

NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
APRIL 19, 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 checked="" type="checkbox"/> Michael Baseler | <input checked="" type="checkbox"/> Sarah Hooper |
| <input checked="" type="checkbox"/> Theresa Bell | <input checked="" type="checkbox"/> Serguei Kozlov |
| <input type="checkbox"/> Rev. David Betzner (regrets) | <input checked="" type="checkbox"/> Dan McVicar |
| <input checked="" type="checkbox"/> Stephen Creekmore | <input checked="" type="checkbox"/> Bradley St. Croix |
| <input checked="" type="checkbox"/> Eric Freed | <input checked="" type="checkbox"/> Lucien Winegar |
| <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 (regrets)

Visitors

- Ted Witte
 Sam Denny (regrets)

APPROVAL OF MINUTES FROM THE MARCH 2016 MEETING

The minutes from the March 15, 2016 meeting were deferred to May meeting. Information regarding the vote to formally notify Dr. Reynolds needs to be captured in the minutes. The March minutes will be reviewed for approval at the May meeting.

ACCIDENT REVIEWS There was a needlestick with a clean needle. A recently hired technician was reconstituting antibiotics and while performing a hard pull to uncap the needle, the hand pulling off the cap retracted back causing the needlestick. Because the needle was clean there was no exposure. This was part of a training exercise, which clearly demonstrated what not to do. Photos of alternative uncapping methods were provided to the technician and additional training was provided by the supervisor.

REVIEW OF PROTOCOLS

NEW REGISTRATIONS

- ❖ Barbara Felber - 16-12: Recombinant adenoviral vector transduction of monocytes for cancer immunotherapy. Adenoviruses have been used as non-integrating viral vectors for gene delivery

NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
APRIL 19, 2016

both in vivo and in vitro. Furthermore, recombinant adenoviruses (rAd) lack the genes necessary to replicate, and are thus a safe way to deliver therapeutic genes in a controlled manner. The objective of this study is to use rAD to deliver genes encoding putative or established immunotherapeutic proteins to murine bone-marrow derived monocytes cultured in vitro. These transduced monocytes expressing the immunotherapeutic proteins will be injected into tumor-bearing mice. We will test the ability of these cells to express the immunotherapy genes within mouse tumors, alter immune response, and potentially lead to regression of established tumors. A motion to approve, pending clarifications, was made by E. Freed and seconded by S. Creekmore. (For: 13; Against: 0; Abstain: 1). Antonio Valentin abstained from the vote.

RENEWAL REGISTRATIONS

(NONE)

OUTSTANDING ITEMS

- ❖ 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 my short registration form for breeding transgenic and KO mice. There is a continuing discrepancy concerning the risks associated with research involving viruses and hot oncogenes. There are concerns regarding the program's recognition of the apparent dangers posed by the pBABE vector with oncogenic RAS. This is a renewal and the renewal research may proceed, however, the program may not initiate work activities with replication competent retroviruses with oncogenic RAS until a SOP has been written, reviewed and approved by the IBC. The program must recognize the risk, ensure these risks are communicated to those performing the work and an observation must be performed to document procedures captured in the SOP are understood and implemented properly. A motion to continue deferral to the May meeting was made by Dan McVicar and seconded by Theresa Bell and all were in favor. The IBC reiterated the need for a letter notifying

NATIONAL CANCER INSTITUTE AT FREDERICK (NCI@F)
INSTITUTIONAL BIOSAFETY COMMITTEE
MINUTES
APRIL 19, 2016

Dr. Reynolds of the situation regarding this registry and the letter was to be delivered within 48 hours of this vote, while members continue to work with the PI to reach agreements and correct registration paperwork. (For: 13; Against: 0; Abstain: 0)

- ❖ 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 was made to defer to May 2016 with the request to resubmit the registration. (For: 13; 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. No update on registration at the time of the April meeting and registry is deferred until May meeting.

AMENDMENTS

Nineteen amendments were processed and approved between March and April IBC meetings.

OTHER BUSINESS

ADJOURNMENT

The meeting adjourned at 1:05 pm.

Next meetings: May 17, 2016 June 21, 2016