

NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
OCTOBER 20, 2015

CALL TO ORDER / ANNOUNCEMENTS

The NCI at Frederick Institutional Biosafety Committee was convened at 12:00 pm in Building 549 Executive Board Room with the following members in attendance:

Voting (Quorum = 8)

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

Sarah Hooper
 Serguei Kozlov
 Dan McVicar

 Lucien Winegar
 Sharon Altmann (regrets)
 Robin Sun

Non-Voting

Walter Hubert
 Karen Barber

Visitors

Gillian Braden-Weiss

APPROVAL OF MINUTES FROM THE SEPTEMBER 15 MEETING

The minutes from the September 15, 2015 meeting were approved. A motion to approve and a second were made. (For: 10; Against: 0; Abstain: 1)

ACCIDENT REVIEWS :

NHP worker – Bethesda – needlestick – need more information.

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

- ❖ Terrence Burke – 15-45: Peptidomimetic Inhibitors Targeting the Polo-like Kinase 1 Polo-Box Domain. This project encompasses the design, synthesis, and evaluation of peptidomimetic inhibitors targeting the polo-box domain of polo-like kinase 1. Novel peptide and small molecule inhibitors are generated using synthetic organic and peptide chemistries. These compounds are then evaluated for inhibition using lysate- and cell-based assays against Plk1. A motion to approve, pending clarification on the labs biosafety level designation, was made by Serguei Kozlov and seconded by Dan McVicar (For: 10; Against: 0; Abstain: 0)

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- ❖ Daniel McVicar – 15-46: Innate immunity to fungal infections. Our laboratory now studies the innate immune response and the regulation of inflammation in the context of metabolism. Specifically we study the metabolic basis for immune cell function in the response of innate immune cells to stimulation with pro-inflammatory stimuli. We have recently found that macrophages require immediate use of their mitochondrial electron transport chain to produce a respiratory burst to phagocytosed Zymosan, a preparation of yeast cell wall components. In this protocol we will challenge in-vitro macrophages with *Candida albicans* or *Saccharomyces cerevisiae* with and without drug treatment. These drugs are the well-used electron transport complex inhibitors rotenone, TTFA, antimycin A, along with the glucose analogue 2-DG and the pentose phosphate pathway inhibitor DHEA. Additionally, mice will be challenged with *Candida albicans* or *Saccharomyces cerevisiae* 7 days after peritoneal infection with lentiviruses containing shRNA against the electron transport protein *Sdha* or nonsilencing control. See 2015-39 / 11-64 for the initial lentiviral protocol, mice after 7 days will have cleared virus, but shall be kept under the lentiviral SOP for the remainder of this experiment (up to 1 week later). A motion to approve was made by Serguei Kozlov and seconded by Rev. Betzner. (For: 9; Against: 0; Abstain: 1)

- ❖ Simone Difilippantonio – 15-47: Pre-clinical study of HPV vaccine immunogenicity: serological responses to L2 peptide. This is a new IBC registration. The project proposed in this submission will involve work with mice. The work with the animals will not be performed in the Human Papillomavirus (HPV) Immunology Laboratory (Building 469/ Rm 111) nor by the staff members of this laboratory. Instead, the work will be performed through the Laboratory of Animal Sciences Program within an animal facility located in Building 539-1CC under the supervision of Principal Scientist, Dr. Simone Difilippantonio. Dr. Ligia Pinto, a Principal Investigator and head of the HPV Immunology Laboratory, will be working closely with Dr. Difilippantonio to conduct this project. The scope of the work will involve vaccination of mice with a non-infectious HPV vaccine. The vaccine under this study is composed of late (L) 1 protein-based virus-like-particles (VLP) of HPV16 (HPV16 L1 VLP), which is also contained in the U.S. Food and Drug Administration-approved HPV vaccines, Gardasil and Cervarix. But in addition, there is a short amino acid sequence from late 2 (L2) protein (positions 17-36) inserted into the part of HPV16 L1 VLP that has a high potential to be seen by the immune system. Like the approved vaccines, this new HPV vaccine (RG1- HPV16 VLP; J Invest Dermatol 2013 133, 2706-2713) is not infectious, as it does not contain any genetic materials inside. Like Gardasil and Cervarix, it is composed of only proteins. The RG1-HPV16 VLP vaccine is also scheduled to be tested in a phase I clinical trial. The primary tasks of this project are: 1) to immunize mice with RG1-HPV16 L1 VLP vaccine (animal protocol is under review), and the vaccine will be provided by NCI and has been contracted to Paragon Bioservices (Baltimore, MD) for production; and 2) to collect serum from vaccinated mice and store them at -80° C. The frozen samples of serum collected from these animals will be transported to the HPV Immunology Laboratory. A motion to approve was made by Melinda Hollingshead and seconded by Serguei Kozlov. (For: 10; Against: 0; Abstain: 0)

- ❖ Jayanta Sinha – DRAFT: Production of Respiratory Syncytial Virus (RSV) vaccine containing the stabilized prefusion RSV viral antigen DS-Cav1 using Chinese Hamster Ovary (CHO) cells. Respiratory syncytial virus (RSV) infects nearly all children by 3 years of age and is a leading cause

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of infant hospitalization and childhood wheezing (Barney et al., 2013). Respiratory syncytial virus (RSV) is a virus that primarily infects infants and the elderly. Currently, there is no licensed vaccine for Respiratory Syncytial Virus (RSV). The VRC has identified a promising immunogen, devised and engineered a coding sequence that consistently generates it, evaluated it in animal models, and developed and transferred manufacturing processes to produce it for clinical trials. Of its three surface proteins, F, G, and SH (short, hydrophobic), only the F protein is essential for infectious virus. RSV F protein, like multiple other Type I viral fusion proteins, adopts distinct metastable prefusion and stable postfusion conformations. Knowledge of these two key facts led VRC researchers to pursue the possibility of eliciting prefusion F-specific, RSV-neutralizing antibody responses as the basis for an RSV vaccine that expresses an stable prefusion-conformation F protein, termed DS-Cav1 (Di-Sulfide; Cavity, first nonclinical molecule). A motion to approve was made by Serguei Kozlov and seconded by Theresa Bell. (For: 10; Against: 0; Abstain: 0)

RENEWAL REGISTRATIONS

- ❖ Dr. S. Perwez Hussain – 15-44 (12-70): The development and cross breeding of genetically altered mice strains and spontaneous tumorigenesis. This proposal covers all the breeding performed in the facility by the investigators of the Laboratory of Human Carcinogenesis (LHC). APPROVED.
- ❖ 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: 10; Against: 0; Abstain: 0)

OUTSTANDING ITEMS

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- ❖ Stephen Lockett – 14-22 (08-46): Ras project 3 and CCR support. Discovery methods to directly target oncogenic Ras protein, and live and fixed cell fluorescence labeling in support of CCR research. A motion to defer final approval pending clarifications to a sub-committee of lead reviewers was made by Dan McVicar and seconded by Theresa Bell. (For: 10; Against: 0; Abstain: 0)

- ❖ 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 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. Mock observation to be performed before work can commence.***

AMENDMENTS

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

OTHER BUSINESS

ADJOURNMENT

The meeting adjourned at 1:20 pm.

Next meetings: December 15, 2015 January 19, 2015