

**NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES**

MARCH 20, 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 type="checkbox"/> Sarah Hooper (regrets) |
| <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 type="checkbox"/> Randall Morin (regrets) |
| <input checked="" type="checkbox"/> Bruce Crise | <input checked="" type="checkbox"/> Shalini Oberdoerffer |
| <input checked="" type="checkbox"/> Eric Freed | <input checked="" type="checkbox"/> Raja Sriperumbudur (left at 1:00pm) |
| <input type="checkbox"/> Melinda Hollingshead (regrets) | <input type="checkbox"/> Lucien Winegar (regrets) |
| <input checked="" type="checkbox"/> Stephen Hughes | |

Non-Voting

- Walter Hubert
- Kim DiGiandomenico

Other

Rose Saad, Clinical Staff - Occupational Health Services

APPROVAL OF MINUTES FROM FEBRUARY 21, 2012 MEETING

The minutes from the February 21, 2012 meeting were approved as written. A motion and second were made. (For: 8; Against: 0; Abstain: 0)

ACCIDENT REVIEWS – No accidents to report

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

Andy Stephen 12-10: Analysis of the metabolic state of tissue culture cells The objective of this registry is to outline a service where NCI staff can use the Biosciences Seahorse XF24 flux analyzer to measure the metabolic state of their tissue culture cells. The XF-24 is an instrument that measures the oxygen consumption rate and acidification rate of tissue culture medium and hence gives information about the metabolic state of the cells. Lead reviewers and the IBC Administrator worked closely with this PI to establish his registry for this service. Aside from needing to reference the SOPs throughout the registry, Bruce Crise moved to approve the registry. Steve Creekmore seconded the motion. For: 10; Against: 0 Abstain: 0

Karlyne Reilly 12-21: Manipulation of gene expression through overexpression and knockdown in mouse and human cells This group is studying how modifier genes affect cancer development using cell techniques and animal models. For in vitro studies, they will overexpress candidate modifier genes using plasmid and lentiviral vectors to observe how changing levels of the protein affect normal and tumor cell phenotypes. Alternatively cells are generated from mice carrying floxed alleles of the candidate genes and will be treated with Adenoviral-Cre in culture to lose gene expression. No adeno- or lenti-transduced cells are used in

NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
March 20, 2012

animals. The committee wanted the PI to include statements in the registry regarding the potential genotoxicity of Cre as well as a higher likelihood for RCA in the Adeno-Cre preps, since they are not tested for RCA by the supplier. With these clarifications included in the registry, Serguei Kozlov moved to approve the registry. Bruce Crise seconded the motion. For: 10; Against: 0; Abstain: 0

Siba Bhattacharyya 12-25: *In vitro* evaluation of radiotracers with cell lines in CIP scientific support laboratory
The CIP Scientific Support Laboratory, Applied and Developmental Research Directorate, provides support to the Cancer Imaging Program of DCTD with development of radio-imaging probes for preclinical and clinical studies. This work will be performed as a part of the preclinical evaluation of the imaging probes. This group has developed radioisotope labeled probes for cancer imaging. In-vitro studies with cell lines need to be completed to determine the suitability of the radio labeled probe for in vivo studies. Theresa Bell brought to the committee's attention that there was a recent publication by Sandy Ruscetti's lab regarding the NCI-60 cell line screen, which is also used in this study. Dr. Ruscetti published that one of the cell lines, EK VX, tested positive for murine retrovirus and for the time being, this cell line has been removed from the NCI-60 panel until additional information is obtained. Some committee members felt that the contamination of the cell line most likely occurred because it had previously been passed through mice. Eric Freed moved to approve the registry. Theresa Bell seconded the motion. For: 10; Against: 0; Abstain: 0.

Ji Ming Wang 12-30: *Use of normal human blood cells for studies of inflammation and cancer in vitro*
This registry is for the use of human peripheral blood neutrophils, monocytes and lymphocytes to study the immune response. While the registry provided the minimum information of what was needed, the committee was concerned with the lack of detail in the SOP regarding safety guidance and the use of human materials, considering the amount of time spent on SOP development with the PI on a prior IBC submission. Theresa Bell also suggested unannounced, post-approval monitoring for this lab based on prior history. Dan McVicar moved to defer the registration pending better SOP development as well as post-approval monitoring. Theresa Bell seconded the motion. For: 10 Against: 0 Abstain: 0

RENEWALS

Ding Jin 12-17 (09-25): *Transcription Regulation in E. coli (K12) and H. pylori*
This renewal is to continue basic research on E. coli K12, a non-pathogenic bacterium, and Helicobacter pylori. For H. pylori, the group will study the gene regulation and transcription regulation in bacterial pathogenesis. The following subset of projects apply to the H. pylori work: 1) Grow H. pylori cultures under different growth conditions in the lab. 2) Study the interaction between H. pylori and several established cell lines. 3) Study the interaction between H. pylori and neutrophils and macrophages to be isolated from human whole blood and mice; and 4) Infect mice with H. pylori (in collaboration with Dr. Ji Ming Wang) to study bacteria pathogenesis. The committee agreed that the paperwork was lacking a safety-oriented SOP as well as relevant details in the main body of the registration form, and that a separate IBC should be provided by Dr. Wang for the administration of H. pylori into mice, since his lab would be conducting those experiments. Dan McVicar summarized the motion as follows: 1. Defer the registration and in vivo work with H. pylori until both groups can establish and demonstrate that operational, safety-oriented protocols have been established; and 2. conduct a successful demonstration of the in vivo work, which will be reported by EHS back to the IBC. Bruce Crise seconded the motion. For: 9 Against: 0 Abstain: 0 (Post-note: PIs were notified of the delay of in vivo research on April 2, 2012)

Scott Durum 12-23 (09-06): *Effects of cytokine-expressing bacteria on the development, progression and treatment of inflammatory bowel disease and colon cancer (L. lactis)* – deferred due to lack of response from PI during pre-review

Howard Young 12-26 (09-57): *The role of probiotics in murine models of cancer and gut inflammation and as vaccine delivery agents (Lactobacillus/ Lactococcus)*
This renewal registration describes three different applications of the use of *Lactobacillus/Lactococcus sp.* to alter the mouse response to inflammation and

NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
March 20, 2012

tumor development. 1. The purpose of the first proposal will be to determine if the administration of genetically modified *Lactobacillus sp/Lactococcus sp.*, common gut microorganisms, can alter the gut microenvironment and block the initiation, development or progression of inflammatory bowel disease or colon cancer; 2. As an adaptation of the above project, *Lactobacillus acidophilus* that has been engineered to express mouse interferon-beta will be injected directly into solid tumors; and 3. *Lactobacillus/ Lactococcus sp.* will be used to deliver foreign antigens to the host in order to determine if an immune response to the foreign antigens can be generated. While the lead reviewers were not overly concerned with the bacteria being used for the studies, they still wanted the PI to have lab staff wear gloves at all times while manipulating materials and requested for that to be revised in the SOP. Additionally, it was difficult to follow what materials were going into what, and they felt that the use of a table or better clarification would help to depict this. Lastly, they wanted the PI to include a statement acknowledging the potential for transfer of the erythromycin resistance plasmid to endogenous bacteria in the gut of experimental animals. Theresa Bell would also confirm with NIH/OBA that the transfer of antibiotic resistance in the organism did not require RAC review. Shalini Oberdoerffer moved to approve the registry pending clarifications as previously noted. Mike Baseler seconded the motion. For: 9; Against: 0; Abstain: 0 (Post-note: This research did not require RAC review)

OUTSTANDING ITEMS

Trinchieri/Noer – IBC 11-66 (formerly 10-60) Flow cytometry core lab: Dan McVicar and Mike Baseler met with the PI to further discuss decontamination of the BSL2* space with laboratory staff before approval being released. Prior to the March meeting, a request had been received by this lab to sort Vero cells (an established non-human primate (NHP) cell line). Per committee discussion and vote, established NHP cell lines would be sorted as if they were well established human cells and be handled at BSL2*. Finalized documents from the PI were still needed as well as a on-site visit to the lab being used at BSL2* so that approval could be released.

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) Clarifications from the January meeting were received and distributed back to full committee for approval. Dan McVicar moved to approve the registry as revised. Steve Hughes seconded the motion. For: 9; Against: 0; Abstain: 0

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.

NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
March 20, 2012

(February 2012 meeting) 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 (March 2012 meeting) – Dan McVicar had met with the PI after the February meeting to discuss the committee’s concerns. As of the March meeting, however, revised IBC documents had not been received. The registry continues to be in ‘deferred’ status.

Anatoli Malyguine 12-12 (P310101MBA02): Immunological monitoring NIH clinical trials and basic research support The PI responded to the outstanding questions lead reviewers had prior to the meeting. Lead review released approval.

Giorgio Trinchieri 12-14 (07-70): Toxoplasma gondii and the innate response Thirteen laboratory and LASP staff received *Toxoplasma gondii* training on February 29, 2012. The PI responded to the outstanding questions lead reviewers had prior to the March IBC meeting. Lead review released approval.

AMENDMENTS

Seventeen amendments were processed and approved between the February and March 2012 IBC meetings.

OTHER BUSINESS

- REMINDER: April IBC meeting is on WEDNESDAY, April 18th in the 549 EBR 12:00 – 3:00pm
- IBC Membership – A member of the VPP technology development group expressed interest in becoming a member of the Frederick IBC. Dr. Dan McVicar would like to meet with her prior to making the recommendation to Dr. Craig Reynolds that she be offered an invitation to join the committee.
- 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. A sub-committee including Theresa Bell, Kim DiGiandomenico, Dan McVicar, Steve Hughes, Bruce Crise and Serguei Kozlov was organized to discuss the form and projected display of data that is input by the PI. This information will be presented back to DMS for discussion at their next bi-monthly meeting.
- 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 was distributed to committee and with a few minor changes was adopted and approved by the committee. Dan McVicar motioned to approve the matrix pending the revisions. Serguei Kozlov seconded the motion. For: 9; Against: 0; Abstain: 0.
- Medical surveillance and monitoring for EBV, CMV, XMRV (tabled)

ADJOURNMENT

The meeting was adjourned at 2:10pm.

Next meetings:

April 18, 2012 (WEDNESDAY)

May 15, 2011