (VCIS) of the HIV DRP, is to understand basic mechanisms of retroviral replication at the molecular level, with an emphasis on the late stages of the HIV-1 replication cycle. Specifically, much of the current effort is aimed at understanding HIV-1 Gag trafficking. Most of this work will involve the use of full-length HIV-1 molecular clones that will be transfected into cell cultures to generate viruses for study. The viruses generated will be examined for replicative properties in cell culture using established cell-lines, or primary cells isolated from humans. The lead reviewers commended the PI for his level of detail in both the training regimen and overall registration, in particular with how the various viral systems will be segregated. Dan McVicar moved to approve the registry. Steve Hughes seconded the motion. For: 10; Against: 0; Abstain: 1 (Eric Freed, as this is his laboratory)

Diane Palmieri 12-18 (09-08): *Preclinical drug testing in models of breast cancer brain metastasis* For the past 6 years this group has been studying breast cancer brain metastasis in mouse models. They have established several models and used them to study the biology of brain metastasis and the inhibitory effects of common and experimental drugs for treatment of this disease. The renewal of their animal protocol will continue these experiments, 8 different drugs will be tested as single agents or in combinations in the proposed experiments. Also, they will be using a second model, the 4T1-BR5 cells in these experiments. This model is a syngenic model as the 4T1 cells are a mouse mammary carcinoma cell line. All safety concerns were addressed during the pre-review. The committee had no additional questions. Melinda Hollingshead moved to approve the registry. Steve Creekmore seconded the motion. For: 11 Against: 0 Abstain: 0

Scott Durum 12-19 (09-06): *Regulation of T lymphocyte development and homeostasis by IL-7* The objectives of this study are to evaluate the development of the immune system following transfer of either 1) genetically modified hematopoietic stem cells or a genetically modified mouse cell line or 2) CFSE labeled lymphocytes. The lead reviewers asked for clarification on restraints being used with the animals during injection since a 'hot' oncogene was being injected. Pending that clarification, Eric Freed moved to approve the registry. Melinda Hollingshead seconded the motion. For: 11; Against: 0; Abstain: 0

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OUTSTANDING ITEMS

Stan Kaczmarczyk 12-02 (07-27): 1. Generation of reporter cell lines using retroviral transduction methods; 2). Generation of virus like particles (VLPs) for intra-tumoral protein delivery; 3). Incorporation of alphavirus replicon into virus like particles (VLPs) As of the meeting date, the clarifications from the January meeting had not been received.

Trinchieri/Noer – IBC 11-66 (formerly 10-60) Flow cytometry core lab: A matrix and request form distributed and discussed at January 2012 meeting by Dan McVicar. The full IBC registry, SOPs and previously noted documents were provided to the committee for full review at the February meeting. Dr. McVicar motioned for he and Dr. Mike Baseler to peruse the registration and further discuss decontamination of the BSL2* space with laboratory staff before approval being released. Mike Baseler seconded the motion. For: 10; Against: 0; Abstain: 1 (Theresa Bell had left the room during discussion)

AMENDMENTS

Thirty amendments were processed and approved between the January and February 2012 IBC meetings.

OTHER BUSINESS

- IBC web-registration update – Theresa Bell, Kim DiGiandomenico and Dan McVicar continue to meet with DMS every other week to forward the progress of the web-registration form.
- Human cell lines and animal biosafety level determinations – the committee drafted a matrix to assist with assigning BSL and ABSL on a more consistent basis. The draft will be distributed to committee prior to the March meeting for final review and comment
- Medical surveillance and monitoring for EBV, CMV, XMRV (tabled)

ADJOURNMENT

The meeting was adjourned at 2:10pm.

Next meetings:

March 20, 2012

April 18, 2012 (WEDNESDAY)