NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE

Minutes
February 19, 2008
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 12:07 p.m. in the Building 549 Executive Boardroom with the following members in attendance:

Ms. Theresa Bell, Secretary	Dr. Henry Hearn
Dr. Randall Morin	Dr. David Garfinkel
Ms. Alberta Peugeot	Dr. Stephen Creekmore
Dr. Bruce Crise	Dr. Stephen Hughes
Dr. Mike Baseler	Dr. Dan McVicar
Ms. Dianna Boissey	

Members not in attendance: Dr. Melinda Hollingshead, Mr. Lucien Winegar

Others in attendance: Dr. Robert Thomas, Dr. Scott Keimig, Ms. Gail Housaman

NEW BUSINESS

08-01 (Keller) Inhibition of Leukemic Cell Proliferation by ID Targeted shRNA: Self Inactivating/Replication Incompetent Lentiviral Delivery

- A5: The language regarding the lentiviral biosafety features is incorrectly stated.
- A8: A roster of individuals working on this project in the lab is needed.
- A9: The research locations form must be completed.
- D5b: Human pathogen testing of the cell lines must be done.
- D7: Will the material be infected with any pathogens as part of this protocol?
- D7a: If yes, what pathogens?
- D9a: What measures are used to perform centrifuging, dissecting, blending/mixing, and pipetting safely?
- E6e1: Why is there no reasonable expectation that the viral segment could help mobilize part or all of the transgene, either by itself or by interaction with other viruses?

- E6f1: Why is there no particular risk if part or all of the transgene was mobilized. What materials (if any) are coming out of the mice? Where does that material go, what hazards are posed by this material, and how are those hazards mitigated?
- E9: How will the animal facility workers be exercising the safe use of sharps (i.e. animal restraints).
- The SOP needs some additional detail regarding the segregation of the lentiviral components from the retroviral components in the lab, contact time with an appropriate disinfectant and how things will be decontaminated, procedures to be used for spill control and clean up, documentation that those with open wounds (especially on the hands) will not be performing this work, and recognition by employees that those with open cuts are at an increased risk of exposure. Given that the shRNA may affect the growth of the lines, extra caution should be used in their handling.

Dr. McVicar made a motion to approve the registration once the appropriate modifications noted above are made, Dr. Crise seconded, and all were in favor.

08-06 (Harris) Purification of Recombinant Adenovirus Vectors by Cesium Chloride Density Gradient Centrifugation and Dialysis
- This study involves the use of 10^{15} adenovirus in a toxic compound (cesium)
- It is not clear how folks will avoid sticking themselves with the needle when performing injections.
- Is there a better way to perform the dialysis?
- What is the gauge of needle being used? Clarification of a "safety needle" is needed.
- Is it possible for the entire apparatus/equipment in use to remain in the BSC the entire time?
- How will the slidealyzer be removed from the container and disinfected?
- What will be done if the tubing leaks or if the slidealyzer does not reseal itself?
- How is the Cesium disposed of? The method of disinfection and disposal for all materials/waste streams must be defined.
- A pictorial diagram to indicate that a one-handed motion to be used for the injection purposes should be provided.
- The work is to be performed in a completely closed system or everything be done in a BSC.
- Why is there limitation to using sharps inside versus outside of a BSC?

Dr. Crise made a motion to defer approval, Dr. Hughes seconded, and all were in favor. Dr. Creekmore abstained from the vote.

08-09 (Palmieri) Effect of Low Hexokinase-2 Expression on Metastatic Colonization of the Brain by Breast Cancer
CONFIDENTIAL
- B5g1: What is "it" referring to?
- B5h1: BSC should be stated rather than "hood".

- D3b: Notes the use of cell lines from the lung of a cancer patient - is there any risk of TB?
- E9: How will injections be performed and will animal restraints be used? This is addressed in Section E of the ASP. Verification of how those performing injections will be careful to not accidentally inject themselves is needed.

Dr. Creekmore made a motion to approve with modifications as noted, Dr. McVicar seconded, and all were in favor.

08-02 (Palmieri) Use of GSK461354 for the Treatment of Brain Metastases

-A3: The vector system needs clarification. It is unclear what is meant by "ex retro or lenti".
- B5h1: Addresses the aerosol hazards, but does not address which activities pose the aerosol risk. How will the potential aerosol hazards present be mitigated?
- How are the animals restrained to ensure that the risks to the person performing injections for self-inoculation are minimized?

Dr. Garfinkel made a motion to approve pending answers to the above questions, Dr. Creekmore seconded, and all were in favor.

08-08 (Melillo) Use of Human and Animal Tissues and Body Fluids to Study the Effect of Therapeutic Agents

- A3: Are non-human primate cells included? What types of tissues will be used? How will tissues and other potentially infectious material be handled safely? Will lung tissue be used, and if so, does this present a TB hazard or need for additional medical surveillance?
- E9: How will the hazards associated with injections be mitigated? Are animal restraint mechanisms mentioned in ASP?
- Does this ASP actually apply to the IBC submitted (IBC title is addressing tissues when the ASP addresses the injection of cell lines into animals). Clarification between the 2 documents is requested.

Dr. Creekmore made a motion to defer approval until issues above are resolved, Dr. Hughes seconded, and all were in favor.

08-05 (Schmidt) Role of Folliculin in Regulation of Nfkappa-B Activation through Retroviral Transduction of Human Cancer Cell Lines with FLCN and FLCN Mutant siRNAs

- A3: The response regarding the integration (the viruses will integrate) must be clarified. The PT67 packaging cell line with MSCV vectors may give rise to replication competent viruses.
- Will the cells be put back into other animals? If the cells are put into mice, the cells will have been exposed to viruses that may mobilize the viral vectors in the cells.

- A6: There are 3 rooms listed so transport does appear to be an issue. This should be addressed or corrected.
- B5f1: Should state that recombination may occur at a low frequency giving rise to replication competent virus.
- B5h1: Tumor suppressors are used in conjunction with amphotropic vectors. The centrifuge safety buckets should be opened under a BSC.
-B5i: Explain what the "derivative"(MSCV) is.
- B6a: How will the hazards noted be mitigated?
- D5: If human cell lines are being injected into the animals, then they must be screened.
- The SOP should note how viral components used in the lab will be segregated, how will those with open cuts or wounds on their hands or those who are immunocompromised be handled, and clarify these materials will only be handled under strict BSL-2 practices and procedures.
- How is a starting dose established?
- How will sterility be maintained?

Dr. Crise made a motion to approve pending resolution of the above noted items, Dr. McVicar seconded, and all were in favor.

RENEWALS

08-03 (Anderson) Analysis of Ly49 Gene Function and NK Cell Development
- A1: Clarification is needed, as it is not evident what is being done (i.e.- identify the material being made in vivo, what will be put into mice, and what will be taken from mice).
- B6a & E9: Hazards must be identified even if they are minimal.
- B6b: Are the LNK and EL4 lymphocyte murine cell lines injected into mice? If not, what are these cell lines being used for?
- B10a: Safety grams are good reference material, but the IBC would like to see a lab specific SOP to address safety issues inherent to this protocol.
- E4: Provide additional information on how animals will be used.
- E6b & E6b1: Need clarification.

Dr. McVicar made a motion to approve once these issues are clearly stated in the registration and an appropriate SOP is completed, Dr. Crise seconded, and all were in favor.

07-71 (Hurwitz) Modulating T Cell Activation in the Anti-Tumor and Autoimmune Responses
- A4a: Clarify the use of sharps, and describe how animal injections with infectious material will be performed safely.
- B5f1: Needs corrected. It is possible to mobilize and pass MLV-based vectors into mice.
- B8b: Hazards must be identified.

- B8b1: Description of how those hazards are mitigated must be provided.

- E6e1: Needs corrected since there is a possibility for mobilizable elements to be present based upon the use of MLV (distinguish the difference between mobilizable and replication competent)
- E9: Any potential for aerosol hazards when performing centrifugation needs addressed.

Dr. Crise made a motion to defer approval, with review of the above noted revisions to occur by a subcommittee, Dr. Hughes seconded, and all were in favor.

07-72 (Hurwitz) Modulating T Cell Activation in the Anti-Tumor and Autoimmune Responses

- A4: Specify what sharps are used for and how will the mice injections be performed safely (i.e. animal restraints).
- E6b1: PI should explain why cells are not permissive to further infection.
- For the strain table provided, the references used and the applicable strain codes should be included.

Dr. Crise made a motion to approve, with the above modifications, Dr. McVicar seconded, and all were in favor.

07-73 (Hurwitz) Chronic Prostatitis as a Model for Prostate Carcinogenesis

- This study requires more information regarding the pathogenesis of the E. coli strain since it is a patient isolate and infectious to humans. Human health hazards, the importance of handling as a BSL-2, hand washing, and whether the material is hemolytic and motile should all be addressed.
- Why are volumes of up to one to two liters needed?
- An upgraded SOP is needed with specific spill procedures and specific practices and procedures used when handling this material to document how this work will be done safely. How will the potential aerosol issues with performing injections into mice with the material be addressed? The importance of handwashing should also be addressed.
- C13a: States that material is prepared for injection on the benchtop. Why is the material not handled in a BSC? How will centrifugation be performed safely?
- Animals are to be in microisolator caging for seven days. Is it known how long viral shedding will occur?
- Since this is a primary isolate for humans was antibiotic susceptibility testing done?

Dr. Baseler made a motion to defer approval, Dr. Garfinkel seconded, and all were in favor.

AMENDMENTS

06-27 (Sei)

- This amendment is to add hepatocytes from cotton rats and hamsters to continue studies to assess hepatocyte toxicity with the already approved adenoviruses from IBC #06-27. There are no issues with this amendment.

Dr. Crise made a motion to approve, Dr. Hughes seconded, and all were in favor.

07-64 (Swing)

- What is the RTTA gene being expressed?

Dr. McVicar made a motion to approve, Dr. Crise seconded, and all were in favor.

06-108, P170705RHA01, & 07-20 (Harris)

- This documentation states that the virus seed stock has been tested in an RCA assay and has shown to be free of RCA. It is still possible to have RCA present even though an RCA test was done and RCA was not found. The limits of detection associated with this assay should be included in the document. It may not be "free" of RCA even though there was none detected given the parameters of the test. The IBC requests acknowledgement of what is known and what is unknown.

The amendments are pending approval with further discussion needed regarding the use of CsCl and dialysis procedures (also related to IBC # 08-06).

OPEN ITEMS

- Ms. Bell briefed the IBC on the outstanding items.

OTHER BUSINESS

- The Bloodborne Pathogen Program is currently 95% compliant. Efforts are continuously made to ensure individuals on the program take their training in a timely manner.
- The IBC form will be updated to reflect changes proposed by the IP Office.
- The Vaccination Policy will be distributed again for revisions before final approval.
- OHS reported there was a non-human primate scratch on 2/11/08 in Bethesda to an SAIC employee. OMS is implementing care. EHS will follow up with an accident investigation in accordance with NIH DOHS.
- The IBC discussed potential new IBC members. An invitation will be extended to several interested individuals to attend the March 2008 meeting.

The meeting ended at 2:35 p.m.

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Theresa D. Bell, MPH, CBSP	Ms. Cara Leitch
IBC Secretary	IBC Coordinator
Biological Safety Officer, EHS	Sr. Safety Specialist, EHS

APPROVED:

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Randall S. Morin, Dr. P.H.	Date
Chairman, NCI-Frederick IBC	
Director, EHS	

xc: Dr. Reynolds
Mr. Wheatley
Dr. Arthur
Mr. Bufter