

NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
NOVEMBER 17, 2015

CALL TO ORDER / ANNOUNCEMENTS

The NCI at Frederick Institutional Biosafety Committee was convened at 12:00 pm in Building 426 Conference Room with the following members in attendance:

Voting (Quorum = 8)

- Michael Baseler (*regrets*)
- Theresa Bell
- Rev. David Betzner
- Stephen Creekmore
- Bruce Crise
- Eric Freed (*regrets*)
- Melinda Hollingshead
- Stephen Hughes (*regrets*)

- Sarah Hooper (*regrets*)
- Serguei Kozlov
- Dan McVicar
- Bradley St. Croix
- Lucien Winegar
- Sharon Altmann (*regrets*)
- Robin Sun
- Jatinder Gulani

Non-Voting

- Walter Hubert
- Karen Barber

Visitors

Gillian Braden-Weiss
Ted Witte

APPROVAL OF MINUTES FROM THE SEPTEMBER 15 MEETING

The minutes from the October 20, 2015 meeting were approved with minor corrections. A motion to approve and a second were made. (For: 9; Against: 0; Abstain: 2)

ACCIDENT REVIEWS :

NHP worker – Bethesda – Bite by NHP: A long-term employee was transferring a Non-human primate from a dirty cage to the clean cage. There were two primates to a dirty cage. The procedure is to take the dirty cage and set it against the clean cage and get one of the two primates in the clean cage. During this procedure, however, both primates tried to enter the clean cage and one got loose. As the employee was trying to catch the loose primate, it bit him.

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

- None presented.

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RENEWAL REGISTRATIONS

- ❖ Daniel McVicar/Jonathan Weiss – 15-49 (11-62): Long term storage of vaccinia virus 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 and no work has been done with these for many many years. However, as significant resources were used to produce them we would like to store the reagents for possible future use. When the time comes that we want to use this material, a full IBC registration will be completed and approved prior to working with the material. The Vaccinia used here is replication competent and a true human pathogen. A motion to approve was made by Theresa Bell and seconded by David Betzner. (For: 8; Against: 0; Abstain: 3)
- ❖ Stephen Lockett – 15-50 (old 14-22 – renewing 08-46): **Notification only.** This registration has been approved, however, we gave it a 2015 number.
- ❖ Ying Zhang – 15-51 (12-64): TGF-beta/Smad Signaling. **Notification only.** Breeding protocol. (Approved by Hollingshead)
- ❖ Brunilde Gril – 15-52 (12-18, 13-33): Models for breast cancer brain metastases. We successfully developed different models of brain metastases of breast cancer using different human cell lines of breast cancer. Those cells are: MCF7-HER2-BR (approved in the IBC #07-12 and renewed in IBC#10-03, renewed in IBC # 13-33), the JIMT-1-BR3-GFP-Luc approved in the IBC#10-03-A2, and the SUM190-BR-GFP-luc, approved in the IBC #09-46-A2, both renewed in IBC # 13-33. The 231-Br-eGFP, 231-Br-eGFP-PC, 231-br-eGFPHER2 and 4T1-BR5 are brain seeking variant developed and approved in IBC # 12-18. More recently we added a modification to IBC 13-33 to add the murine carcinoma E0771 to develop a brain metastases variant of it. Breast cancer is a very heterogeneous disease and the brain metastases which results form it are also very heterogeneous. To represent this heterogeneity observed in patients, we need to work with all these distinct models. Those three cell line are used in the ASP# 14-057. This ASP was initially written to study the effect of drugs such as tyrosine kinase inhibitor (lapatinib and pazopanib) and therefore is entitled “Lapatinib and Pazopanib treatment of Her-2 mediated brain metastases”. However, we added different amendments to this protocol and now we are using it to study the blood-brain barrier permeability. A motion to approve was made by Dan McVicar and seconded by Melinda Hollingshead. (For: 9; Against: 0; Abstain: 2)
- ❖ Rosalba Salcedo – 15-53 (12-60): Cancer and Inflammation Program. Chronic inflammation is associated with highly increased incidence in epithelial cancer. Tumors arise in sites of chronic inflammation, and tumor cells themselves can secrete a large profile of pro-inflammatory mediators within the tumor microenvironment. By utilizing several models of carcinogen and inflammation-associated carcinogenesis, we are investigating the roles of inflammatory mediators and the microbiome in cancer promotion, progression and cancer therapy. In addition we are

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investigating the effect of the microbiota in cancer cachexia, which is a multifactorial syndrome associated with systemic inflammation.

The above research is covered by 3 different ASPs as indicated below:

Project #1. Role of inflammation on Carcinogenesis [ASP 12-450]. Under this ASP several carcinogens are used in colon and skin carcinogenesis models.

Project #2: The role of microbiota in development of cancer cachexia [ASP 12-460]. Under this ASP we use murine tumor cell lines.

Project #3: Basic Research Protocol-Immunomodulation and Immunotherapy in naïve and tumor bearing mice [ASP 13-226]. Under this ASP several murine cell lines and recombinant DNA are used. There is significant overlapping in the materials used under all these ASPs regarding the cell lines, mouse strains, DNA plasmids and biologicals (antibodies, antibiotics, LPS, etc). The carcinogens are specific to ASP 12-450. A motion to approve, with minor clarifications and an observation to be scheduled, was made by Steve Creekmore and seconded by Theresa Bell. (For: 9; Against: 0; Abstain: 3).

- ❖ Drs. Pavlakis and Felber – 15-13 (07-01): Use of lentiviral/retroviral vectors for gene transfer into mammalian cells. The objective is to use lentiviral/retroviral vectors as vehicle for gene transfer into mammalian cell lines. We use this system to insert a gene of interest into the packaging vector, generate pseudotyped virions and generate stable modified cell lines. The advantage of using these systems is that only a few copies of a gene of interest are integrated. Lentiviral/retroviral vector systems consists of 3 independent plasmids expressing (a) the gene of interest such as cytokines, cytokine receptors, HIV/SIV genes; (b) the packaging signal and the marker gene like luciferase or Green Fluorescent protein GFP and/or a selection marker like neomycin; (c) the gene for one single round of replication such as env (VSV-G to enter any cells). For this reason, the pseudotyped virions are only competent for a single round of infection. The separation of the packaging signal, LTRs and gag/pol and env genes into separate plasmids eliminates the chance of recombination. The plasmids are obtained either from other investigators or are generated by us. A combination of the respective plasmids is transiently transfected into human 293 cells (this work is performed in the BSL-2* facility) and the supernatant is directly used to infect the cell line of interest such as HEK293 and primary murine cells. We generate stable cell lines (i.e. selecting for neo resistant cells), generating i.e. cell lines expressing the co-receptors CCR5, CXCR4, cytokine, cytokine receptors, or any gene of interest. ***A motion to defer this registration to schedule a meeting with the PI was made by Serguei Kozlov and seconded by Theresa Bell.*** (For: 9; Against: 0; Abstain: 2)

OUTSTANDING ITEMS

- ❖ Ji Ming Wang – 14-46: The role of mouse mFPR2 in the pathogenesis of Helicobacter Pylori. H.pylori infects human stomach to cause inflammation and sometime H.pylori produces peptides that activate a G-protein coupled receptor FPR2 in human and mFPR2 (in mouse, also termed Fpr2) to induce migration of neutrophils and monocytes, therefore may establish a basis for inflammation. The purpose of this proposal is to use mice deficient in Fpr2 to examine their

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susceptibility to H.Pylori-induced stomach inflammation and potential cancer. A motion to approve with the clarification that a mock observation is to be performed before work begins. ***PI has put this observation on hold due to new staffing and the PI to return to the country. A mock observation to be performed before work can commence.***

AMENDMENTS

Thirty amendments were processed and approved between September and October IBC meetings.

OTHER BUSINESS

- **VINAY VYAS HAS EXTENDED AN INVITATION TO THE COMMITTEE TO ATTEND A TOUR OF THE BDP FACILITY AT THE ATRF. SCHEDULING OF THIS TOUR IS IN PROGRESS.**

ADJOURNMENT

The meeting adjourned at 12:50 pm.

Next meetings: December 15, 2015 January 19, 2015