

NATIONAL CANCER INSTITUTE-FREDERICK (NCI-F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES

MAY 21, 2013

CALL TO ORDER / ANNOUNCEMENTS

The NCI-F Institutional Biosafety Committee was convened at 12:05 pm in Building 549 Executive Board Room with the following members in attendance:

Voting (Quorum = 8)

- | | |
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| <input type="checkbox"/> Michael Baseler (regrets) | <input checked="" type="checkbox"/> Sarah Hooper |
| <input checked="" type="checkbox"/> Theresa Bell | <input checked="" type="checkbox"/> Bhargavi Kondragunta |
| <input checked="" type="checkbox"/> Rev. David Betzner | <input type="checkbox"/> Serguei Kozlov (arrived at 12:15pm) |
| <input checked="" type="checkbox"/> Stephen Creekmore | <input checked="" type="checkbox"/> Dan McVicar (Chair) |
| <input type="checkbox"/> Bruce Crise (regrets) | <input type="checkbox"/> Randall Morin (regrets) |
| <input type="checkbox"/> Eric Freed (regrets) | <input type="checkbox"/> Raja Sriperumbudur (regrets) |
| <input checked="" type="checkbox"/> Melinda Hollingshead (regrets) | <input checked="" type="checkbox"/> Lucien Winegar |
| <input type="checkbox"/> Stephen Hughes (regrets) | |

Non-Voting

- Walter Hubert
- Kim DiGiandomenico

Other

Dr. Ming Zhou (arrived at 1pm/left at 1:30pm)

APPROVAL OF MINUTES FROM APRIL 16, 2012 MEETING

The minutes from the April 16, 2012 meeting were approved as written. A motion and second were made (For: 8; Against: 0; Abstain: 0)

ACCIDENT REVIEWS

No new accidents were reported. Follow-up from the ones presented in April are below:

An LASP worker was bitten by a rat after an oral gavage procedure. The case remained open until it could be determined if the rat had been genetically modified (GMA) prior to the procedure. The rat was not a GMA and therefore, not reportable to OBA.

A post-baccalaureate student punctured her middle finger with a needle while shearing DNA. The injury was not reported to Occupational Health until three days later, and at that time the individual had not notified her supervisor of the injury. It was determined that the needle had previously been used with a lysate of HeLa cells that had been lentivirally transduced with transgenes. The syringe was not full at the time of the incident, but rather had just been used for lysing. An OBA report has been filed and is under review. The IBC recommended that shearing kits be used in place of a needle, and if the kits cannot be used for the purpose of the intended research, then at a minimum, a blunt-ended needle should be used for the shearing.

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REVIEW OF PROTOCOLS

NEW REGISTRATIONS

John Gilly 13-16: Production Hemagglutinin-Ferritin Fusion Protein by Recombinant *Escherichia coli*

The work described in this registration applies to the use of *Escherichia coli* cells to produce a recombinant protein comprised of a fusion between the hemagglutinin (HA) protein of influenza virus and *Helicobacter pylori* ferritin protein hereinafter referred to as HA-Ferritin. There were some questions during the pre-review regarding containment and spills; however, the PI adequately addressed them by revising the SOPs. Steve Creekmore moved to approve the registry as written. Melinda Hollingshead seconded the motion. For: 9; Against: 0; Abstain: 0

RENEWALS

Anne Monks 13-14 (09-34, 09-35): Manipulation of potential drug-target genes with recombinant DNA technology including use of lentiviral based delivery system to express shRNA

This renewal is for the continued use of recombinant DNAs to understand the critical nature of specific targets identified in the response of novel anticancer agents, including use of lentiviral based delivery system to express shRNA (to knock down), or overexpress specific genes identified as potentially critical to the response of novel anticancer agents. For these experiments, the lab does not make their own recombinant DNA; they only purchase pre-made recombinants with the inserts in the vector. Since this was a renewal, there were minimal questions during the pre-review. However, the committee requested for the PI to include a statement in the hazards section acknowledging that some of the cell lines being used, especially the sarcomas, could harbor pro-virus and compliment the lentiviral vector if used in combination. With this addition, Steve Creekmore moved to approve the registry. Theresa Bell seconded the motion. For: 9; Against: 0; Abstain: 0

Howard Young 13-20 (02-08, 04-20): 1) Regulation of Gene Expression in Lymphoid Cells; 2) Use of rDNA for in vivo and in vitro studies

There are two main projects in this renewal. Project 1 involves three parts: the use of mammalian cDNAs encoding genes for cytokines or lymphocyte proteins that will be cloned into a mammalian expression plasmid for subsequent in vivo work, transfection into cells that will be irradiated and introduced into animals for generation of monoclonal antibodies; or transfection into cell lines for the purpose of in vivo expression of the protein of interest with subsequent examination of the effects on the immune system of the rodent and the progression of the tumors in those experiments. Project 2 will analyze the regulation and effects of human/mouse interferons, lymphokines, cytokines, chemokines, kinases and their receptor genes in cell lines, freshly isolated human peripheral blood mononuclear cells, murine NK or T cells and/or transgenic mice. During the lead review, it was clarified that only transfection methods, not transduction, would be used to follow the regulation of cytokines and chemokines and it was confirmed that only murine cells would be used in the in vivo studies. Serguei Kozlov moved to approve the registry. Theresa Bell seconded the motion. For: 9; Against: 0; Abstain: 0

Annamaria Rapisarda 13-37 (10-08): Use of human and animal cell lines in animal studies; Use of lentiviral based delivery system to express shRNA; Use of human and animal cell lines for in vitro research; Use of human and animal tissues and body fluids to study the effect of therapeutic agents; Use of recombinant DNAs for in vitro research

For this renewal, human and animal cell lines will be used in *in vitro* studies to better understand cancer's biology, resistance to therapy, identify novel targets and develop therapeutics that can be ultimately translated in clinical trials. In addition, plasmid DNA containing shRNA sequences or lentiviral vectors will be used to achieve silencing in human cancer cell lines. Lastly, in efficacy studies, mice will be injected with human cancer cell lines and then treated with different anti-cancer agents. It was recommended that EHS visit the lab to determine compliance with containment

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equipment outlined in the SOP. Bhargavi Kondragunta moved to approve the registry with stipulation of a lab visit. Lucien Winegar seconded the motion. For: 9; Against: 0; Abstain: 0 (Post meeting note: lab was visited on 05/22/13. It was indicated that this work is not currently active and EHS will be notified when the project is reinitiated).

Dimiter Dimitrov 13-38 (04-04, 08-20): Developing anti-viral vaccines and human antibodies against infectious diseases and cancer antigens by using recombinant membrane proteins of HIV, Nipah, Hendra, Dengue viruses and cancer antigens The main purpose of the project renewal is to develop human monoclonal antibodies with clinical potentials for treatment of infectious diseases and cancers. The antibodies will be developed with novel recombinant antibody technology and by using recombinant membrane proteins of viruses or targeted cancer antigens. Virus membrane proteins and cancer antigens will be generated with the use of recombinant Vaccinia virus. Vaccinia will be used to promote expression of recombinant proteins in mammalian cells. The primary safety concerns with this registry deal with the use of Vaccinia. The committee requested additional information concerning the detergent that will be used to lyse cells (specify in A1 and B8b1) and how this process will be accomplished. Furthermore, they requested information on how the samples are tested to ensure they are no longer infectious. All materials should be kept and manipulated inside BSC until verification of inactivation. They wanted clarification that up to 10L of cells are first grown and then infected, and how the column used in chromatography is decontaminated. Lastly, they requested a *Vaccinia*-specific SOP, especially since the work is conducted infrequently to ensure that when the work is active, proper safety measures are taken and followed. Additionally, since this work is being performed in a space used for other activities, they wanted the SOP to specify how sufficient decontamination of work space, surfaces, and equipment will be assured. Dan McVicar moved to defer the registry back to lead review pending the aforementioned clarifications. Theresa Bell seconded the motion. For: 9; Against: 0; Abstain: 0

Lino Tessarollo 13-39 (10-14): Generation and analysis of genetically engineered mouse models This laboratory is involved in the generation of mouse models for the entire CCR/NCI scientific community using standard knock-out technology and also has their own research interests focused on the analysis of murine models relevant to study the function of Neurotrophins and their receptors in vivo. There were some questions during the pre-review of this renewal regarding the placement of chemical waste jugs and when they should be disposed as well as use of the UV light inside the biosafety cabinet in the animal facility. EHS offered to visit the animal facility. Bhargavi Kondragunta moved to approve the registry with a follow-up visit from EHS to confirm the aforementioned. Dan McVicar seconded the motion. For: 9; Against: 0; Abstain: 0

Miriam Anver 13-40 (09-23): Support Services on the behalf of NCI investigators in PHL (animal) The Pathology and Histotechnology Laboratory (PHL) provides NCI investigators with histology and Veterinary Pathology services. This renewal is for services offered by PHL including the handling of live animals for collection of blood and body fluids and euthanasia of animals for collection of tissues with the eventual goal being any or all of the following: processing tissues for histologic staining, immunohistochemistry or in situ hybridization, frozen sectioning, DNA or RNA extraction, and pathology evaluation and imaging of slides. There was concern about the use of a razor blade for trimming of tissues. The committee requested an observation of the techniques used in PHL to determine if a safer alternative could be employed. Additionally, the committee requested to see a user request form for how animals/tissues are processed and how it is determined where the respective procedures should occur (i.e. necropsy hood vs BSC). Melinda Hollingshead moved to defer the renewal until the aforementioned could be addressed. Dan McVicar seconded the motion. For: 9; Against: 0; Abstain: 0

Miriam Anver 13-41 (09-41): Support Services on the behalf of NCI investigators in PHL (human) This renewal is for the Pathology and Histotechnology Laboratory (PHL). They provide NCI investigators with

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histology and Veterinary Pathology services. These services include processing of human tissues and cell lines for research purposes for histologic staining, immunohistochemistry or in situ hybridization, frozen sectioning, laser capture microdissection, DNA or RNA extraction, and pathology evaluation and imaging of slides. The committee had no additional concerns with this renewal that were not addressed during the pre-review. Theresa Bell moved to approve the registry. Serguei Kozlov seconded the motion. For: 9; Against: 0; Abstain: 0

John Gilly 13-45 (10-16): Use of HEK 293 Cells for Alphavirus Vaccine Production Tabled until June meeting. Lead reviewers were not present.

Steven Hou 13-46 (10-09): Mouse Models to Investigate Neuron Stem Cell Regulation *Breeding Only_Notification to committee*

Randy Stevens 13-47 (09-43): Repository Support to NIAID-IRC and NIAID-INSIGHT Clinical Trials
The AIDS Monitoring Laboratory (AML), located in building 1066, provides dedicated support for several NIAID-funded human clinical trials conducted by the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) and the NIAID Influenza Research Collaboration (NIRC). The primary function of AML is to receive, inventory, and provide long-term repository storage for frozen clinical specimens obtained from patients participating in several INSIGHT and NIRC clinical trials. The project does *not* involve the receipt or handling of purified pathogen. The frozen clinical specimens are not thawed, the specimen primary containers are not opened, and the specimens are not experimented with or directly manipulated in any other way. The committee had no additional questions or concerns. David Betzner moved to approve the renewal. Serguei Kozlov seconded the motion. For: 9; Against: 0; Abstain: 0

Andy Hurwitz 13-49 (08-39, 08-58): Leukocyte Function in Human and Murine Tumors The goal of this lab is 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, including viral vector technology. There was some confusion for how the adenoviral vector was being used in the research and the committee requested further clarification. Melinda Hollingshead moved to approve the registry pending the aforementioned clarification. Theresa Bell seconded the motion. For: 9; Against: 0; Abstain: 0

Dan McVicar 13-50 (10-26): Maintenance & production of mutant mouse strains for the study of the role of inflammation in the pathogenesis and therapy of cancer *Breeding Only_Notification to committee*

OUTSTANDING ITEMS

Ming Zhou 13-36: Mass spectrometry analysis on clinical and cultured cell line samples The PI attended the May meeting, which greatly assisted with clarifying various aspects of the project which were still not captured in the IBC registry. Theresa Bell and Kim DiGiandomenico offered to summarize the IBC/PI discussions and correspond with the PI to get the paperwork in order. Dan McVicar motioned to defer final approval back to lead reviewers once the documents are revised. Bhargavi Kondragunta seconded the motion. For: 9; Against: 0; Abstain: 0

Jeff Green 13-43: In vivo expression of GFP and IL12 in a syngeneic murine mammary tumor model using VLP technology / Stan Kaczmarczyk 12-02-A2 The committee felt the work would be best covered under Stan Kaczmarczyk's IBC registration (12-02), since his lab is generating the VLPs, and requested for Jeff Green's animal work to also be amended to the 12-02 registry. As a result, the initial submission, 13-43, was withdrawn.

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AMENDMENTS

Fifteen amendments were processed and approved between the April and May IBC meetings.

OTHER BUSINESS

The observation for Robin Dewar's IBC renewal (IBC 13-24) was conducted on April 30, 2013. The observation was a condition of her approval. Theresa Bell participated in the visit and had a few suggestions for conducting some of the research in a safer manner. Overall, there were no major concerns with the observed techniques.

ADJOURNMENT

The meeting was adjourned at 2:27pm.

Next meetings:

June 18, 2013

July 16, 2013