NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
FEBRUARY 24, 2015

CALL TO ORDER / ANNOUNCEMENTS

The NCI at Frederick Institutional Biosafety Committee was convened at 12:05 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
- ☒ Melinda Hollingshead
- ☐ Stephen Hughes *(regrets)*
- ☒ Sarah Hooper
- ☐ Serguei Kozlov *(regrets)*
- ☒ Dan McVicar
- ☒ Raja Sriperumbudur
- ☐ Lucien Winegar *(regrets)*
- ☐ Sharon Altmann *(regrets)*

Non-Voting

- ☐ Walter Hubert *(regrets)*
- ☒ Karen Barber
- ☐ Matthew Nawn *(regrets)*

APPROVAL OF MINUTES FROM THE NOVEMBER 18 MEETING

The minutes from the January 20, 2015 meeting were approved. A motion and second were made. (For: 10; Against: 0; Abstain: 0)

ACCIDENT REVIEWS : Nothing to report

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

- Thomas Doebel – 15-01 – Homeostasis of the skin immune system under germ free conditions. To understand how immune responses are regulated in skin, in particular, how the skin immune system is established and maintained after birth. This study will explore a novel immunological aspect of the hair follicles, and determine whether they could provide specialized niches for skin resident leukocyte precursors, in which direct or indirect interactions with the hair follicle microbiome stimulates proliferation and maintenance of Langerhans cells. A motion to approve with minor changes was made by Bruce Crise and seconded by Melinda Hollingshead. (For: 10; Against: 0; Abstain: 0)
- Vinay Vyas – 15-11 – Process development of RLIP76 – A radiation countermeasure - RLIP76 is being developed as a radiation countermeasure for NCATS (National Center for Advancing Translational Sciences, NIH). RLIP76, is a naturally occurring, membrane-associated human transport protein being produced in E. coli using a recombinant expression plasmid. RLIP76 is a

single chain, 655 amino acid, nonglycosylated amphipathic protein of 76,063 Da. The protein is slightly acidic, with theoretical pI of 5.68, and hydrophobic. RLIP76 has a membrane binding domain and two ATP binding sites, as well as several other known domains important for modulation of biological functions such as protein expression and endocytosis. In solution, RLIP76 assembles into a high molecular weight multimeric complex with a mean hydrodynamic diameter determined by dynamic light scattering of approximately 100 nm. RLIP76 is an endogenous, transmembrane-associated protein that is active in the clearance pathway for reactive oxygen species. The objectives of the project for this milestone/feasibility phase are:

- Fermentation process development to optimize production and yield
- Purification process development which includes optimization of various chromatographic steps, and
- Product Evaluation and Assay development

An amendment will be submitted to the IBC, if this project progresses beyond the initial R&D stage to the Clinical Manufacturing phase. Attachment I provides more details of the tentative process

A MSDS (Material Safety Data Sheet) is available with the company (Terapio Corp.) and will be attached to this submission as soon as it becomes available to the BDP. A motion to approve was made by Eric Freed and seconded by Dan McVicar. (For: 9; Against: 0; Abstain: 1)

- Raja Sriperumbudur – 15-08 – Breeding and cohort production of mouse models for leopard syndrome - Leopard syndrome (LS) is a rare, autosomal dominant, multisystem congenital anomaly caused mainly due to mutations in the gene PTPN11 and affecting the cutaneous, skeletal and cardiovascular systems. Pre-clinical drug studies utilizing two mouse models (Y279CPtpn11 and Q510E-Shp2) ofLS, which are focused on the development of therapies for hypertrophic cardiomyopathy (HCM), a manifestation seen in over 70 % of LS patients, will be conducted by LASP in response to a Yellow task request. The primary objective of this study is to characterize and validate the efficacy of two candidate pharmaceutical agents (rapamycin and afinitor) in treating HCM pathogenesis as the basis for subsequent clinical testing in LS patients. In order to produce cohorts for experiments, we need to breed heterozygous mutant mice with wildtype littermates. These breeders will be the foundation for colony maintenance as well as production of mutant males (up to 16) used in IVF procedures for the generation of experimental cohorts for future studies conducted for the National Center for Advancing Translational Sciences (NCATS), a NIH institute. A motion to approve was made by Eric Freed and seconded by Dan McVicar. (For: 10; Against: 0; Abstain: 0)

RENEWAL REGISTRATIONS

- 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 the work begins. Motion made by Melinda Hollingshead and seconded by Steve Creekmore. *The PI has put the observation on hold until he completes his staffing. It is understood that no work will commence until the observation has been performed by Safety.* (For: 108; Against: 0; Abstain: 0)

- Amy Hutchinson – 14-47 – DNA Extraction & Staging Lab (DESL)- The DNA Extraction and Staging Laboratory is responsible for extraction of nucleic acids (DNA and RNA) from a variety of human-derived source materials including but not limited to whole blood, various blood products, saliva, and tissue (both frozen and fixed). DNA is then QC's and prepared using an automated staging pipeline for use in downstream applications such as sequencing and genotyping. A motion to defer for further clarification was made by Eric Freed and seconded by Mike Baseler. (For: 10; Against: 0; Abstain: 0)
- Stefan Ambs – 15-02 (11-41) – Nicotine-induced extraprostatic disease spread int eh TRAMP mouse model of prostate cancer. To study whether low-dose nicotine treatment induces accelerated lung metastasis in TRAMP mice. A motion to approve was made by Raja Sriperumbudur and seconded by Melinda Hollingshead. There is no current ASP. The PI must submit an ASP and have it approved by the ACUC before work can begin. (For: 10; Against: 0; Abstain: 0)
- Ira Daar – 15-03 (11-12)- Proto-oncogene Signal Transduction. Our laboratory examines the signaling pathways involved in morphogenetic events during development. Our model system is Xenopus laevis, but we use mammalian tissue culture as well. We use prokaryotic vectors to subclone genes involved in this process and use in vitro tanscription of RNA that we inject into Xenopus oocytes. The oocytes are then examined biochemically (western analysis, immunoprecipitation immunofluorescence). In tissue culture cells we express proteins for the same purpose using pCS2+ vector and typical transfection using Fugene6. For expression of RNAi in established human cell lines we use a lentiviral vector (pLK0.1). Generally, we express proteins which are harvested and analyzed by immunoprecipitation and Western analysis. A motion to approve was made by Steve Creekmore and seconded by Dan McVicar. (For: 10; Against: 0; Abstain: 0)

OUTSTANDING ITEMS

- Peter Gorelick – 14-26 (08-27). Serological diagnostic testing of non-human primates for the presence of potentially adventitious viruses - Diagnostic serological testing for routine health monitoring of NHPs. (Bell) Deferred to full committee in August. Awaiting additional documentation.

- 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. (Zudaire/Hughes/Altmann) Deferred to full committee in August. Awaiting additional documentation. ***ON HOLD. WAITING ON CHANGES IN THE DEPARTMENT BEFORE SUBMITTING***. **As of October 14, 2014, no updates have been made.**

- 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.* Committee requested additional clarifications and a Vaccinia-specific SOP as well as a lab visit. Post-meeting, Theresa Bell learned that the lab was relocating and suggested that the space that will be used for the Vaccinia work should not be evaluated until the move has been completed. No Vaccinia work is being performed at this time. **Approved. Need to visit lab space once moved for Vaccinia work**. For: 8; Against: 0; Abstain: 0

AMENDMENTS

Twenty five amendments were processed and approved between January and February IBC meetings.

OTHER BUSINESS

ADJOURNMENT

The meeting adjourned at 1:10 pm.

Next meetings: ***March 17, 2015*** ***April 21, 2015***