

**NCI-FREDERICK  
INSTITUTIONAL BIOSAFETY COMMITTEE  
MINUTES**

**DECEMBER 20, 2011**

**CALL TO ORDER / ANNOUNCEMENTS**

The NCI-Frederick Institutional Biosafety Committee was convened at 12:10 p.m. in Building 549 Executive Board Room with the following members in attendance:

Voting (Quorum = 8)

- |  |  |
|--|--|
| <input type="checkbox"/> Michael Baseler (regrets)       | <input checked="" type="checkbox"/> Sarah Hooper                         |
| <input checked="" type="checkbox"/> Theresa Bell         | <input checked="" type="checkbox"/> Serguei Kozlov (arrived at 12:30 pm) |
| <input checked="" type="checkbox"/> Rev. David Betzner   | <input checked="" type="checkbox"/> Dan McVicar (Chair)                  |
| <input type="checkbox"/> Stephen Creekmore (regrets)     | <input checked="" type="checkbox"/> Randall Morin                        |
| <input type="checkbox"/> Bruce Crise (regrets)           | <input type="checkbox"/> Shalini Oberdoerffer (regrets)                  |
| <input checked="" type="checkbox"/> Eric Freed           | <input checked="" type="checkbox"/> Raja Sriperumbudur                   |
| <input checked="" type="checkbox"/> Melinda Hollingshead | <input checked="" type="checkbox"/> Lucien Winegar                       |
| <input checked="" type="checkbox"/> Stephen Hughes       |  |

Non-Voting

- Walter Hubert (arrived at 12:55pm)
- Kim DiGiandomenico

Other

Capt. Darrell Laroche

**APPROVAL OF MINUTES FROM NOVEMBER 15, 2011 MEETINGS**

The November 15, 2011 meeting minutes were approved as written.  
(A motion and second were made. (For: (10) Against: (0) Abstain: (0))

**ACCIDENT REVIEWS**

There were no accidents to report.

**REVIEW OF PROTOCOLS**

***NEW REGISTRATIONS***

Patricia Steeg / Natascia Marino 11-68: Role of candidate genes downstream to multiple metastasis suppressors on lung colonization by metastatic breast cancer cells The investigator will analyze the function of UGT1A1 and UGT1A9 using the same surgical procedure on the animals (tail vein injection) as described in IBC 11-45. In order to increase the efficacy of the gene down-regulation, instead of using transfection method (as described in 11-45), the investigator used a lentiviral infection method (lentiviral transduction). The lentiviral infection allows the integration of the external DNA, such as the interfering sequences (shUGT1A1 and shUGT1A9), into the cellular genome. Only after two months from the infection (performed in Bethesda) and the appropriate pathogenic testing, the cells will be sent to the animal facility in Frederick. The cells will be injected into the animals through the tail vein. At the end of the experiment, 8-12 weeks, the animal will be sacrificed and their lungs collected in

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order to count the lung metastasis. Theresa Bell moved to approve the registry as presented. Eric Freed seconded the motion. For: 10; Against: 0; Abstain: 0

Frank Cuttitta 11-70: *In Vitro/In Vivo Models of Angiogenesis/Lymphangiogenesis – used to assess anti-angiogenic or anti-lymphangiogenic compounds for the potential clinical management of malignant disease* This is a new IBC submission to evaluate small molecule compounds for their ability to block tumor induced blood vessel formation in nude mouse xenograft models using a variety of human tumor cell lines as targets. Based on how the current registration is written, the committee has concerns with approving the work without further expansion of the animal work. Specifically, these are the concerns: These xenografts can/will come out of these mice infected with xenotropic retrovirus which are capable of infecting humans. This work is not covered by the current paperwork. To include dissection etc., the PI needs to add information about the precautions of tissue harvest from these mice. This would include limiting sharps for the harvest, harvest in BSC, fixations times etc. before the materials go to PHL and how the RNA extraction would be handled safely. Once the animal work is clarified, the edited registry can be approved by lead review, Dan McVicar and Steve Hughes. Theresa Bell moved to approve the registration with clarification. Randall Morin seconded the motion. For: 10; Against: 0; Abstain: 0

**RENEWALS**

Robin Dewar 11-60 (P080494MBA03, P080201RDA02, P080201RDB02): *Virus Isolation and Serology Laboratory: Work with Clinical Specimens from Patients Infected with the Bloodborne Pathogens, Human Immunodeficiency Virus Type I and Type II, Hepatitis B Virus and Hepatitis C Virus* One of the main functions of the Virus Isolation and Serology Laboratory (VISL) is to test clinical specimens from patients with HIV disease or other emerging/re-emerging infectious diseases during their treatment with a variety of antiviral and immunomodulatory agents. To do this, the laboratory receives whole blood, leukapheresed packs, serum, blood plasma, purified PBMC, CNS fluid and biopsies of the gut and lymph nodes for testing. Testing procedures include: Serologic assays to determine seroreactivity to viral proteins, Viral Load assays that quantify virus concentrations in a variety of clinical samples, and Genotyping assays that identify viral subtypes and drug resistance mutations. These procedures require pipetting and centrifugation of clinical samples. Even though this was a renewal registry, some members of the committee expressed concerns with the SOPs and how aerosols may be generated. It was suggested that EHS visit the lab for clarifications on a few of the procedures. Steve Hughes motioned to defer the registry back to full committee via email once the lab visit was completed and reported back to committee. Eric Freed seconded the motion. For: 10; Against: 0; Abstain: 0

Dan McVicar 11-62 (08-74): *Storage of Vaccinia virus Stocks for Later Use* This proposal is for the storage of recombinant Vaccinia virus constructs. These vectors carry receptors or signaling proteins in replication competent Vaccinia viruses. At this time there is no work being done with these viruses. However, as significant resources were used to produce them the PI would like to store the reagents for possible future use. The PI would notify the IBC (via the IBC Administrator and biosafety officer) when active research with the materials commence. There was a question during the pre-review regarding the type of tubes / freezer boxes used for the long-term storage and their integrity. It was determined that there were higher hazards if the contents of the tubes were to be transferred into different storage tubes. In addition, it was confirmed that the freezer used for storage was locked at all times. Steve Hughes motioned to approve the registry. Serguei Kozlov seconded the motion. For: 9; Against: 0; Abstain: 1 – Dan McVicar, as this is his lab

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Dan McVicar 11-64 (05-56): *Retroviral Transduction of Leukocytes and Murine Bone Marrow for the study of Innate Immune Receptors* This proposal involves the use of Lenti-and Retroviral-based vectors for the expression of genes and/or specific gene silencing using shRNA (small sequences of RNA that lead to destruction of endogenous RNA and downregulation of gene expression). These experiments are not underway and details for shRNA studies will follow within an amendment to this protocol. The experiments are largely based on two approaches. The first involves the expression of chimeric and other forms of innate immune receptors and/or Signaling proteins in primary innate immune cells and on cell lines derived from mice some of whom may carry mutations in signal transduction proteins. The second approach involves the construction and use of bicistronic viral constructs that will be used to reconstitute the immune cell compartment under study while incorporating a gene or shRNA of interest. The PI specifies that the only vector system that will go back into mice is the MSCV system. Additionally, the PI plans to keep mice in microisolator caging throughout the experiment. Serguei Kozlov motioned to approve the registry. Eric Freed seconded the motion. For: 9; Against: 0; Abstain: 1 – Dan McVicar, as this is his lab

Dan McVicar 11-65 (08-74): *Signal Transduction of Leukocytes* This work includes the expression of multiple tyrosine kinases, signal transduction proteins such as adaptor proteins and signaling chains, and the immune receptors themselves. In addition, to facilitate the study of signaling, these immune receptors are often modified and/or fused with other known receptors permitting the deployment of reagents previously developed for signaling work. These chimeric receptors are expressed in cell lines, engaged by antibodies or soluble ligands and signaling intermediates are studied. In some cases reporter constructs are used to determine the effects of receptor ligation on specific genetic events. In still other cases, genomic fragments are isolated to study the promoter regions of the receptors and/or signaling proteins. In addition to this work, the group proposes experiments that use Staphylococcal Enterotoxins and Convulxin as super-antigens to study the involvement of multiple receptor/ligand interactions in the regulation of immunity. There were some concerns regarding the toxins being used and how DNA would be sheared. The PI confirmed that protein concentration would not be checked with experiments involving the toxin and also stated that their group only uses 'shredder columns' for shearing DNA, rather than a syringe and needle. The committee felt that the 'blanket roster' provided to the PI for LASP staff involved with his research was not acceptable. Melinda Hollingshead moved to approve the registry once a more definitive LASP roster was provided. Theresa Bell seconded the motion. For: 9; Against: 0; Abstain: 1 (Dan McVicar as this is his lab)

Simone Difilippantonio 11-67 (08-64): *Development of in vitro and in vivo experimental approaches applicable for the generation, analyses, and application in preclinical drug evaluation of genetically engineered mouse cancer models* The Center for Advanced Preclinical Research (CAPR) aims at designing, construction, and validation of a portfolio of genetically engineered mouse models with the aim of exploring such models for evaluation of novel therapeutic compounds and drug candidates available through research and development efforts in both academic laboratories and pharma industry. In the course of the proposed renewal of research activities, CAPR personnel will apply the recombinant DNA methodologies in combination with state-of-the-art cell culture techniques to derive cell lines with genetic defects that predispose such cells to oncogenic growth in the context of transgenic animal tissues. For some methodologies, viral vector technologies are employed. The renewal registry was well written and had minimal questions during the pre-review. Dan McVicar requested for the PI to clarify that the Diphtheria toxin gene noted in B8a is only the alpha chain and cannot gain access to secondary target cells. With this clarification, Dr. McVicar moved to approve the

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registry. Theresa Bell seconded the motion. For: 9; Against: 0; Abstain: 1 – Serguei Kozlov as he is part of the CAPR group.

James Phang 11-69 (08-60): *The proline metabolism in cancer and other diseases* The objective of this research is to determine the importance of proline metabolism, particularly the function of proline oxidase, prolidase, P5C synthase and P5C reductase, in various regulatory processes, including cancer development, progression and apoptosis. The committee expressed concerns with the transport of the materials (potentially containing adeno-infected cells) across campus and then being opened on an open bench. It also was not clear in the documentation what was being performed in vitro and what was being performed in vivo. Melinda Hollingshead moved to defer the registry until further clarification was obtained and for a representative from EHS to visit building 469 to evaluate the area where instrumentation will be used. Dan McVicar seconded the motion. For: 9; Against: 0; Abstain: 1 (Steve Hughes, not present for the vote)

**OUTSTANDING ITEMS**

Jonathan Keller 11-57 (08-67): *Transduction of human hematopoietic cells and cell lines with replication incompetent retroviral vectors* (Hollingshead / Creekmore) Waiting for clarifications from PI

Jonathan Keller 11-58 (08-72): *Hematopoietic Stem and Leukemic Gene Investigation (General Cloning-no viral vectors)* (Baseler / McVicar) Waiting for clarifications from PI

R. Gorelick 11-03-A1 – Hepatitis C Virus work – (Lead reviewer requested full committee review) Steve Creekmore, Steve Hughes, Theresa Bell and Kim DiGiandomenico visited Dr. Gorelick's lab on December 2, 2011 for the mock-run of the HCV work. Unfortunately, the fluorescein was not available and the actual experiments could not be conducted. However, Drs. Creekmore and Hughes discussed the research in greater detail with Dr. Gorelick; and it was decided that Dr. Gorelick would conduct the mock runs on his own to determine any safety flaws in the proposed research, attempt to correct those flaws, and then contact Ms. Bell and/or DiGiandomenico to observe. As of the IBC meeting, no additional correspondence had been received from Dr. Gorelick.

Ji Ming Wang 11-43 (08-53): *The role of mouse G protein receptor FPR2 in infection, inflammation and cancer* (Deferred and project suspended in September) PI provided comments and updates to SOP based on feedback from initial mock observations. Theresa Bell and Melinda Hollingshead conducted a second mock observation on December 15, 2011. Dr. Hollingshead was impressed with the implementation of the suggestions provided by her/Ms. Bell and the IBC. The only outstanding issue, which had been resolved the day of the observation, was the process for final waste disposal. Dr. Hollingshead moved to lift the suspension on the *Listeria* research and reinstate full access to the animal facility. Theresa Bell added to that motion post-approval monitoring in approximately 6 months, once the standard operating procedures of the pathogen challenge room have been modified and implemented. Dan McVicar seconded the motion. For: 10 Against: 0 Abstain: 0

Trinchieri/Noer – IBC 11-66 (formerly 10-60) Flow cytometry core lab: Dan McVicar briefly discussed updates made to the matrix and services request form; but due to time, further discussion was tabled to the January 2012 meeting.

**AMENDMENTS**

Thirteen amendments were processed between the November and December meetings. One remained outstanding as of the meeting date, while twelve were approved.

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**OTHER BUSINESS**

- Membership appointment policy – revised and approved by committee. (For: 9; Against: 0; Abstain: 0)
- Medical surveillance and monitoring for EBV, CMV, XMRV (tabled due to time)
- BSC training (tabled due to time)

**ADJOURNMENT**

The meeting was adjourned at 2:25pm.

*Next meetings:*

*January 17, 2012*

*February 21, 2012*