

**NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)**  
**INSTITUTIONAL BIOSAFETY COMMITTEE**  
**MINUTES**  
**FEBRUARY 16, 2016**

**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)

- |  |  |
|--|--|
| <input type="checkbox"/> Michael Baseler (regrets)       | <input checked="" type="checkbox"/> Sarah Hooper     |
| <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      |
| <input checked="" type="checkbox"/> Stephen Creekmore    | <input type="checkbox"/> Bradley St. Croix (regrets) |
| <input checked="" type="checkbox"/> Eric Freed           | <input type="checkbox"/> Lucien Winegar (regrets)    |
| <input checked="" type="checkbox"/> Melinda Hollingshead | <input checked="" type="checkbox"/> Sharon Altmann   |
| <input checked="" type="checkbox"/> Stephen Hughes       | <input type="checkbox"/> Robin Sun (regrets)         |
| <input checked="" type="checkbox"/> Antonio Valentin     | <input checked="" type="checkbox"/> Jatinder Gulani  |

Non-Voting

- Walter Hubert
- Karen Barber

Visitors

- Ted Witte
- Sam Denny

**APPROVAL OF MINUTES FROM THE DECEMBER 2015 MEETING**

The minutes from the January 19, 2016 meeting were approved. A motion to approve and a second were made. (For: 12; Against: 0; Abstain: 0 )

**ACCIDENT REVIEWS** : An employee was reaching into a basket of scissors that had been decontaminated when one of the scissors nicked her finger. The scissors had been soaked in either Virkon or bleach for at least 5 minutes prior to the incident. ASP 14-059. This was determined to not be a biological exposure incident.

**REVIEW OF PROTOCOLS**

***NEW REGISTRATIONS***

Federico Bernal – 16-01: Development of inhibitors of the Ebola Fusogenic Complex. The goal is to develop synthetic peptides capable of inhibiting the formation of the complex that leads to Ebola infectivity. The experiments in the laboratory are limited entirely to biochemistry assays (characterization of compounds, binding to recombinant proteins, etc.) All assays involving the actual virus are being carried out at the IRF. A motion to approve pending clarifications was made by S. Hughes and seconded by E. Freed. (For: 11; Against: 0; Abstain: 1)

**NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)**  
**INSTITUTIONAL BIOSAFETY COMMITTEE**  
**MINUTES**  
**FEBRUARY 16, 2016**

Federico Bernal – 16-02: Control of Bacterial transcription factor function. In our efforts to study ways of controlling oncogenic transcription factors with designed molecules, we are carrying out a pilot study aimed at modulating the function of the bacterial transcription factor sigma 54. Sigma 54 is responsible for the pathogenic properties of several microorganisms. The experiments revolve around compound design and activity in bacterial cells using E.coli as our model organism. A motion to approve pending clarifications was made by D. McVicar and seconded by D. Betzner. (For: 12; Against: 0; Abstain: 0)

Javed Khan – 15-61: Molecular targeting of rhabdomyosarcoma with combinations of small molecule drugs. Rhabdomyosarcoma (RMS) accounts for 3% of all childhood cancers, constituting approximately 350 new cases annually in the US. This tumor, which is derived from skeletal muscle progenitors, is sub-divided into two major genetic and histologic subtypes: embryonal (ERMS, PAX3-FOXO1 fusion negative) and alveolar (ARMS, PAX3-FOXO1 fusion positive). ERMS has a better prognosis than ARMS, with relapse-free survival rates approaching 70- 80% for ERMS patients with localized disease. However, the 5-year survival rate for patients with metastatic RMS at diagnosis or relapsed disease is poor irrespective of the subtype: 25% for ERMS and 10% for ARMS. Addition of targeted agents are needed to improve overall survival in relapsed or refractory RMS. We have identified several novel drug combinations that are effective in RMS cell killing in culture. In the planned experiments, we will test the efficacy of these drug combinations in mouse models of RMS. A motion to defer this registration to the March Committee meeting, for further clarification, was made by J. Gulani and seconded by S. Altmann. (For: 12; Against: 0; Abstain: 0)

***RENEWAL REGISTRATIONS***

Peter Johnson 16-03 (11-37): Molecular genetics of the C/EBP family of transcription factors. Our laboratory is interested in the regulatory pathways that distinguish normal cells from cancerous cells, focusing on the control of gene expression by specific DNA-binding transcription factors. In particular, our research involves the C/EBP (CCAAT/enhancer binding protein) family of transcription factors. We aim to understand the regulation of C/EBPs by oncogenic signals as well as their target genes that contribute to tumorigenesis or tumor suppression. We employ genetic approaches involving genetically engineered mice (GEM) and cells derived from these animals, cell biological studies in tissue culture, and biochemical experiments using mammalian cell extracts or recombinant proteins produced in E. coli. Experiments using mammalian cells in culture involve transient or stable introduction of exogenous vectors expressing normal or mutant genes of interest and determining their effects on cell proliferation, oncogenic transformation, and activation of target genes. We also use transfected cells to conduct protein activity assays and to assess protein: protein or protein: DNA interactions, as well as to ablate expression of specific genes using RNA interference approaches. Experiments in mice will use GEM animals as detailed in

**NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)**  
**INSTITUTIONAL BIOSAFETY COMMITTEE**  
**MINUTES**  
**FEBRUARY 16, 2016**

my short registration form for breeding transgenic and KO mice. A motion to defer this registration to the March Committee meeting, for further clarification, was made by S. Kozlov and seconded by A. Valentin. (For: 12; Against: 0; Abstain: 0)

- ❖ Elaine Jagoda – 16-04 (12-36): General protocol for testing molecular imaging agents (Radiopharmaceuticals of Short-lived Radionuclides and optical probes) in Rodents. The goal of these studies is to develop new imaging probes including primarily radiopharmaceuticals for Positron Emission Tomography (PET) or Single Photon Emission Computed Tomography (SPECT) and fluorophore conjugates for optical/fluorescent imaging. Successful imaging probes will be able to detect, follow the pathophysiology, and monitor therapeutic responses of various disease states to be used for clinical imaging in humans. These imaging agents are molecular probes designed to target a specific biochemical pathway (ie enzyme activity, receptor expression) which has been altered due to the disease state. After these imaging probes have been developed, preclinical testing in rodents is necessary to determine the in vivo distribution and specific uptake of the agent at the target sites before proceeding with studies in higher animals and finally to humans. A motion to approve was made by E. Freed and seconded by S. Creekmore. (For: 12; Against: 0; Abstain: 0)

***OUTSTANDING ITEMS***

- ❖ Andre Nussenzweig – 15-60 (12-63): Expression of MLL fusion proteins in BM cells for transplantation to assess tumor formation in vivo. Our lab is studying the role of DNA repair response genes in tumorigenesis. We believe that deletion or inhibition of proteins in the DNA repair response pathways can impair or reverse MLL fusion induced acute myeloid leukemia (AML). To test this in vivo we will 1) transfect HEK293T cells to produce murine ecotropic retrovirus carrying DNA encoding a murine MLL fusion protein, 2) infect wildtype or knockout mice BM cells to stably express the MLL fusion protein, 3) IV inject these transformed cells into recipient mice, either C57BL6 or NRG, 4) follow progression of leukemia to up to 140 days. A motion to defer to February 2016 with the request to resubmit the registration. (For: 11; Against: 0; Abstain: 0)
- ❖ Vinay Pathak – 15-62 (07-37): Mechanisms of retroviral replication. We seek to understand how retroviruses replicate and how they evolve to acquire resistance to antiviral drugs and human antiviral defense proteins called restriction factors. We are studying how APOBEC3 proteins, a family of host cytidine deaminases, inhibit HIV-1 replication, and how the viral Vif protein overcomes these host defenses. We are screening for small molecule inhibitors of APOBEC3-Vif interactions, elucidating the structure and function of APOBEC3 proteins, and identifying host genes that facilitate the Vif-APOBEC3 interactions. We are exploring mechanisms of antiviral drug resistance and retroviral replication. We are also using APOBEC3 proteins tagged with fluorescent proteins such as yellow fluorescent protein to label HIV-1 virions that can complete one cycle of replication but have defects in many essential genes such as envelope and/or reverse transcriptase, and accessory genes such as Vif, Vpr, Vpu and Nef. A motion to defer this registration was made, pending clarifications and an observation, by Steve Creekmore and seconded by Serguei Kozlov,.

**NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)**  
**INSTITUTIONAL BIOSAFETY COMMITTEE**  
**MINUTES**  
**FEBRUARY 16, 2016**

(For: 11; Against: 0; Abstain: 0)

- ❖ Lisa Ridnour – 15-63 (12-77): Role of Nitric Oxide in Breast Cancer Disease Progression.  
We hypothesize that NOS2-derived NO perpetuates feed-forward inflammatory signaling loops that promote tumor progression to more aggressive metastatic and drug resistant phenotypes. A goal of our group pertains to the elucidation of this pro-tumorigenic role of NO in cancer through the identification of NO-driven molecular mechanisms that promote disease progression. Moreover, we propose to utilize this mechanistic information for the development of novel drugs that target specific biomarkers, or combinations of biomarkers, for improved therapeutic response.  
**February meeting:** Awaiting the safety syringes to perform the injection observations. We propose to test the anti-tumor effects of NOS3 inhibitors and novel NSAIDs designed and synthesized by our collaborators for their abilities to suppress the above biomarkers and reduce tumor growth and metastasis in mice. A motion for a conditional approval, pending clarifications and an observation, was made by Sharon Altman and Bradley St Croix. (For: 11; 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 was made to inactivate/retract the previous approval for the H.pylori registration (14-46), which is now 2 years old. JiMing Wang will have to resubmit a new registration at the time a new employee (tasked with this scope of work) is hired. The registration will tell us about the work scope, location, training, SOP's and an observation will be required with the new employee, prior to releasing approval to do the work. NO work with H.pylori will be approved until the staff can sufficiently demonstrate competence with an innocuous agent first (such as H2O). A brief discussion was held regarding the use of the H.pylori breath test which costs approximately \$100 per test and is not sufficient for medical surveillance purposes, mainly because the source of the H.pylori cannot be isolated to lab exposure potential.**

**AMENDMENTS**

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

**OTHER BUSINESS**

**ADJOURNMENT**

The meeting adjourned at 2:05 pm.

**Next meetings:**

**March 15, 2016**

**April 19, 2016**