ANIMAL CARE COMMITTEE MEETING MINUTES
AUGUST 18, 2020

Attendees: Member 6, Member 8, Member 9, Member 10, Member 11, Member 24, Member 30, Member 42, and Member 43

Absent: Member 42

Guest: Member 44 and Member 45

1. **Minutes**

   None

2. **Announcements**

   New Director of OACIB was introduced to the committee.

3. **Old Business**

   a. Protocol 20-043 update

   Member 6 updated the committee on the status of the protocol and meeting with PI. It is anticipated that protocol and all associate SOPs will be presented at the next ACC meeting for review and final approval by committee.

   b. Protocol 20-112

   Member 9 informed the committee that this protocol was deferred at the last meeting and the PI had revised the protocol based on the committee's requested clarifications. The Committee reviewed the revised protocol and discussed that the PI needed to address clarifications listed below and that Members 6 and 9 should contact the PI and discuss the committee's concern with the lack of personnel with surgical training. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

   COI #1: Once a trainer has been identified, PI's staff must be trained with all aspects of surgical procedures and surgical procedures may be revised based on the needs of the procedure.
   COI # 2: PI and staff must notify the BRL Vet when the trainer is identified and are ready to start the training of PI's staff.

   a. In Form A, item 8g, please address the following:
      i. In The 2nd paragraph, PI indicates meloxicam will be injected "via subcutaneously via IV injection", please correct to just indicate "subcutaneously".
      ii. In the 4th paragraph, PI indicates that endpoints will be "group specific, but most common timepoints are 1,4, 8 and 24 weeks", please remove that statement and indicate the exact timepoints.

iii. Please clarify if both knees for each animal get the same implant material. This is not clear from the experimental design table.
iv. The last 4 compounds listed in the table in Form A, 7d2, are not part of the description of groups in the experimental table, please clarify.

b. In Form A, item 8h Please address the following:
   i. Please provide the effect size used to calculate the group size.
   ii. Please clarify if male and female animals will be used in equal numbers within each group.
c. In Form A, item 10a, please remove the concentration of pentobarbital.
d. In Form A, item 14, Personnel lack experience with surgical procedures and need to be trained by experienced person. Once a trainer is identified, all personnel involved in surgical procedure must be trained prior to involvement in any surgical procedures.
e. In Form B, item 6c, please address the following:
   i. Please correct the following statement: "Baytril (10mg/kg) SQ via IV" to "Baytril (10mg/kg) will be administered SQ ".
   ii. Please clarify the approximate duration of the procedure.
f. In Form B, item 6f, please indicate the route of delivery for Baytril.
g. In Form B, item 9, please clarify what it means by "unusual or lethargic behavior".

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c. Protocol 20-125

Member 9 informed the committee that this protocol was deferred at last meeting and PI had revised the protocol based on the committee's requested clarifications. The Committee reviewed the revised protocol and discussed that the PI needed to address clarifications listed below and that Members 6 and 9 should contact the PI and discuss the committee's concern with the lack of personnel with surgical training and an understanding of the proposed immunosuppression regimen . Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

COI #1: Once a trainer has been identified, PI's staff must be trained with all aspects of surgical procedures, changes to the surgical procedures should be updated as appropriate based on the needs of the procedure and the recommendation of the trainer. PI should incorporate the use of Cadaver animals for training personnel on surgical procedures.

COI # 2: Conducting a pilot study to determine the correct immunosuppression regimen.

COI # 3: PI and staff must notify the BRL Vet when the trainer is identified and are ready to start the training of PI's staff.

a. In Form A, item 8g, this item needs to be revised to incorporate a new immunosupporession regimen based upon the literature and/or to include a pilot study to evaluate an immunosuppression regimen to be used in the main study. PI should include methods of training staff in the procedures to be performed in this protocol.
b. In Form B, item 6c, this item needs to be revised upon identification of an experienced surgeon who will both perform the procedure and train staff. The revisions should be based upon the

surgeon's experience with the proposed surgical procedures and include specific details related to the surgical procedure.

4. BRL Director's Legislative and Facility Update

Member 6 directed the Committee's attention to the report and updated the Committee on the following: 1) COVID 19 update: that BRL veterinary staff will be reaching out to the research community to re-initiate lab visits and that the lab visits will be done in a manner that takes into account social distancing, lab occupancy limits and the use of face coverings, 2) that the [redacted] is getting closer to opening to support BSL3 COVID 19 work and EHSO will soon begin investigator training and that the first studies proposed for the [redacted] will only involve bench work, i.e. no animal work, 3) that the helicobacter and mouse norovirus outbreak in room [redacted] has been contained and the room has undergone 2 cycles of negative testing and as a result the room is no longer under quarantine, 4) that the AAALAC description has been submitted on July 31st and that. AAALAC will be reaching out to us toward the end of August to schedule a site visit, which is hoping to be within the first part of December and that most likely, due to COVID-19, parts of the site visit will be done remotely, and to recognize to recognize the BRL veterinary staff for their significant efforts in putting together the program description documents, 5) that the rodent training module for UIC research continues to be under revision and videos on techniques in mice and rats are being updated over the next two weeks with the intent to roll out the revised training module by October 1st, 6) that the BRL veterinary staff will be rolling out a new training wet lab on perioperative care in rodents with the first training session scheduled in September and that will be done on a very small scale in a manner consistent with UIC OCVID 19 guidelines and 7) that the BRL veterinary staff are in the process of updating the ACC's policy on Euthanasia to take into account recent changes that occurred in the AVMA guidelines.

5. OACIB Update

a. Modifications

Member 9 updated the Committee to the following activity during the past month: there were 15 modifications approved at the administrative level, 25 modifications approved administratively following veterinary consult, and 6 modifications approved via designated review this month. In addition, there were 12 protocols that added personnel, 0 with personnel deletions, 3 that added new funding, and 0 in which animals were added to the holding protocol.

b. Continuations and Terminations

Member 9 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal of the protocols was passed by the following vote: 9 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

20-131

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, please list only staff who are co-investigators on supported grants or who are to be included on project related correspondence in this section.
b. In Form A, item 4, please address the following:
    i. Line a, if these are wild-type BL/6 mice please remove "+/+", otherwise specify gene.
    ii. Please specify here how PBEF +/+ is distinct from the BL/6 WT animals (e.g, littermate controls).
    iii. Use 2 is listed for several groups. This use is "breeders" whereas the animals described are clearly experimental (this includes, for example, 750 neonates to be euthanized at P1-2); please clarify.
    iv. Please add animals bred in Appendix 1 that are excess and not used in experiments. These should be categorized here as uses 3 and 4. All mice not acquired from outside vendors (i.e. any that are bred and listed in Appendix 1) must be counted here and these two sections must match exactly.
c. In Form A, item 5c, please address the following:
    i. Replace "rat studies" with more specific description of work to be performed in [redacted].
    ii. List the locations for MRI and toxicity studies.
d. In Form A, item 6c, please address the following:
    i. Please specify animals that will require single housing.
    ii. Provide appropriate justification for single housing.
e. In Form A, item 7c, please add [redacted] as building in addition to room number.
f. In Form A, item 7d, please define or spell out full name for compound "NAM" the first time mentioned.
g. In Form A, item 8c, please provide a summary of what has been accomplished during the past three years.
h. In Form A, item 8d, this is a generic justification of animal research lacking in any project-specific details. Please replace with specific rationale for using animals in the current studies.
i. In Form A, item 8e, PI should list all wild type and transgenic mice and provide justification for each mouse line.
j. In Form A, item 8g, please address the following:
    i. Please identify actual source for PBEF transgenic mice.
    ii. Please replace instances of "animal facility" with actual locations where experimental or monitoring will occur.
    iii. The committee recommends that clean cages be used to transport animals, in lieu of paper container.
    iv. Based on previous experience with the procedure described in this protocol, PI should consider performing neurological scoring without veterinary consultation. Also define "intermediate" score and how this classification will be assigned.
    v. In cardiac arrest protocol, epinephrine injection is described, but in item 13a, norepinephrine is listed. Please reconcile. Also, will PI be using pharmaceutical grade epinephrine? If not please add to Form A, item 7d.

vi. Describe method for how corneal reflex will be assessed.
vii. Humane endpoint criteria are listed as part of the neurological scoring criteria on page 2 of 13. Additional discussion of humane endpoints on this page is redundant and can be removed.
viii. Details on experiments prior to euthanasia (e.g, culturing conditions for cultured myocytes) are not salient to this protocol and can be removed.
ix. Despite it being a core target of this study (e.g., majority of the animals requested), the function of PBEF and the rationale for selecting it as a target are discussed only minimally in this section and throughout this proposal. Please expand upon the description of this pathway to justify use of overexpressed, floxed, and heterozygote mice at such high numbers.
x. It is postulated in several places that "with intervention, 70% of wild-type mice will survive". This seems to refer to survival beyond the 5-day monitoring period, but as described it may also refer to survival from the surgery, please clarity.

k. In Form A, item 8h, please address the following:
i. Experimental details are included in this section which belong in section 8g. Most of the information under this heading on pages 4-6 belongs in 8g, and in some cases can be consolidated with existing text in that section.
ii. Studies requiring 0 animals (e.g., "pilot studies" that have been completed) can be removed.
iii. Please include power analyses performed prior to discussing the mathematical variables of the analysis.
iv. In Project 1, part 5, 12 breeding females are requested, and are predicted to give birth every 4 weeks with litters of 6 pups each. But this would result in 18 pups/week, whereas 25 are needed for the experiments, please clarify. Also, these pups are not counted in form A.4 (unless they are the same animals as used in Project 9, in which case they are counted twice in this section), please rectify here and in A.4.
v. For Project 5, description lists 50 mice needed but summary lists 40. Please reconcile.
vi. Across projects 1-7, 859 BL/6 animals are counted, but 981 are listed in Form A4, Please reconcile.
vii. In Project 8, please define how "moribund" will be determined.
viii. In Project 9, define "data point". Please explain why "10 data points are required" using statistical analysis. Also, 198 adult animals are requested across PBEF genotypes, but 246 are requested in A.4. Please reconcile these numbers.
ix. In Form A, item 9, all sick animals are to be sacrificed, but it appears from the description of this study that a large percentage of the animals are expected to meet standard humane endpoints as part of the experimental design. It may be preferable to amend this to "contact PI" if the investigators wish to perform their neurological assessment to evaluate experimental variables on these animals prior to disposition.

l. In Form A, item 10a, please confirm if pharmaceutical grade Nembutal or non-pharmaceutical grade, if non-pharmaceutical grade, add to A7d2 including source, scientific justification, method of preparation and sterilization.
m. In Form A, item 13a, please remove retro-orbital injections from this section, but add and justify toxicity study as well as the survival cardiac arrest surgical procedure.
n. In Form A, item 13b, please remove reference to Harvard Apparatus catalog.
o. In Form A, item 14, please provide mouse/rat training dates for personnel.

p. In Form B, item 4, Nembutal dose listed here is too low and inconsistent with dose listed previously, please reconcile.
q. In Form B, item 6, monitoring for recovery should be performed until animals are sternal, irrespective of time required.
r. In Form B, item 6d, cap, and surgical drape are appropriate for this surgery; please add to existing aseptic equipment.
s. In Form A and Appendix 1, address the following:
t. PBEF -/- animals are not used due to poor survival, and so are replaced by a PBEF flox/flox mouse crossed against MHC-cre for conditional KO instead. In this case, would not an MHC-cre:PBEFflox/+ provide a more adequate heterozygous model than the global het?
u. 30 PBEF+/- are listed for breeding purposes. These should be listed as use category 2 in Form A, item 4. Please reconcile.
v. In breeding table e, the pairing described would result in only heterozygous flox excision, not conditional KO, as the listed females would carry a wild-type allele of the PBEF gene which would not be altered by cre expression,, please clarify
w. Two copies of Appendix 1 are listed with the same text in boxes 1-2. Instead, please attach a supplementary breeding table (available for download on ACC website) and include specific purpose and origin for bred animals on second copy of this form in the first instance Appendix 1.

20-143

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, Spell out the acronym "DRA"
b. In Form A, item 8g, please address the following:
   i. Under "Induction of Colitis" on the line "Preventative", specify state that the mice undergo imaging after compound dosing as is done in the line "Therapeutic" (as written, it is not clear that the "Preventative" group will undergo imaging).
   ii. Under "Imaging", in the last sentence, the word "overdose" of isoflurane is used. Either list the overdose dose to be given above the anesthetic dose listed, or simply rephrase to describe cervical dislocation under anesthesia as the euthanasia method.
   iii. In the flow chart figure, add when euthanasia will be performed, and remove the "Ex-vivo imaging" box as it is not clear that these procedures occur after the animal is euthanized, and procedures after euthanasia are not required for animal use protocols.
c. In Form A, item 8h, please indicate the proportion of males and female in each experimental group
d. In Form A, item 9, under "Dead Animals," check box for Contact PI and Contact Other, and list contact # for PI
e. In Form A, item 10b, please remove check box if CO_2 euthanasia will not be used.
f. In Form A, item 13b, please reconcile "Date of Search" with "Period of Years of Search"
g. In Form B, item 6a, skin preparation is described in A8g (i.e., clipping fur, iodine/alcohol scrub) but left blank here, please reconcile.

20-149

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Form A, all sections - Please use consistent nomenclature throughout the protocol when referring to specific mouse strains.
b. Form A, item 5c, in A7c PI indicated that isoflurane will be administered in room [redacted], please add this location in item 5c.
c. Form A, item 6c, the veterinarians recommend the use of acidified water only. If PI plans to use acidified and antibiotic water, include justification for requiring both.
d. Form A, item 7b, please check "Yes" for murine biologicals and list specific biological include source.
e. Form A, item 7d2, please add Herceptin and 851c/Herceptin to the table including scientific justification, source and method of preparation and sterilization for each compound
f. Form A, item 8g, please address the following:
    i. Under study 1(A), PI indicated that mice will be bled by terminal exsanguination. Will this procedure be performed under anesthesia? If yes, indicate anesthetic and dose, skin preparation, duration of restrain, amount of blood to be collected, and if this is the same procedure as the saphenous vein procedure described in the methods. Further, clarify the use of 'terminal' since these mice will be used for multiple blood collections.
    ii. Under study 1(A), the total number of mice listed for this study is inconsistent with the number listed in A8h, please reconcile.
    iii. Under study 1(B), the total number of mice listed for this study is inconsistent with the number listed in A8h, please reconcile.
    iv. Under study 2-3, list method of euthanasia.
    v. In Form B, item 3, PI indicated that i.p injections will be done under anesthesia, please clarify if i.p injection of cytokine fusion/control constructs will also be done under anesthesia.
    vi. For all studies and in Form B, item 9, include "body condition score of <2 (OACIB Guidelines) as humane end point criteria.
    vii. For all studies, PI indicated that endpoint is 'approximately 3-6 weeks', please define a specific endpoint such as 'no longer than 6 weeks'
    viii. Under method of euthanasia, please update the AVMA guidelines from 2008 to 2020.
g. Form A, item 8h, please address the following:
    i. Since this is a funded study and a 3-year renewal, a pilot study is no longer justifiable. Provide a full power analysis and sample size calculation for each experimental group. Further, justification of only female mice is necessary.
    ii. Please clarify if both the BALB/c and C57BL6 strains will be used or indicate criteria that will be used to determine appropriate strain for this study.
    iii. The total number of mice listed in the justification do not match the number of total mice listed in the study design (Form A, item 8g).
    iv. It appears that a total of 15 mice are requested for the control saline injection group (10 more than the experimental groups), please provide clarification and justification for this difference.
    v. Under study 2C, based on the groups the total number of mice is incorrect, please reconcile.
h. Form A, item 10a, add method 5, exsanguination under anesthesia

i. Form A, item 10c, in A8g PI indicated that "blood will be collected via cardiac puncture". check box for 'exsanguination' in 10c.
j. Form A, item 13b, perform literature search for *in vivo* induction and/or alternatives in mice.
k. Form A, item 15, signature from the BRL director is required.
l. Form B, item 3, clarify that anesthetics will only be used for blood collection.
m. Form B, item 3, clarify that anesthesia will not be used for IP injections and tail vein injections.
n. Form B, item 9, since there are concerns regarding ulceration at the site of intratumor injections, we recommend that ulceration be removed from the humane endpoint criteria for the intratumor injection procedure

20-132

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 6 and 10 for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, please provide institutional approval form numbers for funded studies and number assigned by NIH for the pending application.
b. In Form A, item 5c, please address the following:
c. PI should note that [redacted] is not for housing but for post-surgical monitoring
d. PI should note that [redacted] is no longer applicable and should update location for this procedure.
e. In Form A, item 4, PI should reconcile the number of Balb/c nude mice with A8g and A8h. Also, account for the number of excess mice and inappropriate genotype.
f. In Form A, item 6c, PI should uncheck “Yes” and check “No” and remove the justification since the procedure described is post-surgical monitoring.
g. In Form A, item 7c, please address the following:
    i. Please remove [redacted] and list [redacted] location for use of isoflurane.
    ii. If isoflurane will be used in [redacted] as described in A8g, this location should be added.
h. In Form A, item 7d2, please address the following.
    i. PI should define or spell out BIO the first time used.
    ii. The scientific justifications for Tamoxifen and Tideglusib should be changed to 2 or 3 not 1
    iii. Add DMSO and corn oil including scientific justification, source, method of preparation and sterilization. Also, indicate the final concentration of DMSO that will be administered to mice.
i. In form A, item 8f, check “yes” and move the answer from A8g (highlighted paragraph about $Rosa^{mT/mG}$:$Nanog^{fl/fl}$: $Cdh5^{CreERT)}$ to here.
j. In Form A, item 8g, please address the following:
    i. PI should provide tamoxifen dose in mg per kg body weight.
    ii. Under procedure 1, PI indicated that tamoxifen will be administered prior to AMI but the description of the procedure is not for AMI but tamoxifen mediated Nanog deletion-induced cardiomyopathy, please clarify.
    iii. Under procedure 1, PI indicated that “in the absence of therapeutic intervention, these mice die of heart failure” will these mice receive any treatment? If yes, indicate specific treatment(s) including dose(s), injection volume and route of administration.

iv. Under procedure 2, TOG should be TDG.
v. Under procedure 2, PI should indicate time interval between the three doses of BIO or TDG
vi. Under procedure 2, PI should indicate when oral BIO or TDG in drinking water will be initiated.
vii. Under monitoring post AMI, please clarify monitoring frequency. Example, should it be "mice will be monitored once daily during the 1 first 3 days post-surgery and once every 3 days until euthanasia?
viii. Under procedure 2, PI should clarify if [redacted] will be used for isoflurane euthanasia, if so, this location should be listed in A7c.
ix. Under collection of hearts at day 7 and 14 after MI, PI should clarify the need CO_2 euthanasia if echo will be performed under isoflurane anesthesia and mice euthanized immediately afterward.
x. Under hind limb ischemia, PI should remove "we will use only male mice to exclude the confounding effects of cyclic estrogen on cardiovascular system in female mice" and provide appropriate justification for not using female mice.
xi. Under hind limb ischemia, the doses for BIO and TDG should indicated in mg or mg per kg body weight.
xii. Under monitoring for hind limb ischemia, PI should define "mild" toe or foot necrosis and include a score or rating scale for mild necrosis. Also, PI should refer to the previous approved protocol and incorporate the language on necrosis here.
xiii. Under hind limb ischemia, PI should indicate method for euthanasia.
xiv. Under procedure 5, PI should define or spell out LDI
xv. Under tissue processing and microscopy, PI should clarify if mice will be anesthetized for perfusion fixation.
xvi. Under A7a, PI indicated that AAV9 encoding cDNA, hTERT and ERG1 will be used but there is no indication for when these will be used and/or description of experiments involving AAV9, please clarify.
xvii. PI should use [redacted] SOP and attach the SOP with revisions of the protocol

k. In Form A, item 8h, please clarify the following:
i. In all the table, the number of extra mice requested should be 10% not 20%
ii. PI should include additional explanation for requesting 10% extra mice for all experiments.
iii. PI should define the 50% effect size of interest.
iv. Under power analysis PI indicated "Analysis of variance (ANOVA) with posthoc comparison using unpaired T-test or Mann-Whitney tests; you cannot use ANOVA for two groups, please use appropriate statistical analysis.
v. In Form A, item 4, PI is requesting male and female mice but is only using male mice, please clarify.
vi. In Form A, item 4, PI is requesting 40 male and female Balbc nude mice but provided justification for 99 male mice, please clarify.
vii. In Form A, item 4, PI indicated that excess breeders and inappropriate genotypes will be generated but these are not accounted for in here, A8g, or appendix 1 completed, please clarify.

l. In Form A, item 10a, in the column for anesthetic, PI should remove N/A and list CO_2 and in the column for route of administration indicate inhalation.
m. In Form A, item 13a, PI should list cardiomyopathy, AMI, HLI and include the justification for each procedure.

n. In Form A, item 13b, this section pertains to appropriate alternative models, therefore the combination of search terms should include the models described in this protocol. Please redo literature search using the models described and update search accordingly.
o. In Form A, item 14, please address the following:
    i. Update ACC regulatory training dates for personnel.
    ii. PI should remove [redacted] personnel since they are covered under the [redacted] protocol.
    iii. Please provide specific training and expertise for personnel with HLI.
p. In Form B, item B3, please add i.p. and SQ route of administration.
q. In Form B, item 6a, PI should move the surgical description to surgery #2. Also reconcile the duration for transient ligation (20 min) with A8g (45 min).
r. In Form B, item 6c, as indicated in A8g above, PI should adopt [redacted] surgical procedures for AMI and Echo and attached SOP as addendum.
s. In Form B, item 6e, PI should list AMI as class 4 surgical procedure.
t. In Form B, item 9, PI should include justification for all the procedures described in this protocol and add monitoring, and humane end point criteria for cardiomyopathy.
u. In table A4 and A10a, PI indicated excess breeders and inappropriate genotypes and euthanasia of these mice but did not complete appendix 1, please clarify.

20-135

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5c, in row #3, there is no [redacted], please clarify the correct location here and throughout the protocol.
b. In Form A, item 7a, check "yes" for chemical hazards and list bleomycin here.
c. In Form A, item 7d2, please address the following:
    i. PI listed a several FDA approved albumin nanoparticles but according to A8g, only piceatannol albumin nanoparticles will be used, please clarify.
    ii. The committee suggests that the PI switch from to non-pharmaceutical to pharmaceutical grade bleomycin because several PI's have had difficulties with data reproducibility with the non-pharmaceutical grade.
d. In Form A, item 8g, please address the following:
    i. Under study 1 and 2 h post-LPS treatment, PI should list the different preparations of nanoparticles that will be used.
    ii. PI will be injecting a buprenorphine 0.1 mg/kg SC as post-surgical analgesia; this should be added to table B4.
    iii. Under i.p LPS-induced ALI, PI should indicate the timeline for nanoparticle treatment post-LPS treatment.
    iv. PI should also include timeline for monitoring post-LPS treatment.
    v. Under monitoring disease progression and ALI/ARDS pathology, PI should indicate the duration for restraint during arterial pressure monitoring.
    vi. Under study 2, PI should use future tense for experimental description and throughout the protocol.
    vii. Under study 2, PI should indicate method for euthanasia.

viii. Under study 2, last sentence, PI indicated that "recipient mice will be monitored and analyzed as described above" This is the first mention of this experimental procedure and there is no experimental description above, please reconcile.
ix. Under experiment 3.1, the cecal content to be collected from each donor should be enough for adaptive transfer into more than 1 recipient mouse, however the donor to recipient ration is 1:1; PI should provide additional explanation and/or justification.
x. Under study 3.4, PI should indicate method for euthanasia
xi. Under experiment 3.9, PI should indicate timeline for administration of Fluorochrome-labeled ANPs post-LPS treatment.
xii. Under experiment 3.10, PI indicated that "sham procedures as previously approved" please provide complete description since previous approved protocol was not available at the time of the current review process.
xiii. Under experiment 3.12, please indicate injection volume for BrdU and indicate which strain or transgenic mice will be used for this experiment.
xiv. Under experiment 3.12, PI should specify treatments that will be administered concomitantly, and indicate when ANPs treatment will be initiated. Also remove time points after tissue removal.
xv. Under study 6, please indicate the strain or transgenic mice that will be used. Also remove last paragraph because this is a repetition.
xvi. The experimental description has several repetitions and makes it difficult to follow, please revise accordingly.
xvii. PI should clarify if male and female mice will be used, if yes, indicate the proportion of male and female mice for all experimental groups.

e. In Form A, item 8h, please address the following:
   i. The justification for study 1 & 2 indicates that only piceatannol ANPs will be used, however A8g indicated that different formulations will be used, please reconcile.
   ii. In all the tables, PI should also indicate the experimental or study group for the respective animal groups.
   iii. PI should clarify why the same power analysis was used for all the experimental groups.
   iv. PI should define effect size of interest.
   v. Please indicate the proportion of male and mice that will be used for all experimental groups.
   vi. Table A4 listed B6.SJL-Ptprca Pepcin/BoyJ mice but there is no justification for this group of mice or applicable experimental description in A8g, please reconcile.
   vii. PI should indicate the strain or transgenic mice that will be used in study 6.
   viii. The justification for C57Bl/6-L6gtm2621C57BL/6, C57BL/6, CXCR4 KO, and FycRIII$^{+/+}$ do not match the numbers in A4, please reconcile.
f. In Form B, item 3, in the row for blood collection, add site for i.v blood collection.
g. In Form B, item 4, please add buprenorphine 0.1 mg/kg, SC
h. In Form B, item 6c, please reconcile the dose of ketamine/xylazine with the description in A8g.
i. In Form B, item 6d, PI should check appropriate PPE that will be required for the surgical procedures described in this protocol.
j. In Appendix 2, please add TGF SiRNA

20-144

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, please indicate the New ACC# 20-144
b. In Form A, item 2b, please indicate the role of personnel by number and provide UIC email contact for [redacted].
c. In Form A, item 4, numbers requested do not match with the tables given in A8h and those in Appendix1; please reconcile.
d. In Form A, item 7d2, please address the following:
    i. Please include corn oil
    ii. Please remove "3" under scientific justification for Tamoxifen.
    iii. Remove " no PG is available" under scientific justification for SRBCs.
e. In Form A, item 8c, please provide a summary of the animal experiments conducted during the last three years and remove the details regarding the procedures indicated in this section.
f. In Form A, item 8e, please remove the details regarding source and procurement for hMT-gamma1-/- mice from this section.
g. In Form A, item 8g, please address the following:
    i. Under study 1, please remove 'LPS stimulates expression of the AID promoter. The Cre in these mice is inactive in the absence of tamoxifen. AID is critical for CSR to occur. Thus, LPS activation of these mice in vivo will indicate whether AID is induced in early B cells in vivo' It is repeated twice.
    ii. Include doses for LPS and clarify whether tamoxifen gavage will be for 4 or 5 days.
    iii. Please remove the description for Tamoxifen administration
    iv. On page 15b and c, under mouse Strains used for CSR in mature B cell studies, remove the strain 'Msh2', as this is not included in item A4 and include HS3b4-/- here.
    v. Under study II, please verify volume of SRBCs. As 0.1 ml appears to be too small a volume. Also, indicate duration of observation for this study.
    vi. Under study II, please clarify whether mice sacrificed 11 days post booster refers to day 11 from first injection or second injection.
    vii. Under study III, PI should include justification for group size determination and add power calculation in A8h
    viii. Under study IV, please remove reference to Friend of Site 1 mice and row "r"
h. In Form A, item 8h, please provide power calculation for group size of 25 including the parameters used for power calculation.
i. In Form A, item 9, please provide PI's contact number.
j. In Form A, item 10, please address the following:
    i. Please indicate the anesthetic and dose as well as the route for both method 1 and 2.
    ii. For method 2, please check 10c.
k. In Form A, item 13b, please correct the year for row#2.
l. In Form A, item 14, Please address the following:
    i. Please list correct ACC regulatory training dates for personnel.
    ii. Provide UIC email contact for personnel.
    iii. For personnel, please check relationship to UIC.

iv. Please indicate personnel that will be responsible for non-irradiated diet feeding and unsterilized water.

m. In Form B, please correct the ACC# and in item 9, change deceased activity to decreased activity.

n. In Appendix 1, item 2, remove reference to Msh2-/- mice and recalculate the numbers in the breeding table and reconcile the numbers table A4.

20-147

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, please complete Funding Support information including Title of Proposals, Funding status etc.

b. In Form A, item 4, please address the following: Reconcile age of mice here with the experiment description in A8g and indicate the purpose of the animals in the use column.

c. In Form A, item 4, please define or spell out KPC the first time used.

d. In Form A, item 6d, PI checked acidified water for animals, include justification.

e. In Form A, item 6d,4, please remove answer provided

f. In Form A, item 8e, please address the following:

i. PI should provide additional explanation and/or justification for requiring KPC mouse model. Also, include information on the uniqueness of this pancreatic tumor model in this project.

ii. Please provide additional background information (genetic background etc.) on the KPC mouse strain.

f. In Form A, item 8f, please address the following:

i. Please include tumor kinetics for facial papillomas and vaginal masses for KPC transgenic mice.

ii. Please remove the last paragraph (pertaining to Balb/c Nu/Nu mice).

g. In Form A, item 8g, please address the following:

i. Under the pancreatic cancer model, please change the first sentence “Pancreatic cancer will be induced in KPC mice” to “KPC mice will develop pancreatic cancer” since this is genetic and not an inducible mouse model of pancreatic cancer.

ii. Under the pancreatic cancer model, please change “20 months” to 20 weeks.

iii. Und the lung Cancer model, please specify whether the A549 cells are human or murine cell lines.

iv. Under the xenograft model, please remove details for shaving since Balb/c Nu/Nu mice will not require shaving

v. Under euthanasia, PI should specify that “if tumor reaches 2cm in diameter” regardless of time, mice will be euthanized. This is also applicable to Form B9.

vi. Please reconcile monitoring criteria and frequency here with B9.

i. In Form A, item 8h, it is still unclear why 25 animals will be used; please provide justification for how a total number of 25 was determined including power analysis.

j. In Form A, item 10a, please specify building number ([redacted] for the listed location.

k. In Form A, item 11, please clarify if the extra animals refer to Balb/c nude mice. PI should note that only Balb/c nude and not KPC mice can be used for training

l. In Form A, item 12a, please check yes and add ketamine/xylazine injection for the subcutaneous injection of A549 cancer cell line.
m. In Form A, item 13a, please list the two tumor models and provide justification for each model.
n. In Form A, item 13c, PI should indicate alternatives found and provide appropriate justification for not using the alternative models found.
o. In Form A, item 14, please address the following:
   i. Please indicate the specific procedures/techniques which personnel will be involved with. PI should note that only personnel who will be directly handling and using animals should be listed here.
   ii. For each personnel, PI should only list training and expertise that are relevant to the experiments described in this protocol.
   iii. Personnel which will only be responsible for growing cancer cell lines and will not be handling or using animals and therefore should be removed here.
p. In Form A, item 15, please provide PI signature.

7. **Review from Subcommittee #2**

20-076

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:
Note to PI: This protocol needs to be divided into two protocols, one for cancer studies and the other one for Diabetic model and device testing

a. In Form A, item 4, Add "Mice" before C3H.
b. In Form A, item 7b, Murine Biologics – the fibrosarcoma cells will need to undergo testing prior to being transferred to UIC mice.
c. In Form A, item 8a, Project, 2nd part of this section that lists other institutions should be deleted. Also, PI needs to clarify how EPROI would enhance diabetes therapy and the rational for using both mice and rats for two different studies.
d. In Form A, item 8b, please clarify how EPROI will address hypoxia.
e. In Form A, item 8d, please provide background and reference for using rat donor for C57BL/6 recipients without immunosuppression. Most islet transplant models involve the same species/strain for host and donor.
f. In Form A, item 8g, please address the following:
   i. MRI and EPROI are in separate buildings. Are both these imaging modalities occurring on the same day? Also, describe the acronym JIVA-25?
   ii. Under Timelines, please clarify the animal numbers as it is very confusing. Day 0 states 20 mice, but then below it describes 12 mice and 8 rats.
   iii. Please clarify the glucose monitoring as stated in the table glucose monitoring is every day, but below it describes twice weekly testing, please reconcile.
   iv. Please delete the last sentence about housing in the density as it is incorrect.

v. Under induction of Type I Diabetic Mice, it is not recommended to fast rodents, especially prior to diabetes induction.
vi. Why is anesthesia needed for an IP injection? With adequate training, this can easily be done without anesthesia.
vii. Part V. – Please clarify how often glucose is checked and how often animals are given STZ.
viii. Under Surgical Procedure, If isoflurane and the anesthetic vaporizer is available for use, committee recommends using this method over ketamine/xylazine since animals will recover more rapidly.
ix. Describe the control device. For the Theracyte device, the size 22X12X1 mm appears to be quite large for a mouse. For the UF Device it states, "Implantation devices will likely not exceed 3x the diameter", therefore is the device 15 mm. Please Clarify.
x. Change Ketoprofen to Meloxicam 1-2 mg/kg SC q 24 hours.
xi. Section IV., last sentence – are mice euthanized after removal of the device?
xii. Under Study Design for Tumor growth, is anesthesia needed for injection of tumor cells. It is generally not recommended to inject tumor cells into the leg muscle of the mouse as it is a very small area. Additionally, to keep everything consistent and have less variables, we recommend using the same route of administration in all animals.
xiii. Tail vein cannulation, 1.5 hours is a long time to have an animal under anesthesia for the purposes of catheter placement. Does anyone in the lab have experience with this technique? Please clarify.
xiv. Bladder Cannulation, please clarify if males are difficult to catheterize, then should this part of the study only involve female mice. Delete sentence describing expense of contrast agent.
xv. Identification, Inspection of Well-Being, and Treatments; the current dose of insulin listed is very high and not recommended. Additionally, even administering 0.25 Units of insulin was not shown to be beneficial and most animals with very high blood glucose levels require a constant administration of insulin via an osmotic pump. This is also not recommended as this protocol is very complex and we want to minimize the number of variables. In general, if glucose levels are excessively high and mice have lost weight and are lethargic, they should be euthanized.
xvi. According to UIC ACC policy and guidelines any animal with an ulcerated tumor should be euthanized.
xvii. Animals in severe pain should be euthanized as this should not occur with a minor surgery. Additionally, the dose of meloxicam listed is very high and should be 1-2 mg/kg.
xviii. Endpoints – delete "in the span of a week" under weight loss as this should be over any time frame. Describe tumor size in mm/cm not volume. Any animal that is unable to feed or drink should be euthanized as supplementing with saline will likely not help. Additionally, any animal that reaches a BCS of < 2 should be euthanized.

20-139

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with

designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 8b, please define CNO.
b. In Form A, item 8g, please address the following concerns:
    i. As indicated above, this section of protocol seems to be a copy of the grant application. References and descriptions of photograph referencing other institutions and their funding source should come out.
    ii. Please clarify how pus is monitored while isolated and placed in the cup which is then placed in water bath. Please confirm personnel will observe animals, while animals in isolation.
    iii. Please add the description of foot shock test here (could be removed form item 13a), also clarify the number of trials and number of days the test will be conducted.
c. In Form A, item 8h, please address the following concern:
    i. Please remove the section labeled as "***Overview of the n calculation***".
    ii. Please Justify the numbers requested in the tables. Is not clear why group sizes are variable, please clarify.
d. In Form A, item 9, under dead animals, please either check save or discard.
e. In Form A, item 10a, please address the following:
    i. Please change method 5 to 4.
    ii. Please change [redacted]
    iii. PI has indicated that animals will be decapitated (as secondary method) using PI's owned guillotine, please clarify how PI will ensure the guillotine is maintained and is sharp?
f. In Form A, item 13a, please move the last paragraph to 8g.
g. In Form B, item 3, please address the following:
    i. Under "Percutaneous Catheterization", please add IP catheter to deliver chloral hydrate and check "yes" box
    ii. Under "Stimuli producing…", please move your answer to item B7 and uncheck "No".
h. In Form B, item 4, please address the following:
    i. Please add Meloxicam at dose of 1 mg/kg SC.
    ii. Please clarify why lidocaine instead of bupivacaine? Since this is a 5-hour procedure, the longer acting bupivacaine is recommended.
i. In Form B, item 6a, please change lidocaine to bupivacaine, see above for explanation.
j. In Form B, item 7, please provide an answer, please describe foot shock/conditioning here.

20-145

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In form A, item 4, Male and female animals are listed but in 8g only males are indicated., please request only males.
b. In Form A, item 8a, please rewrite the section in more lay person terms, section of 8b, can be moved here and information on 8a, can be moved to 8b.
c. In Form 8e, please justify using only males due to size issue and number of implants.

d. In Form A, item 8g, please address the following:
    i. Under procedure A, please remove “forearm”,
    ii. PI should combine procedures A and B so there is only one section for implantation of all sites (IP and SQ). Move retrieval to section with terminal laparotomy for retrieval.
    iii. In Part A, “arm” has been indicated as one the sites for implantation, committee suggest that PI reconsider using different site due to size of the arm, not much SQ fat and too small for size of device.
    iv. Under Part B, last paragraph, please change the suture pattern to Continuous pattern and change muscle to Subcutaneous layer.
    v. Under Part C, please also add SC site for retrieval in addition to intraperitoneal sites. Last sentence, please also clarify if animals also undergo pancreatectomy.
    vi. Under Part D, please remove stapling the duodenum as part of pancreatectomy procedure.
    vii. Under Part 1, study 1, please remove arm as site of implantation since not much SQ fat and too small for size of device.
    viii. Please clarify how 20 devices are going to be divided up. Does each site get the same device within each animal? Please in provided tables for both studies under devices/cells please indicate the type of devices/site.
    ix. PI has listed only 3 kinds of devices that are being tested, does each animal get implanted with same device on all sites or all kind of devices get implanted in all 4 animals.
    x. Does each animal have one or multiple adhesives used? If multiple, which sites with which adhesive?
    xi. Under procedure # 2, last paragraph, please change the suture pattern to Continuous pattern and change muscle to Subcutaneous layer.
    xii. Under procedure # 3, please also add SC site for retrieval in addition to intraperitoneal sites.
e. In Form A, item 9, please change the disposition of dead animals to refrigerator from freezer.
f. In Form B, item 4, please address the following:
    i. Please change meloxicam to meloxicam SR and dose to 0.6 mg/kg SQ.
    ii. Please change the ketamine dose to 10 mg/kg.
    iii. Please delete bupivacaine pre-op.
g. In Form B, item 6c, please address the following:
    i. Please combine surgery 1 and 2 as one surgery and move retrieval with terminal laparotomy.
    ii. For all surgeries please indicate the methods used to monitor the state/depth of anesthesia.
    iii. Under surgery # 3, please add SQ retrieval to this surgery.
h. In Form B, Item 6f2, please remove Cefazolin for immunosuppressed animals, since animals are not going to be immunosuppress for this study. Please change meloxicam to meloxicam SR at 0.6 mg/kg SC.
i. In Form B, item 9, please provide answer.

8. Review from Subcommittee #3

20-146

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

The PI proposes to conduct this class remotely with video recordings of mice in the lab accessible via the internet. The subcommittee 3 expressed serious concerns about this to the ACC. The ACC discussed in depth the potential ramifications of conducting the studies proposed in this protocol and streaming the videos of mice treated with amphetamines and lithium to students as part of a virtual lab. The consensus of the committee was that the blackboard platform did not have the capability of ensuring a secure stream that would prevent downloading or recording of the labs by the students, which could place the institution at risk from a public relations perspective. As a result, the ACC approved the protocol with the understanding that it could not be used for remote learning purposes during the COVID-19 pandemic, i.e. the protocol could only be used for in person wet labs once the campus allowed for their re-institution. As part of the ACC's decision the committee recommended that the PI seek out alternative model systems that could be streamed without risk to the campus to demonstrate the scientific process/method for this course under the current restrictions of COVID 19.

a) In Form A, item 8g, the sodium appetite experiment please replace the word "mice" with "rats" in the rationale. In the amphetamine study please provide specifics about when the control rats may be used again – will this be on the same day or is there a longer lag time between experiments for these rats, i.e. the committee is concerned that if a sufficient wash out period is not provided that the rats would receive two doses of amphetamines in one day.
b) In Form A, item 13a, please provide information about the type and severity of distress that can result from lithium chloride injections.
c) In Form A, item 14, please provide ACC training dates for personnel.
d) In Form B, item 7, please provide the requested information for the distressful lithium chloride treatment.

20-141

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Condition of Initiation: ***The PI needs to provide IDEX reports on the cells obtained from Canada to the ACC and [redacted] prior to using these cells in mice at UIC.***

a. In Form A, item 7c, please add the word "charcoal" to the method of scavenging.
b. In Form A, item 8e, please indicate that FVB or CD-1 mice will be used to be consistent with the information in Form A, item 4.
c. In Form A, item 8g, please address the following concerns:
    i. Please indicate that the saline that will be used for vaginal lavages will be sterile.
    ii. Please indicate the site for SC injection.

iii. Please clarify if 10 months is experimental endpoint for all studies, if not clarify.

d. In Form A, item 13a, please change "mammary" to ovarian".
e. In Form A, item 14, please update the ACC training for personnel
f. In Form B, item 3, please remove intrabursal injection here as this is described under surgery in item 6c.
g. Form B, item 9, please remove first sentence "It is not certain….".

20-142

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please reconcile the numbers of animals and their anticipated use with the numbers in the breeding protocol and those mentioned in Form A, item 8g. Please contact oacib@uic.edu for help.
b. In Form A, item 6d, please provide more specifics about the timing of the sucrose drinking water administration; will this be done during the first 48 hours after the first or the last STZ injection?
c. In Form A, item 7d2, please address the following:
    i. please provide the concentration of sodium citrate
    ii. The anticipated amount of dihydrate sodium citrate that will be added.
    iii. The method of sterilization of corn oil and change the source of the corn oil from a commercial product to Sigma.
    iv. Change the justification for STZ from 1 to 2 or 3.
    v. Change the justification for RU486 to pharmaceutical grade since it is available.
    vi. Please submit Appendix 2 and move the chemical hazard information for ZTZ to Appendix 2.
d. In Form A, item 8e, please provide a justification (i.e., the scientific reasons) for each mouse model listed. As written the only information provided is what these mice are and sometimes what they will be used for. Some models are not addressed in items 8a. and/or 8b, so their purpose is nebulous; please expand the justification of the mouse lines. The rationale for using rats is unclear as they will be used only for one type of experiment in item 8g. and it is not clear what is meant with "doesn't show satisfactory results".
e. In Form A, item 8g, please provide the following clarifications:
    i. Although it is mentioned up front that males and female will be used and that this is taken into account for statistical analysis, there is no evidence of this in item 8h and some groups sizes (n = 5) make it impossible to use 50% males and 50% females. Please clarify this.
    ii. The humane endpoint of un-relieved pain requires a definition of this and the approach of how to recognize un-relieved pain.
    iii. For all studies, please provide a justification of why the not-injured eyes cannot be used as controls rather than having separate control groups.
    iv. For the studies A and B of Notch-1 Conditional knockout mice it is not clear why these experiments will be done and what the hypothesis is that they will address. In particular the rationale for the tarsorrhaphy is nebulous. Furthermore, it is unclear

why the group size for the tarsorrhaphy experiment is 10, rather than 16 as justified in item 8h. Please clarify these issues.

v. Please justify why this model is needed if the effect is the same as Cre-ERT (conditional deletion of Notch). (Notch1 flox/flox, K15-crePR1+/-)

vi. For the B study with Notch-1 Conditional knockout mice provide volume and concentration of the RU486 and the concentration of the DMSO which cannot be used undiluted.

vii. Under Chemical injury, please clarify the volume for "Drop".

viii. In the Wild-type mice study it is not clear why the group size for the tarsorrhaphy experiment is 5, rather than 16 as justified in item 8h. Also describe how the removal of the entire corneal epithelium is done - is any epithelium left on the eyes and is this different from the scraping injury mentioned in the studies A and B of Notch-1 Conditional knockout mice? Please clarify these issues.

ix. For the studies with Pax6+/- mice Pax6+/-/Thy-1 mice it is not clear why these experiments will be done and what the hypothesis is that they will address. Please clarify. And please clarify why the group size of these mice is 5 and not 16 as justified in item 8h.
Please clarify what is special about the Thy-1 mice that makes them suitable for the proposed experiments; this could also be addressed in item 8e. And please clarify how the microscopy is precisely done. Please explain how corneal epithelium is abraded.

x. Clarify why the group size in the experiments with the Thy-1 mice, the diabetic mice and the rats is 10 and not 16 as justified in item 8h.

xi. In the experiment with rats please replace the word "mice" with "rat".

xii. Please either remove the list of references or refer to them in the text as a means to justify specific models and techniques in items 8e. and 8g.

f. In Form A, item 9, please explain how sick animals can be treated and sacrificed at the same time and how dead animals can be discarded and save at the same time.

g. In Form A, item 13a, please provide a rationale for the need to protect an eye with tarsorrhaphy from bacteria.

h. In Form A, item 13a, please explain why some searches have been limited to the last 10 years and others have been done for all available years.

i. In Form A, item 14, please indicate who will do the NaOH treatments and update the ACC training date for personnel.

j. In Form B, item 3, please move the "under 21 day old" text to the tail snips which is where it was intended to be.

k. In Form B, item 6d, please clarify whether surgical instruments will be autoclaved between use on different animals or another method will be used, such as a hot bead sterilizer.

l. In Appendix 1, please reconcile the animal numbers and nomenclature of the various mouse strains with those listed in From A, item 4, and explain why B6.Cg-Serpinf1tm1Craw/J(homozygous) mice are listed here but not mentioned anywhere else in the protocol.

m. Appendix 2 (For STZ) is needed.

9. Designated Review(s), Exemptions, and Lab Visits

a) **Protocols**

Member 6 updated the Committee on the review of protocols 20-136, 20-138, 20-140 and 20-148 by DMR process. Protocols 20-136, 20-138, 20-140 and 20-148 were approved

b) **Exemptions**

There were none

c) **Lab Visits**

None – due to COVID-19 campus restrictions

10. New Business

a. Modification of Protocol 19-008 (12)

The Committee reviewed PI's request for: 1) addition of two chronic bowel inflammatory models to the protocol to further define the role of different macrophage lineages in the development of mesenteritis associated with intestinal inflammation, 2) addition of new mouse strains, 3) additional animals of approved strains and 4) addition of new funding source. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. item 5a, please address the following items:
    i. Aim 2-5 Please clarify if neonatal mice will be administered salmonella and DSS at day 7 and 14. Also, clarify how PI will administer salmonella and DSS to day 7 and day 14 mice. It is not clear how the PI can conduct this study. Please provide more details and how the time points fit into the context of the study.
    ii. In Aim 2-4 and 2-5 PI refers to 10b which in the original protocol is the intravital imaging of the lungs. Will PI be imaging the lungs in the mice in Aim2-4 and 2-5 or will the PI be imaging the gut mesentery. PI needs to clarify organ system imaged. If the gut then the PI needs to add this as an acute surgery under section 5g.
b. Item 5b, please address the following:
    i. PI lists 2,030 animals; however, the total in the table adds up to 1955. Please reconcile the difference.
    ii. Aim 1a, 1-4 It is not clear what is meant by ACC# 19-182 being linked to this protocol. This protocol must stand on its own. Therefore PI must add the parabiosis surgery to this protocol under 5,g as well as a description of the respective parabiosis studies in item 5 c. of this modification or PI needs to remove all reference to the parabiosis studies in this modification and add the specific parabiosis studies to protocol 19-182 including the mice strains and mouse numbers. I would strongly recommend that the PI do the latter and link the protocols (19-182 and 19-008) via a Form G. Please discuss with [redacted].
    iii. Aim 1a, 2-2 PI should clarify if he will be harvesting blood via submandibular vein and conducting BALs in mice that are 1 and 2 weeks of age. PI should clarify how the techniques are performed in young mice of that age. PI should provide more specific details for these studies.
    iv. PI needs to provide similar information on Brdu and when in the context of the study each agent is administered to the mice.

v. Item 2 = Determining the role of CX3CR1 – PI needs to indicate when in the context of the salmonella acute gut inflammation model the clodronate liposome is administered and when animals are euthanatized thereafter.

c. Item 5c, PI needs to include a detailed description of the salmonella acute gut inflammatory model including dose. PI must provide an IBC number that covers this work and PI must include an appendix 2 to the modification describing appropriate safety precautions for working with the agent.
d. Item 5g, PI needs to include acute surgical procedure for the imaging of the gut mesentery, if it is being conducted.
e. Item 5i, PI needs to be completed for the salmonella acute gut inflammatory model and possibly the gut mesentery imaging study.
f. PI should remove parabiosis studies from this modification and add under ACC 19-182 (where these procedures are approved already), in addition PI should request animals for these studies and request the addition of funding to protocol 19-182.

b. Modification of Protocol 19-140 (01)

The Committee reviewed PI's request for change of PI. Following discussion, a motion to secure approval following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Policies and Guideline Review

The Committee reviewed the following policy: Zebrafish Research Policy. The Committee discussed and that there were no changes required for Zebrafish Research Policy. Following review, a motion to approve the changes were passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. COMRB Helicobacter/norovirus outbreak update

Member 6 presented the committee with summary of events surrounding the helicobacter/norovirus outbreak associated with the MSK mice and presented the information regarding the cause of the outbreak of mouse helicobacter and norovirus to the ACC as well as an overview of the subsequent meeting with PI's Department Head. As part of the discussion PI's Department Head's action plan was presented to the Committee as listed below:

1. PI's Department Head and/or senior faculty meet with PI after the ACC meeting to reinforce ACC's conclusions.
2. PI's Department Head and/or senior faculty meet with PI on a regular basis (quarterly to semi-annually) to review PI's animal use and animal protocols.
3. Request that PI repeat the Animal Training requirements by retaking the online training courses
4. Request that PI take the Responsible Conduct of Research course: https://research.uic.edu/compliance/research-integrity/responsible-conduct-of-research-training/.

5. If PI successfully completes steps 1-4, then PI's Department may ask PI to develop an "ethics in research" seminar for the benefit of the Department which will be given to faculty, students, and other research trainees.
6. The Committee discussed the unusual circumstances around this event including: the potential impact it could have had on the UIC animal care and research programs, the impact on animal welfare, whether the PI's research should be suspended, whether this was an integrity/departmental human resources issue, whether the action plan went far enough in making sure the junior faculty member understood the significance of her actions.

Following discussion, the committee made the following determinations:

a. That this was not a reportable item and that a suspension of research was not necessary as the action of the PI had already resulted in a six-week suspension of her research program while her animal room was under quarantine.
b. That the IO should be notified of the situation and its potential to be an integrity issue and the Attending Veterinarian at MSK should be notified.
c. That the Department Head and PI would complete the following action plan:
    i. Department Head and senior faculty would meet with the PI after the ACC meeting to reinforce the conclusion of the ACC.
    ii. The PI would pay for the costs ($3650) of all testing conducted as part of the outbreak.
    iii. Department Head and senior faculty would meet with the PI on a regular basis (quarterly to semi-annually) to review her animal use and animal protocols.
    iv. The PI would retake the Animals and Research at UIC and the Working with Mice and Rats at UIC training modules.
    v. The PI would take the Responsible Conduct of Research course: https://research.uic.edu/compliance/research-integrity/responsible-conduct-of-research-training/
    vi. The PI would develop an "ethics in research" seminar for the benefit of the Department of Physiology, to be given to faculty, students, and other research trainees.

ANIMAL CARE COMMITTEE MEETING MINUTES
SEPTEMBER 15, 2020

Attendees: Member 6, Member 8, Member 9, Member 10, Member 11, Member 24, Member 30, and Member 43

Absent: Member 42

Guest: Member 44 and Member 45

1. **Minutes**

   None

2. **Announcements**

   New Director of OACIB was introduced to the committee.

3. **Old Business**

a. Protocol 20-043 update

Member 6 updated the committee on the status of the protocol and the Committee reviewed the revised protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Condition of Approval: PI must submit an approved copy of SOPs pertaining to this protocol to OACIB, prior to obtaining approval and initiation of the project.

a. In Form A, item 8f, please remove your answer, and add IL10-/- animals and their deposition for inflammatory bowel disease and colitis.
b. In Form A, item 8g, please describe how animals will be transferred from [redacted] lab in [redacted] to PI's lab in [redacted].
c. In Form B, item 13b, 2nd search, please redo the search by extending the Period of Years of Search to 2020.
d. In Form A, item 14, please address the following:
   i. For personnel # 4 and 5, please clarify their relationship to UIC and mark the appropriate box.
   ii. Please only indicate procedures/techniques specific to this protocol.
   iii. For personnel # 2, please remove experience regarding BSL2.

4. **BRL Director's Legislative and Facility Update**

Member 6 directed the Committee's attention to the report and updated the Committee on the following: 1) COVID 19 update: That BRL veterinary staff initiated lab visits in August/September and list of labs visited were presented to committee members as part of the DMR report, 2) that training for the first group of research staff to work in the BSL-3 facility was essentially completed, 3) that it is expected that SARS-COV-2 virus will be on campus by 9/18/20, 4) that the first studies

proposed for the [redacted] will only involve bench work, i.e. no animal work, 4) that the BRL animal husbandry staff and the BRL technical staff have been working without a contract since 10/3/19 and 12/16/19, respectively. Though contracts are currently in mediation and the union (SEIU) has yet to submit a formal contract proposal to the University there is the chance that the animal husbandry and veterinary technical group will strike along with the Hospital's nurses, who are scheduled to strike on 9/12/20. The situation is very fluid, but it should be noted that there are provisions in place to ensure animals are fed, watered and receive appropriate veterinary care, 5) that Dr. Jim Strake of Pfizer has been assigned to lead the AAALAC site visit team which will be conducting UIC's AAALAC accreditation site visit and that visit will be in Nov 2020, and will be conducted in two parts, initial portion through zoom (Nov 5 and 6) and the other part will be in person on site (Nov 10 and 11), 6) that the rodent training module for UIC research is nearing completion and should be available on the AALAS learning library website by October 1st and 7) that the BRL veterinary staff rolled out a new training wet lab on perioperative care in rodents. It should be noted that the wet lab was well received by the attendees.

5. OACIB Update

a. Modifications

Member 9 updated the Committee to the following activity during the past month: there were 10 modifications approved at the administrative level, 25 modifications approved administratively following veterinary consult, and 5 modifications approved via designated review this month. In addition, there were 12 protocols that added personnel, 0 with personnel deletions, 5 that added new funding, and 0 in which animals were added to the holding protocol.

b. Continuations and Terminations

Member 9 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal of the protocols was passed by the following vote: 9 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

20-150

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Form A, item 2 - Use consistent nomenclature for mouse strains throughout the protocol.
b. Form A - correct old protocol number.
c. Form A, item 2a, please provide contact address and email address for the PI.
d. Form A, item 2b, please correct emergency contact phone number for [redacted]
e. Form A, item 4, please address the following:
    i. Use consistent nomenclature for mouse strains throughout the protocol.

ii. M/F mice are requested for all mice. A justification for sex as a biological variable is required in item 8.h. Also, it is not clear if the total animal numbers requested reflect only one sex or both; please clarify.
iii. Form A, item 4e-g - The age of the Pak1ko, TG-Tm 180, and control mice are listed at 6 months; please confirm that 9-month-old mice will not be used as is stated in A8g.
iv. C57BL6 and C57/cTnl-ND mice are justified for use in the protocol but not listed in the table. Further, these mice are not listed in item 8h and do not have a sample size power analysis justification; please revise for clarify.

f. Form A, item 5c - [redacted] are both listed twice. [redacted] and [redacted] are listed in item A10a but not listed here; please clarify.
g. Form A, item 8f; PI described the existence of a phenotype, please check the "yes" box and reference Form B, item 9. Also, include age of onset, monitoring criteria, and applicable humane endpoint.
h. Form A, item 8g, please address the following:
    i. Under experimental design, procedures, and data analysis, remove the reference to "Associated with table 4 c, e, h, and i" or clarify the contents of this table.
    ii. Move all sample size and power analysis and justifications to item 8h.
    iii. Under location of surgery, remove personnel information from this section.
    iv. Under pre-op analgesic, indicate that the Buprenorphine will be administered SC.
    v. Under terminal hemodynamic measurements, please reconcile the dose of isoflurane for induction and maintenance with A7c & B6c.
    vi. Under terminal hemodynamic measurements, indicate how frequent osmotic pump will be replaced and describe the replacement procedure in detail.
    vii. Form A, item 8h, please address the following:
    viii. Add power analysis and number justification for c57BL6 and c57/cTnl-ND mice.
    ix. Move all sample size and statistical justification from A8g here and indicate the proportion of male and female mice that will be used.
i. Form A, item 10a, please address the following:
    i. All the locations listed here need to be listed in section item 5c.
    ii. For method 5, please verify that there is a CO_2 station in [redacted].
    iii. For method 1, add [redacted].
    iv. For method 2, change room number to [redacted].
j. Form A, item 12a and b, please check only one applicable box.
k. Form A, item 13a, if dilated cardiomyopathy is a potential endpoint criterion for the study, a brief justification for the use of the model is required here.
l. Form A, item 13b, please correct the period of years searched for the dilated cardiomyopathy.
m. Form A, item 14; please note that all personnel listed here have adequate experience and will not need a trainer.
n. Form B, item 3, please uncheck "no" for tail snips.
o. Form B, item 4b - change isoflurane dose from 1=4% to '1-4%' and remove buprenorphine from this section.
p. Form B, item 6a, please specify that the hair will be shaved or removed with Nair, scrubbed with betadine, and 70% isopropyl alcohol as described in A8g.
q. Form B, item 6b, please remove the answer provided and indicate anesthetic and supplemental dose to be used for each procedure.
r. Form B, item 6c, please address the following:
    i. Remove the reference to buprenorphine SR.

ii. Under surgery 1, please include a summary or description of the osmotic pump replacement as described by Gaffin et al.
iii. Please verify that the incision for subcutaneous implantation is about 4.5 cm since this seems large for a mouse. If so, consult with the veterinary staff.
iv. Surgery 2, PI indicated that catheter will be placed under microscopic guidance; if the heart will be exposed during this procedure, provide details on the surgical approach including the size and location of the incision.

s. Form B, item 6d, in A8g PI indicated that a mask and cap will be worn during surgical procedures; please check the "mask" and "cap" box for consistency.
t. Form B, item 9, please address the following:
    i. Indicate the specific primary and secondary method of euthanasia that will be used.
    ii. Please reconcile the frequency of pump replacement here with A8g and B6c.
u. General comment: Please correct the misspelling of administered drugs: 1) isoflurane to "isoflurane" (Form A, item 7c -). 2) Xylazine to "Xylazine" - isoflurane to "isoflurane" throughout the document.

20-153

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, PI should check appropriate box for personnel and indicate role on protocol.
b. In Form A, item 3, PI should provide institutional approval number for funding support 2 and uncheck box under funding support 5.
c. In Form A, item 4, please address the following:
    i. Remove information on rows i-j
    ii. PI should include inappropriate genotype listed in appendix 1
d. In Form A, item 5b, PI listed radioactive procedures in [redacted], please remove.
e. In Form A, item 5d, PI checked “Yes” for maintaining animals outside approve facility and indicated [redacted] (surgical room) and [redacted] (Biohazard room), please clarify.
f. In Form A, item 7a, list specific liposomal cDNAs described in A8g.
a. In Form A, item 7c, PI should clarify whether in addition to isoflurane, sevoflurane will also be used.
b. In Form A, item 7d2, please address the following:
    i. Indicate only one scientific justification for tamoxifen.
    ii. The scientific justification for corn oil should be 1.
    iii. Add SUMO-siRNA, clodronate, cholesterol, dimethyl-dioctadecyl-ammonium bromide, and glucose, including scientific justification, source, method of preparation and sterilization.
    iv. Please change scientific justification for corn oil to 1.
c. In Form A, item 8c, please address the following:
    i. PI should provide more details on what was done with the different types of microcapsules tested.
    ii. Include a brief description on the proposed modifications of microcapsules to improve rate of achieving normoglycemia at 1-2 months post-transplantation.

d. In Form A, item 8e, third paragraph under Rab43, please clarify whether Rab43 siRNA or Yap siRNA.
e. In Form A, item 8f, include description of the phenotype, age of onset, monitoring and humane end point.
f. In Form A, item 8g, please address the following:
    i. Under LPS nebulization, PI should indicate how mice will be handled after the first 24 h observation.
    ii. PI should indicate injection volumes for all compounds that will be administered systemically.
    iii. Under CLP, please provide more information of mid-grade CLP and high-grade CLP. Also include justification for using both models.
    iv. Under macrophage manipulation, please clarify if these mice will be anesthetized with Ketamine only. Also, include dose or concentration for clodronate.
    v. Under thioglycollate and isolation of peripheral macrophages, please include dose or concentration thioglycollate and indicate method of euthanasia.
    vi. Under isolation of bone marrow derived macrophages, please provide a full description of bone specific isolation of macrophages.
    vii. Under bone marrow harvest and transplantation, please provide more information on how mice will be euthanized by rapid cervical dislocation without anesthesia. Also include scoring scale for humane end point criteria here and in B9.
    viii. Under isolation of neutrophils, indicate if pharmaceutical grade heparin will be used.
    ix. Under isolation of lung endothelial cells, as described it is not clear how cells will be isolated after cannulation of trachea and pulmonary artery, please clarify with more additional information.
    x. Under in vivo studies PI indicated that lung tissue analysis at 0 and 12 h post CLP have been completed, however 24 h post CLP analysis has not been done but PI is proposing to repeat time 0 and 12 h post CLP. Please include justification or additional explanation for the need to repeat these two time points.
    xi. Method for isolation of lung endothelial cells is not well described and should be re-written to include more specific details of the procedures involved.
    xii. Under in vivo studies, PI should include route and injection volume for SUMO-1 siRNA.
    xiii. Under project 3, experiment 3; please indicate if pharmaceutical grade imipenem will be used.
    xiv. PI should indicate method of euthanasia for each experiment.
g. In Form A, item 8h, please address the following:
    i. The PI used the same power calculation to determine experimental group size for all experiments, please clarify.
    ii. Please indicate the proportion of male and mice that will be used for all experimental groups.
h. In Form A, item 10, please address the following:
    i. In the first row, please list CO_2 under anesthetic and inhalation for route of administration.
    ii. In the second column (Method) use the numbers for method of euthanasia.
    iii. List [redacted] for CO_2 euthanasia.
i. Under item 10c, please check box for exsanguination.

j. In Form A, 10e &10f, in A8g, PI indicated that for collection of bone marrow derived macrophages, mice will be euthanized by rapid cervical dislocation without anesthesia, so these sections should be answered including scientific justification for not using anesthesia. Also, personnel that will be responsible for this procedure should be identified in A14 and will need to demonstrate proficiency with this procedure with veterinary staff.
k. In Form A, item 11, please move answer here to A10f.
l. In Form A, item 13a, include justification for mid-grade and high-grade CLP
m. In Form A, item 14, please address the following:
    i. Indicate personnel that will be responsible for rapid cervical dislocation without anesthesia.
    ii. Please list training and expertise with all the techniques and procedures described in the protocol for all personnel listed in the protocol.
n. In Form B, item 3, please include tail snips for genotyping as indicated in appendix 1. Also include intracheal instillation of *P. aeruginosa* and nebulization of LPS.
o. In Form B, item 6a, please remove last sentence because CLP is not a terminal surgery.
p. In Form B, item 9, please address the following:
    i. Reconcile the LPS doses and volume for IT instillation with the experimental description A8g.
    ii. Reconcile the monitoring frequency post P. aeruginosa IT with the experimental description in A8g.
    iii. In paragraph 3, please change "Himan" to Humane.
    iv. Reconcile the monitoring frequency and duration post irradiation with A8g.
    v. Monitoring and humane end point for irradiated animals should be redone.
q. In Appendix 2, this should be redone; also add all liposomal cDNAs.

20-157

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please clarify if breeders will be set up for the KO mouse strains or not. If yes, please modify the form (numbers, ages, and usages) accordingly and complete Appendix 1. If these mice will be transferred from other protocols, please clarify.
b. Form A, item 5a, please also check [redacted], for post-surgical housing is in [redacted]).
c. Form A, item 7b, please add Matrigel.
d. Form A, item 7d2, please address the following:
    i. Please include sterilization of Pellet and Luciferin substrate.
    ii. Add VEGF, including scientific justification, source, and method of preparation.
    iii. Add Matrigel, including scientific justification, source, and method of sterilization.
    iv. The committee recommends that corn oil be purchased from Sigma not grocery store.
e. Form A, item 8a, second paragraph, please remove the reference to "the site at which tumor in injected does not represent the local tumor environment and the absence of this environment may result in cancer development that differs from that observed in human pathology" here and in A8g or include additional explanation and justification for using this model.
f. Form A, item 8e, please provide separate justification for each mouse strain listed in table A4.

g. Form A, item 8g, please address the following:
    i. Under goal of the study, please remove the reference to "the site at which tumor is injected does not represent the local tumor environment and the absence of this environment may result in cancer development that differs from that observed in human pathology"
    ii. In Protocol #1, please clarify how DMEM and Matrigel will be prepared/sterilized and if commercially available indicate so.
    iii. Under Protocol #1 humane endpoint criteria, please specify "tumor mass >2cm in any dimension".
    iv. Please reconcile humane endpoint criteria here with Form B9.
    v. Under Protocol #2, as indicated the stock cell suspension will be $5x10^6$/ml, and therefore, 100ml cell suspension should contain $5x10^5$cells; please reconcile.
    vi. Please describe how metastatic nodules will be counted.
    vii. Under humane endpoint for tumor metastasis, add weight loss >20% and body condition score of <2 or weight gain >15% with abdominal distension.
    viii. Under Protocol #3, please indicate the concentrations for Tetracaine drops and Meloxicam.
    ix. PI should include experimental procedures for luciferin injection and IVIS imaging and frequency of imaging.
h. Form A, item 8h, please include power analysis and justification for experimental group size of 8. Also, note that Rosner equation cannot be used for calculation of sample size, please reconcile.
i. Form A, item 9, please also check "Save Refrigerate" for Dead Animals.
j. Form A, item 13b, a literature search performed using the same search terms as indicated, yielded more outcomes that listed; please re-do the literature search and update accordingly. Also, include endothelial vascularization permeability and angiogenesis in the combination of search terms used.
k. Form A, item14, please address the following:
    i. Please complete Trainer and Expertise for personnel.
    ii. Please update the ACC Regulatory training date for personnel.
l. Form B, item 4, please indicate the concentration of tetracaine
m. Form B, item 6c, please indicate monitoring for depth of anesthesia.
n. Form B, item 9, last sentence of the first paragraph, please indicate "2cm diameter in one dimension". Also, reconcile humane endpoint criteria and monitoring with A8g.

20-158

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5b, please uncheck [redacted] and check [redacted]zard [redacted].
b. In Form A, item 6c, please change "caged individually" to housed individually.
c. In Form A, item 7d2, please add HBSS including scientific justification, source, and method of sterilization.
d. In Form A, item 8c, please provide additional details on what was done with respect to the different types of microcapsules. In addition, PI should include a brief description on the proposed microcapsule modifications to improve the rate of normoglycemia at 1-2 months post-transplantation.

e. In Form A, item 8b, please address the following:
    i. The information provided here is experimental procedure; please provide scientific background for the experiments described in this protocol.
    ii. Please define and/or spell out PFO here and throughout the protocol.
    iii. Please specify that human islet cells will be used.
    iv. PI should also include a description of how the viability of the human islet cell is determined or ascertained.
f. In Form A, item 8e, please address the following:
    i. The species/strain justification provided here suggests that nude mice will be used to test the efficacy of microcapsules-containing islet cells while C57 mice will be used to test biocompatibility and immune response to microcapsules; however according to A8g both nude mice and C57 mice will be used in all experiments; please clarify
    ii. Please remove the reference to non-human primate islets here and throughout the protocol.
g. In Form A, item 8g, please address the following:
    i. It appears PI has experience with STZ-induced diabetes therefore a specific dose of STZ should be provided instead of dose range, except if PI will be performing STZ-dose response.
    ii. PI should indicate method of euthanasia for each experimental procedure.
    iii. PI should indicate source, dose, and volume of islet cells for kidney capsule transplantation.
    iv. PI should include a description of the method of blood collection by retroorbital route, and if anesthetic will be required, specify the anesthetic that will be used and the volume of blood that will be collected by this route. The committee recommends that PI considers using facial vein for blood collection since more blood can easily be obtained by this route.
    v. PI should specify that 20 different microcapsules formulations will be evaluated.
    vi. PI should ensure that the frequency for blood glucose monitoring and the time points for OGTT are consistent here and throughout the protocol.
h. In Form A, item 8h, is sex a biological variable in the proposed experiments? If yes, PI should include a justification for using male mice only.
i. In Form A, item 13b, the literature search should include the model and experimental procedures that will be performed in mice.
j. In Form B, item 3, please address the following:
    i. PI indicated that anesthetics will be used for tail snips, please specify anesthetic in A8g.
    ii. PI should remove reference to insulin injection.
    iii. Uncheck box for use of anesthetic under other treatments.
k. In Form B, item 5a, PI should also check multiple survival surgery for mice receiving kidney capsule transplantation and nephrectomy followed by 48 hours of blood glucose monitoring.
l. In Form B, item 5b, PI should answer for multiple surgeries.
m. In Form B, item 6e, both surgery 3 and 4 should be listed under class 3.
n. In Form B, item 9 please reconcile frequency for blood monitoring and duration of studies with A8g.

20-160

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with

designated member review following full committee review via subcommittee of members 6 and 9 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 2b, please add a scientific consultant here.
b. In Form A, item 3, please uncheck the boxes for funding support 2 and 3 if these will not be used.
c. In form A, item 4, please address the following:
    i. Please account for BL/6 WT animal use in this table along with all transgenic lines or EAE models.
    ii. Several mouse lines are listed as use code 2 (breeders) but are used before adulthood (<4 weeks); please rectify.
    iii. Several transgenic lines (rows g, h, i) animal totals are given but do not match the number of use codes and ages listed. Please specify numbers for each age and use code listed in the adjacent columns.
d. In Form A, item 7d2, please address the following:
    i. Change the scientific justification for corn oil category to #1.
    ii. Add incomplete Freund's adjuvant include scientific justification, source, method of preparation and sterilization.
e. In Form A, item 8e, 2D2 mice are mentioned but are not listed elsewhere in the document; please remove or else describe their use.
f. In Form A, item 8f has been changed to 8a, please correct the formatting of this page and the next page.
g. In Form A, item 8g, please address the following:
    i. Please describe how the presence of bladder atonia will be assessed and indicate in A14 the personnel with experience for this assessment.
    ii. Under experiment 1A, will oral medications be given by oral gavage or by drinking water. If the former, please include description and add to Form B3. If the latter, please complete Form A, item 7d2.
    iii. Please clarify decrease of core body temperature of 7^{o}C as humane endpoint criteria if this will be used and if not, please remove.
h. In Form A, item 8h, please address the following:
    i. The Cav1-/- mice appear to be undercounted. Between experiments 2A, 2C, 2D, 3A, 3B and 5, the table lists (20+33+66+40+40) *2(for both sexes) = 398 experimental animals, but only 300 are requested in item 4. Please clarify the numbers or reconcile counts in the table.
    ii. Similarly, (20+67+100+40+40+36) *2 = 606 WT Bl6 are listed in the first summary table but only 370 are listed in the second. (34+18) *2 = 104 CXCR3-/- are requested in the first table but only 68 are listed in the second. Several other lines are off by smaller amounts, please reconcile the numbers in A4 with A8g, A8h, and Appendix 1.
    iii. Please describe how a 15% loss of sample due to human error was obtained.
    iv. PI should maintain consistency with the power calculations for the respective experimental groups.
i. In Form A, item 10.a, please address the following:
    i. Please clarify if methods 4 & 5 will both be used in this protocol.
    ii. In the second row, please list CO_2 and list the specific [redacted] for this procedure.
j. In Form A, item 13a, please address the following:

i. Alternate methods of genotyping are available that are adaptable to neonatal mice. Please provide a justification for using toe clips, which is a non-preferred method at any age.
ii. Please provide justification for using two acute EAE models.

k. In Form a, item 13b, please address the following:
i. Please list actual dates of search range. Please perform search for alternatives to acute model and include justification for alternatives, if found.
ii. Please include EAE and Biozz in your literature search terms and update accordingly.

l. In Form A, item 14, please remove consultant from this section and add to A2b as scientific consultant.

m. In Form B, item 3, please add oral medication to account for treatments administered by oral gavage.

n. In Form B, item 6d, please use hot bead sterilization between animals.

o. In Form B, item 7, please justify Freund's Complete Adjuvant here as a nonsurgical technique causing unalleviated pain.

p. In Appendix 1, please address the following:
i. Please adjust numbers and disposition to account for surplus animals. For example: in Breeding 1, 6 litters * 5 litters/female * 21 breeding females would result in 630 progenies. 552 are requested for experimental and breeding purposes, meaning the remaining 78 should be accounted for as surplus or maintenance. This should be done for all breeding groups such that the number of generated animals predicted from pups/litter * litters/dam * # of dams matches the total numbers and the sum of all animals in the disposition column.
ii. Please ensure that enough breeders are accounted for to ensure necessary animals are generated. E.g.: in Breeding #3, 4*6*6 = 144 animals would be generated using the numbers listed in the upper box, but 328 are listed under total numbers below. Please check numbers for all breeding groups to ensure adequate numbers of animals are generated to meet goals as set out by power analysis.
iii. In breeding #4 more animals are disposed of than are listed under total numbers, which in turn does not reflect the numbers that would be generated by the number of breeding animals listed above. Please rectify.
iv. In breeding #7, the Cldn5 genotype of the females is missing. This should probably read +/- as its listed below. However, this table and breeding 6 use imprecise nomenclature to describe these animals. From the PI's previous work, these appear to result from a transgenic insertion of eGFP-Claudin 5 after an epithelial promoter, in which case they should probably be referred to as eGFP-Cldn5$^{Tg/0}$, to make clear that the -/- animals are not Cldn5 knockouts. While this nomenclature could be used throughout to accurately describe hemizygous transgenic animals, it is most critical for Cldn5 to distinguish animals with this background from others where the native locus of Claudin 5 is manipulated. (Similarly, in Breeding #8, the heterozygous animals should be described as Claudin-5 Fl/+).
v. In breeding #6 and #7, the proportions are not correct. e.g., in Breeding #6, the progeny of a eGFP-Cldn5$^{Tg/0}$ female with a WT male would be 50% of each: 50% of the pups receive the Tg and 50% receive the null from the dam, and all receive the null from the sire (in the absence of any phenotype affecting survival of the progeny, which should be noted if the case). These calculations are performed correctly in other sections of this appendix.

vi. BL/6 WT animals are used throughout this protocol but are not easily tracked in Appendix 1, please reconcile.
vii. As written, Appendix 1 seems to generate 1175 such mice, of which 370 are used for experiments per table in 8h (see clarification "h" above). Please use Form A4 to account for all BL6 "WT" animals from other breeding.

q. Complete and attach Appendix 2 (for pertussis toxin) with revisions.

20-165

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 6 and 9 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 3f, please check the funding status box.
b. In Form A, item 5c, please change room number to [redacted] and the procedure for all the BSL2 agents that will be administered and list the procedures that will be performed.
c. In Form A, item 7a, please check "No" for all applicable hazardous materials.
d. In Form A, item 7b, check yes, and list cells, macrophages, and neutrophils
e. In Form A, item 7c, please add isoflurane here for IVIS.
f. In Form A, item 7d2, please address the following:
    i. Please indicate source for all pathogens and cells (PI needs to obtain IBC for using cells)
    ii. Please remove macrophages and neutrophils and list under 7d for murine biologicals.
    iii. Please remove ketamine/xylazine, dendritic cells, and Nair from this section.
    iv. PI should specify if sterilized antibody will be procured, if not, include method of sterilization.
    v. PI should note that ketamine is a controlled substance and therefore will need to obtain State control substance license to procure ketamine. In addition, pharmaceutical grade can be purchased from the Hospital Pharmacy while xylazine can be obtained from the BRL.
g. In Form A, item 8d, please reconcile the scope and scientific abstract with the rationale for using animals.
h. In Form A, item 8f, please uncheck the box as there are no genetically engineered mouse lines that are used.
i. In Form A, item 8g, please address the following:
    i. Include mode of administration for all the agents listed under treatment procedures.
    ii. Under imaging procedures indicate that the pathogen will be fluorescent tagged and explain the entire imaging procedure including the time point, anesthetic (isoflurane), and duration.
    iii. In the study design, please include a schematic representation of the experimental design including the start and end of special diet, pathogen administration dose, time, age of mice and at what point the other treatments will be administered.
    iv. Please clarify if pathogen and the other agents will be simultaneous or there will lag time between treatments.
    v. Please include details for alveolar macrophage adoptive transfer.
    vi. Under project 2, Aim 2, please remove reference to 1.5 genes.

vii. For each model, specify monitoring criteria and monitoring frequency for each pathogen.
viii. Under methods of euthanasia, please remove "forced" in the sentence "all animals will be euthanized using forced inhalation of compressed CO_2 in a sealed chamber" Also in the last line please remove "has been approved by IACUC."
ix. PI should include additional explanation and/or justification for the differences between retroorbital and intranasal route of infection in terms of the experimental outcome or study endpoints.

j. In Form A, item 8h, please address the following:
   i. Remove the lines pertaining to why C57BL6 mice are suitable for the study.
   ii. Please specify if equal numbers of male and female mice will be used in all the studies.
   iii. Please include a tabulation for the number of animals requested for each study to make it easy to comprehend as there are number of variables that are to be considered.
   iv. Under Aim 1, remove the word "approximately"
   v. Under statistical analyses, please remove methods for statistical analysis of the data obtained and include the Statistical test/design used to determine the sample size, effect size, alpha level (significance, or "p" value; typically 0.05), power level used in the analysis (typically 60-80%).
   vi. Please remove the whole section on testing ketamine/xylazine because only pharmaceutical grade formulations are used, and historically, there should be any issue with this anesthetic.
k. In Form A, item 9, please uncheck the contact other box.
l. In Form A, item 10a, please address the following:
   i. Please indicate that 30-70% CO_2 will be used and remove the reference to euthanasia solution.
   ii. Please use the number codes (1 for CO_2, 6 for ketamine/xylazine, and 7 for euthanasia solution) for method of anesthesia.
m. In Form A, item 13b; i) please redo the search by including all the pathogens used in the study, ii) please justify in 13c why alternatives are not being used.
n. In Form A, item 14, i) please list all the procedures that PI will conduct, ii) indicate that PI will be responsible for providing the special diet to experimental mice and iii) state the experience that PI has with intranasal and retro-orbital injections.
o. In Form B, item 4, please remove ear punch or include reason for ear punch in A8g.
p. In Form B, item 4, please remove "a" since this ketamine/xylazine dose is used for euthanasia. Also, reconcile dose with A10a.
q. In Form B, item 5d, uncheck the box for chemical sterilant.
r. In Form B, item 5e, uncheck the box for PI acknowledgement.
s. In Form B, item 6e,4, please uncheck box.
t. In Form B, item 7, please remove the answer provided.
u. Please complete and attach Appendix 2 with revision

7. **Review from Subcommittee #2**

20-076

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5b, please uncheck "other", and remove [redacted].
b. In Form A, item 5c4, please indicate TBD for location.
c. In Form A, item 8b, please address the following:
    i. Please clarify why MRI imaging is needed? Is it for comparison of imaging modalities?
    ii. Please justify xenotransplant model and provide reference if available. If not reference (Committee is suggesting PI to conduct a pilot study with ~ 10 mice if no references are available).
d. In Form A, item 8d, the yellow highlighted paragraph should be moved to 8b (see comment c2 above). Also, the reference provided is for NHP study not rodents, please provide more appropriate reference, if no reference available (Committee is suggesting that PI should conduct a pilot study with ~ 10 mice).
e. In Form A, item 8e, please justify why only male rats will be used.
f. In Form A, item 8g, please address the following:
    i. Please delete the 2nd timeline table, since the timelines indicated does not match what is describe in table # 1 and text.
    ii. Please clarify what is the control device and is the same control device used for the other implants?
    iii. Please clarify that both MRI and [redacted] will be used.
    iv. Please clarify if both Male and female mice are going to be used as indicated in A4 and 8e, since only male mice are indicated in 8g.
    v. Please clarify how often glucose levels will be measured, every day or twice/week. It is indicated both ways in the protocol, please correct accordingly.
    vi. Please change the dose of meloxicam form 1-2 mg/kg to 2 mg/kg.
    vii. Please clarify if animals will be survived after implant removal to show that glucose control is due to the device and explain how that is done.
    viii. Under tail vein cannulation, please remove the last sentence regarding how long it takes to cannulate the tail vein.
    ix. Under surgical procedures, please clarify if animals will be survived after removal of the sensor to show that glucose control was due to the device, and if yes, how will animals be monitored and for how long.
    x. Under Bladder cannulation, please address the following:
        1. clarify if cannulation is also done for MRI imaging.
        2. Please change AB ointment to sterile lube ointment.
    xi. Under identification, please remove the last paragraph.
    xii. Under endpoints, please remove text about veterinary intervention. The criteria listed here are humane endpoint criteria and animals will need to be euthanized at this point. Please add the body score <2 to the list of humane endpoint criteria. Also indicate how often animals will be weighed.
    xiii. Under euthanasia, please remove reference to use of CO2 after iso exposure.
    xiv. Under imaging, please address the following:

1. Please remove consultation with OACIB. Any movement of animals between facilities, needs to be consulted and coordinated with BRL vet.
2. Please remove the paragraph regarding cancer studies.

g. In Form A, item 8h, please address the following:
   i. please clarify what is group 4.
   ii. Please justify your need 20 extra animals (almost double the number of animals needed.
h. In Form A, item 10a, please delete the description for rats with method # 1 in ILF, since in 8g describes use of iso + thoracotomy.
i. In form A, Item 14, please clarify who from staff, will be responsible for preparing the glucose water and providing it to the animals.
j. In Form B, item 4, ketamine/xylazine is listed but not mentioned in form A, item 8g. Please remove it.
k. In Form B, item 5a, please clarify if animals will be survived after 2nd surgery (removal of the device) and if so please check "multiple survival" and justify the second surgery,
l. In Form B, item 5c, for both surgery #1 and 2, Ketamine/xylazine is listed, please remove.
m. In Form B, item 6e3, please remove wording about intervention and change AB ointment to sterile lube ointment
n. In Form B, item 6e4, please remove wording about use of lidocaine jelly.
o. In Form B, item B9, under endpoints, please remove text about veterinary intervention. The criteria listed here are humane endpoint criteria and animals will need to be euthanized at this point. Please add the body score <2 to the list of humane endpoint criteria. Also indicate how often animals will be weighed.

20-152

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 8g, please address the following:
   i. Under Short term Treatment, in the table and text, there is discrepancy for blood collection timeline, Day 5 in the table but Day 6 indicated in the text, please correct accordingly.
   ii. Under Effect of Bfue., study A, last paragraph for signs of toxicity, please change "inability to eat and drink and retain food over a period of >7 days" to "weight loss > 20%".
b. In Form A, item 8h, please change 6 to 7 for number of requested animals.
c. In Form A, item 10a, under method, please change "anesthesia" to "euthanasia"
d. In Form A, item 13a, it indicates that "No animal will undergo more than 3 bone marrow aspirations within a single year in our studies", in Form A, item 8g, indicates 3-4 times for BM aspiration, Please reconcile.
e. In Form B, item 4c, Buprenex please change "2nddose only if animal appears painful" to "as needed"
f. please uncheck the "No" box.
g. In Form A, item 8d, please remove the first sentence.
h. In Form A, item 8g, please provide timeline/single animal. How many different studies can a single animal go through and what determines that animal is fit to undergo another set of experiments.

20-159

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 8a, please add a statement about clinical relevance of this project since the compounds being evaluated are to be used to treat heart failure in humans.
b. In Form A, item 8g, please indicate that animals are continuously observed and monitored while the animals are in restrainer.
c. In Form B, item 8b, please add statement regarding the impact of heart failure on the human population.

20-163

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5c1, please remove the [redacted] and location OR in the description of the procedure.
b. In Form A, item 6f, please uncheck the box.
c. In Form A, item 8g, please address the following:
    i. Under implantation, please clarify if both locations (IP cavity and Lesser sac) will be used in one animal and implantation to different locations will be done as separate surgeries or not.
    ii. Under procedure C, please remove the word “small” in front of the incision, since midline incision extended for laparotomy.
    iii. Please remove reference to non-diabetic animals, this project does not involve diabetes.
d. In Form A, item 9, provide contact phone number.
e. In Form A, item 14, The following personnel must update ACC Regulatory Training by updating online course "Animals and Research at UIC”: Personnel # 1 and # 2. Please see attached instructions. Training must be updated every 3 years and completed prior to protocol approval.
f. In Form B, item 5b, please justify implant and retrieval surgeries.
g. In Form B, item6c, surgery # 3, please remove the word “small” in front of the incision, since midline incision extended for laparotomy.

20-155

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, please uncheck the box.

b. In Form A, item 4, indicate the age as >20 , but 8b, indicates > 22, please reconcile.
c. In Form A, item 7d2, please add a-Syn-PFFs to the table.
d. In Form A, item 8d, please remove "Surgical procedures cannot be effectively mimicked by tissue culture and to the best of our knowledge" since this phrase is not relevant to this section.
e. In Form A, item 13b, please redo your lit search for "PD , animals model", using a less general search term (Narrow your search) since large number of publication both on PubMed and ALTBIB were found (360,000 and 157,000).
f. In Form A, item 14, The following personnel must update ACC Regulatory Training by updating online course "Animals and Research at UIC": Personnel # 5. Please see attached instructions. Training must be updated every 3 years and completed prior to protocol approval.

20-161

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5c1, please remove the [redacted] and location OR in the description of the procedure.
b. In Form A, item 6f, please uncheck the box.
c. In Form A, item 8a, please rewrite this section in layperson's language and provide an explicit reference to human health (diabetes) which would be useful.
d. In Form A, item 8e, please justify why only male animals are requested.
e. In Form A, item 8g, please address the following:
    i. Under implantation, please clarify if both locations (IP cavity and Lesser sac) will be used in one animal and implantation to different locations will be done as separate surgeries or not.
    ii. Under procedures H and I, please replace ketamine with dexmedetomidine/midazolam.
f. In Form A, item 9, provide contact phone number.
g. In Form A, item 14, The following personnel must update ACC Regulatory Training by updating online course "Animals and Research at UIC": Personnel # 1 and # 2. Please see attached instructions. Training must be updated every 3 years and completed prior to protocol approval.
h. In Form B, item 5b, please justify implant and retrieval surgeries.
i. In Form B, item 9, please clarify how the failure of the transplant is determined (e.g. High glucose level)?

8. Review from Subcommittee #3

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a) In Form A, item 8c, please indicate how many people were trained and re-trained in the past three years.

b) In Form A, item 8g, please provide the following clarifications and changes:
   - **i.** Re-write the second paragraph on page 12 of 47 which is confusing and difficult to understand by more clearly describing the training regimen; also make this paragraph consistent with the text of the first paragraph.
   - **ii.** In the last sentence of the paragraph labeled "a" on page 12 of 47. Rats and mice, please delete the word "humanely".
   - **iii.** In the paragraph labeled "b" on page 12 of 47. Rabbits, under techniques indicate which vein will be used for catheterization and add this procedure to the detailed description of the routine techniques.
   - **iv.** In the section F. BLOOD COLLECTION FROM THE RETRO-ORBITAL SINUS IN RATS OR MICE, restate the frequency of this technique and add that alternate eyes will be used. The committee recommends that the interval between samplings is specified (e.g., two or three days) and that this will be done on alternate eyes, no more than 3 times in any one week, followed by at least one week recovery period. The total number of samplings of mice (4) and rats (no more than 8) is agreeable.
   - **v.** In the section D. INTRAVENOUS INJECTIONS IN MINIPIGS, indicate the needle size (only the catheter size is indicated).
   - **vi.** In the section F. BLOOD COLLECTION IN MINIPIGS, under the descriptions of sampling from saphenous, cephalic, and epigastric veins, the line labeled "1." indicates "injection" which should be changed to "collection".
   - **vii.** Listed under each of the blood collection sites (ear veins, saphenous veins, cephalic veins and abdominal epigastric veins) for the minipig the PI states "A catheter may be placed to aid in the administration of larger volumes through the "designated" vein. Placement of a catheter in the description is for agent delivery not blood collection and should be removed or clarified.

c) In Form B, item 4, please add ketamine/xylazine for rodents and acepromazine/buprenex for rabbits.

20-167

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

The protocol, particularly Form A, item 8g, is written in ways that makes it impossible to understand. It is recommended that the PI reaches out to Dr. Jeffrey Fortman for guidance on how to develop the scope and timeline of the project for submission of the protocol to the UIC Animal Care Committee.

9. Designated Review(s), Exemptions, and Lab Visits

a) **Protocols**

Member 6 updated the Committee on the review of protocols 20-151 and 20-164, by DMR process and that protocols 20-151 and 20-164 were approved

b) **Exemptions**

There were none

c) **Lab Visits**

Member 6 informed the Committee that the following labs were visited as part of the post-approval monitoring program.

The following labs/investigators were visited during the last month:

Lab	ACC
[redacted]	17-174, 19-011 18-023, 18-157, 20-096 17-136, 17-203, 17-204, 18-032, 19-052 18-201 20-063 19-061 18-129 19-153 18-130 17-137, 18-204 17-189, 19-188 18-076, 19-041, 19-160, 20-122 18-248

10. New Business

a. Modification of Protocol 18-240 (05)

The Committee reviewed PI's request for: 1) addition of new mouse strain (K18-hACE2), 2) request for additional RGS2, LyzM-GFP mice (40), 3) addition SARS-CoV-2 infection model and 4) addition of parabiosis model; in order to determine the role of epigenetic modifications in treatment of Covid-19 mediated lung vascular injury and use of parabiosis to test for involvement of genetically altered monocytes derived macrophages and the cytokines and chemokines released from them in regulating lung inflammatory injury. The Committee reviewed the modification request and discussed that PI needed to submit a separate modification for studies involving the SARS-CoV-2 infection model from other requests. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. PI needs to submit two separate modification requests: one for parabiosis model and the other one for studies involving SARS-CoV-2 infection model.
b. In Form D, item 5a, please indicate experimental groups and number of mice per group/sex.
c. In Form D, item 5c, item # 2, please clarify if the same group of animals that are getting infected with SARS-Cov2 virus will be injected with DNMT3a inhibitor, 5-aza-2′deoxycytidine and S1PR1 specific agonist, CYM-5442, or is this being done in a different group of mice?

d. In Form D, item 5g5, please provide an answer and indicate the surgery class and mark the analgesics.

e. Modification of Protocol 19-089 (05)

The Committee reviewed PI's request to conduct a second major operative procedure to inject a-synuclein in to the gut to see if that will transmit to the brain and result in pathology ultimately leading to neurologic deficits since the animals have gone approximately 6 months from first surgery and had shown no signs of neurologic deficits. The Committee reviewed the modification and discussed if there would be the possibility to validate the a-syn gut injection model by euthanatizing 1 or 2 animals and looking at brain tissue pathology before conducting a second major operative procedures on the animals. Following discussion, a motion that clarifications are needed prior to rereview by the full committee and to defer this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. PI needs to provide results from rodent studies referenced in Item 4.
b. PI need to clarify if there would be possible to euthanatize 1 or 2 animals to look at brain tissue pathology to validate the a-syn gut injection model.

f. Modification of Protocol 20-041 (03)

The Committee reviewed PI's request for an additional group of NHPs ("Group 5") (n=4) to be allocated for long-term assessment of pericapsular fibrosis (PFO) after implantation of microencapsulated cells at the following timepoints: approximately Day 7, Day 14, Day 30, Day 60, and Day 90 (terminal timepoint) based on the request from FDA. Following discussion, a motion that clarifications are needed, and that revised modification would be sent for designated review determination was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. PI needs to provide copy of correspondence with FDA, for requesting additional group of animals for long-term assessment.
b. PI needs to justify the need for earlier assessment timepoints (Day 7, 14 and 30) if the goal is the long-term assessment timepoint.
c. PI needs to clarify what kind of findings from biopsy samples would result in termination of the study/animal prior to 90 days. Please clarify if study will be continued to Day 60 and 90 time points if microencapsulated cells are dead and fibrotic at day 14 and 30 would.

g. Modification of Protocol 20-065 (01)

The Committee reviewed PI's request to perform preclinical imaging studies using the UIC preclinical core imaging (PCI) facility for better understanding of the HSV-1 spread and pathogenesis in murine eye and the nervous system. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form D, Item 5c, please address the following:

i. PI needs to obtain IBC approval to take HSV infected animals/carcasses to a central imaging core.
ii. PI needs to define what is the PCI, what type of imaging is performed there and what is the building and room number.
iii. PI needs to include a picture of the isolation/containment device that will be used for the imaging.

h. Modification of Protocol 18-074 (13)

The Committee reviewed PI's request to conduct a pilot study to induce seizures in mice of varying genotype by performing chemical induction using Pentylenetetrazol (PTZ), a GABA receptor antagonist to establish a reliable method of seizure induction in these mice and to confirm that the E4FAD mice in fact have lower GABAergic inhibitory function, as evidenced by a lower effective dose of PTZ compared to the E3FAD mice. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form D, item 5b, please address the following:
   i. Please clarify the number of animals needed to be tested at each dose, is N=8/dose level? If there is need to test higher than 60mg/kg, would additional animals be needed? Please reconcile how many animals will be needed in total.
   ii. Committee recommends increasing the monitoring of animals between 24-48 hrs. (addition of monitoring in the afternoon and next day).
b. In Form D, item 5c, please clarify the expertise of personnel that will be scoring the animals for seizure intensity with this scoring system.

i. Modification of Protocol 20-037 (11)

The Committee reviewed PI's request for: 1) additional 48 animals, 2) addition of a GLP safety/toxicity biodistribution study in NSG mice to evaluate a novel natural killer (NK) cell delivery system for the potential treatment of cancer, and 3) addition of IVIS imaging. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form D, item 5d, please clarify how BINATE-K will be prepared for IV administration by TRL staff.
b. In Form D, item O, please address the following
   i. Please provide information on the expected tumor kinetics for the Daudi cell line.
   ii. Please provide a brief description of the IVIS imaging including anesthesia, expected duration and whether luciferin is administered.
   iii. Please complete item 5I for the proposed metastatic tumor model.
   iv. Please provide description of restraining device and clarify how long the animals will be in restrainer.

j. Policies and Guideline Review

The Committee reviewed the following policies: policy on Sanitation of Behavioral and Specialized Research Equipment and Euthanasia Policy. The Committee discussed the following: 1) that there was

no change required for Sanitation of Behavioral and Specialized Research Equipment Policy and 2) that there were minor changes required to Euthanasia Policy. Following review, a motion to approve the Sanitation of Behavioral and Specialized Research Equipment Policy and a motion that the revised Euthanasia Policy would be sent for designated review determination was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

ANIMAL CARE COMMITTEE MEETING MINUTES
OCTOBER 20, 2020

Attendees: Member 6, Member 8, Member 9, Member 10, Member 11, Member 24, Member 30, Member 42 and Member 43

Absent: None

Guest: Member 45

1. **Minutes**

July and August 2020 minutes were approved by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

2. Announcements

Members 6 and 9 reminded the committee on the upcoming AAALAC Site visit and the tentative schedule.

3. Old Business

a. Modification of protocol 19-215 (Mod 1)

Member 6 informed the committee that this modification was deferred at the last meeting and the PI had revised the modification based on the committee requested clarifications. The Committee reviewed the revised modification and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form D, item 5c, under experimental design; please address the following:
   i. On page 4, please define the study endpoint is it 21 days or 7days?
   ii. Under "Clinical signs of disease progression and mortality rate", please clarify the following statement "The intranasally infected mice displayed significant clinical symptoms on day 2, rapid *weight loss between days 3 and 5, and 0% survival by day 5* (natural death or euthanasia at 20% weight loss), and clarify if this means death is an end point of the study?
   iii. PI needs to clarify study endpoints verses humane end points.
   iv. Please clarify which weight loss criteria (15% or 20%) will be used for euthanasia purposes. Please correct accordingly in all sections.
   v. Please indicate IV infusion procedures will be done as approved in the protocol, and please clarify the volume that will be administered.
   vi. Group 2, the unit for volume administered should be 50 microliters not 50 ml.
   vii. Please clarify what is the difference between Groups 4 and 5. Please also correct the table.
   viii. Based on 30% mortality indicated by PI the group size should 9 not 12. Please correct the total number of requested animals accordingly.

ix. Under "HINI nasal inoculation", # 7, PI indicates animals will be euthanized at two time points (5 and 7 days post inoculation) but only enough animals are accounted for one time point (day 7), please reconcile.

b. In Form D, item 5d, please describe aseptic conditions for production of virus.
c. In Form D, item 5i, please remove the 3rd search regarding COVID-19 ARDS, not related to this modification.
d. In Form D, item O, please remove your answer.
e. Appendix 1, Breeding tables, please correct your breeding scheme accordingly. As indicated 2 breeder X 3 litters X 6 pups/litter= 36 pups total. For producing 160 animals, PI needs to increase the number of breeding pairs accordingly.

b. Modification of protocol 19-089 (Mod 5)

Member 6 informed the committee that this modification was deferred at the last meeting and the PI had revised the modification based on the committee requested clarifications. The Committee reviewed the revised modification and discussed that the PI still had not addressed the committee's main concern. Following discussion, a motion that members 6, 9, 24 and 30 should meet with PI to discuss the committee's concern prior to PI's submission of the next revised modification and to defer this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Update on ACC Mod # 19-061 (07)- Bleomycin

Member 6 informed the committee that this modification was deferred at the last meeting and the PI had revised the modification based on the committee's requested clarifications. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarification:

a. The main study can proceed by the following conditions:
   i. New modification must be submitted by PI outlining the full study.
      1. In Form D, item 4, for the new mod, PI needs to indicate that following pilot study it was determined that the use of pharmaceutical grade Bleomycin will result in better and consistent outcome in comparison to non-pharmaceutical grade bleomycin and therefore pharmaceutical grade bleomycin will be used.
      2. New modification must use the same humane end point criteria that was set for the pilot study (Mod # 7) as detailed below:
b. Post inject monitoring, treatment of biohazard/chemical hazard:
   ii. Mice to be observed for any signs of pain or distress daily until euthanized. Animals should be weighed twice a week. Frequency of weighing to increase if animals show signs of weight loss >10%. If animals show any severe signs of tachypnea, dyspnea, weight loss >20%, a body condition score (BCS) of less than 2, or signs of discomfort, the animals will be euthanized, or the BRL veterinary staff will be contacted immediately for consultation.
   C. The monitoring and humane endpoint criteria approved in this modification will be used for all bleomycin studies moving forward.
   a. All animals receiving the compound listed above will be housed in [redacted] animal facility chemical hazard room. Animals will be housed in this room for 7 days following administration of bleomycin and then moved to [redacted].

b. PPE in biohazard room will be nitrile gloves, head cover, Tyvek suit/gown, shoe covers, and masks.
c. All procedures including inoculation will take place in the chemical fume hood in this room.
d. Should an animal need to change cages, cages will be reassembled with bedding in the fume hood and bagged and placed on the designated shelves in the room for decontamination by BRL staff per SOPs for these rooms.
e. If an animal is euthanized in this room, carcasses will be placed in bags and bags will be placed in designated refrigerators in rooms for disposal by BRL staff.
f. All surfaces will be decontaminated with chlorine dioxide.
g. All personnel listed on the protocol and working with this hazard will receive initial training by BRL veterinary staff.

d. Update on protocol 20-146

Member 6 updated the committee on the status of this protocol and indicated that the PI has decided to use crawfish rather than rodents in response to the concerns of the committee regarding the video recording of animal experiments and making the video accessible to students via the internet for a virtual class. At this time PI is not required to submit protocol for use of crawfish.

e. Update on non-compliance issue under 18-184

Member 6 updated the committee on the final status of the noncompliance issue.

a. Protocol 20-043 update

Member 6 updated the committee on the status of the protocol and the Committee reviewed the revised protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Condition of Approval: PI must submit an approved copy of SOPs pertaining to this protocol to OACIB, prior to obtaining approval and initiation of the project.

a. In Form A, item 8f, please remove your answer, and add IL10-/- animals and their deposition for inflammatory bowel disease and colitis.
b. In Form A, item 8g, please describe how animals will be transferred from UIC PI's lab in [redacted] to PI's lab in [redacted]
c. In Form B, item 13b, 2nd search, please redo the search by extending the Period of Years of Search to 2020.
d. In Form A, item 14, please address the following:
    i. For personnel # 4 and 5, please clarify their relationship to UIC and mark the appropriate box.
    ii. Please only indicate procedures/techniques specific to this protocol.
    iii. For personnel # 2, please remove experience regarding [redacted].

4. BRL Director's Legislative and Facility Update

Member 6 directed the Committee's attention to the report and updated the Committee on the following: 1) COVID 19 update: that BRL veterinary staff have re-initiated the mouse handling and technique training labs and the first training lab will be the first week of November and will be limited to 4 trainees, and that there were 9 BRL animal care staff exposed to COVID during the SEIU strike and only one staff member tested positive; however, this created a hardship as nine employees were out in quarantine for 10-14 days and that BRL is looking into provisions to take in lieu of the holidays and a possible surge of COVD-19 following the holidays; 2) that the BRL animal husbandry staff went out on strike on September 14th for 10 days (7 animal care staff and four veterinary technicians) and therefor 8 members of the veterinary staff provided daily care to over 38,000 animals. Although cage changing schedules were pushed back all animals were checked daily by the staff for food, water, and health issues. Moreover, there was not hold placed on PI's being able to conduct research and Five days into the strike a targeted group of investigators were asked if members of their lab would assist the BRL staff in cage changing and for the record, they were very receptive to helping out. All staff that worked during this time should be commended for their significant efforts in providing care and supporting the research program, 3) that [redacted] is currently supporting in vitro COVID-19 research and the tentative plan to start the first mouse COVID 19 project in [redacted] is in the week of November 30th; and 3) that a lot has been happing in preparation of the institution's upcoming AAALAC site visit. A BRL Bulletin describing the AAALAC accreditation process has been sent out to investigators as well as an email to all investigators and their staff on how to prepare both their animal rooms and labs for the upcoming inspection. In addition, the BRL veterinary staff will hold two virtual town halls the last week of October to review with investigative staff on how to prepare for an AAALAC site visit and finally, the veterinary staff has conducted walk-throughs of all animal facilities on campus, updated signage, validated cleaning procedures for cleaning investigator equipment such as behavioral equipment and visited in the last 2 months all labs in which survival surgery is conducted.

5. OACIB Update

a. Modifications

Member 9 updated the Committee to the following activity during the past month: there were 8 modifications approved at the administrative level, 20 modifications approved administratively following veterinary consult, and 5 modifications approved via designated review this month. In addition, there were 12 protocols that added personnel, 0 with personnel deletions, 5 that added new funding, and 0 in which animals were added to the holding protocol.

b. Continuations and Terminations

Member 9 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal of the protocols was passed by the following vote: 9 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

20-153

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

COI #1: PI must obtain Radiation safety approval prior to initiation of any experiments involving ^{125}I-albumin.

COI # 2: PI must contact BRL Director prior to initiation of the experiments involving ^{125}I-albumin regarding the location where studies will be conducted.

a. In Form A, item 2b, PI should indicate role for personnel in protocol.
b. In Form A, item 4, PI should include inappropriate genotype and breeders listed in appendix 1
c. In Form A, item 5c, PI should add location (room and building number) for IV infusion of ^{125}I-albumin.
d. In Form A, item 5d, please verify location for maintaining animals for more than 12 hours outside approved animal facility. If location is outside approved facility, update current justification to include reasons appropriate justification for maintaining mice in the identified facility is necessary.
e. In Form A, item 7a, PI should check "Yes" for IV infusion of ^{125}I-albumin for lung permeability studies.
f. In Form A, item 7d2, please add ^{125}I-albumin including scientific justification, source, and method of preparation.
g. In Form A, item 7c, PI should clarify whether in addition to isoflurane; sevoflurane will also be used as described in A8g.
h. In Form A, item 8f, please include body score condition less than 2 as humane end point criteria. Also, note that animals with signs of abscess and granuloma should be euthanized immediately.
i. In Form A, item 8g, please address the following:
    i. Under CLP, PI should include a brief description of the differences between mid-grade and high-grade CLP. Also include a justification for using mid- and high-grade CLP.
    ii. Under Lung injury using LPS nebulization, PI should include a logistics of how the experiment will be executed including duration and timeline for the study.
    iii. Under IT route, please indicate the duration of the study.
    iv. As a general observation, the current Ketamine/xylazine doses (74/3 mg/kg, i.p.) are too low for all the surgical processes described and should be increased to 100/5 mg/kg i.p.
    v. Under PAR1 peptide, please indicate approximate duration for the restraint procedure.
    vi. Under monitoring frequency, please change monitoring to 4x for the first 3 days, then when stable, twice daily.
    vii. Under in vivo lung permeability studies, PI should check "yes" for use of radiation in A7, and provide approved RPN number for use of ^{125}I-albumin.
    viii. Under project 1 and other projects, PI is requesting separate groups of animals for the 4 analysis (Lung edema/permeability, tissue biochemistry, BAL protein, leukocyte content) proposed; PI should include justification for requiring separate groups of animals for each analysis/measurement.
    ix. Under effects of LPS and CLP on lung inflammatory injury, please reconcile the dose for BMDM cells with the dose listed under bone marrow harvest and transplantation.
    x. Under A8h, PI indicated that the same power analysis calculations will be used for all experiments, however, under LPS/CLP survival study the group size for WT and MAFIA mice is different, please clarify.

xi. Under effects of Pseudomonas aeruginosa and lung inflammation injury, please reconcile the dose for BMDM cells with the dose listed under bone marrow harvest and transplantation. Also, include justification for requiring separate group of animals for the 4 analyses proposed.

xii. Under project 2, in vivo studies, please include injection volumes for Ginkgolic acid and TAK.

xiii. Under project 3, evaluation of the role of macrophage p120 in bacterial clearance and lung injury during sepsis, include injection volumes for *E. coli and P. aeruginosa*.

xiv. Under project 3, evaluation of the role of macrophage p120 in bacterial clearance and lung injury, second to the last paragraph, is mid-grade CLP the same as Sham? Please clarify.

xv. Under project 5, PI should specify LPS dose and indicate timeline for LPS administration in all the different experimental groups.

xvi. Under project 6, role or macrophage TLR4 resolution of ventilator-induced lung injury, PI should include timeline for the procedure and indicate when animals will be anesthetized.

xvii. PI should contact veterinary staff for whole body radiation endpoint training prior to initiating these studies.

j. In Form A, item 8h, PI used the same power calculation to determine experimental group size for all experiments and yet different experimental group sizes (n=6 in project 1study 3; n=7 & 8 in project 5 study 3 & 3 respectively) will be used, please clarify.

k. In Form A, item 13a, please define mid-and high-grade CLP and include a justification for using both CLP procedures.

l. In Form B, item 6c, PI should include descriptions for mid- and high-grade CLP or remove references to these CLP procedures in A8g and throughout the protocol.

m. In Form B, item 6d, please avoid using 70% ethanol for sterilization and use hot bead sterilization for sterilization of instruments between surgeries.

n. In Appendix 1, all inappropriate genotypes, breeders, and excess animals should be listed in table A4.

20-169

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 3e, please provide PAF number for funding support 1 & 2.

b. In Form A, item 7a; please that IBC#17-065 renewal is pending.

c. In Form A, item 7d2, please address the following:

i. Please add phosphate buffered saline, DMSO, alcohol (used in DID studies) saline, tamoxifen (used in study 7.2) and AAV-DJ/8-EF1α-FLEX-DTR-P2A-EYFP-WPRE-hGHpA.

ii. Scientific justification for testosterone, aldosterone, and corticosterone should be changed to something other "1"

d. In Form A, item 8b (page 16 of 34)- 4th paragraph, last line "we hypothesize that MeA aromatase is important for estrogenic regulation of physical activity and adiposity, especially in males. We plan

to generate both LOF and gain-of-function (GOF) mouse models to test it". Please add that 'this will be tested in both male and female mice'.

e. In Form A, item 8e, please address the following:
   i. Please provide full form for DREADD,
   ii. Include justification for C57Fopo-10-TG/+ and C57 Cx3cr1-YFPCreER/YFPCreER.
f. In Form A, item 8g, please address the following:
   i. In the table for volume and doses for viral vectors- add the route of delivery for clarity.
   ii. Include full forms for BAT, iWAT, gWAT that will be used.
   iii. Under study 3.6, please include the duration for administration of NaCl, corticosterone and aldosterone in drinking water.
   iv. Under study 3.4, please include the duration for HFD feeding.
   v. Under Project 1, indicate the duration for restraining.
   vi. Under Project 6; please change 'stated' to 'fasted.'
   vii. Under Project 8, please include reference or justification for selecting a two day 'wash-out period'.
g. In Form A, item 10a; please include PI's laboratory room number.
h. In Form A, item 13b; please use appropriate combination of search terms including estrogen receptors, high fat diet, and other treatments given to experimental mice and update search results accordingly.
i. In Form A, item 14, please address the following:
   i. Please indicate personnel that will be responsible for HFD, fasting and the experiments utilizing metabolic cages.
   ii. PI is advised that PI should contact veterinary staff for training on adrenalectomy.
   iii. Please complete trainer and expertise section for all personnel.
   iv. For personnel, please complete the training and expertise section.
j. In Form B, item 3 please address the following:
   i. Add cardiac puncture for blood collection.
   ii. Add ear punch for genotyping under transient pain.
k. In From B, item 6, please include monitoring criteria as described in A8g.
l. In Form B, item in 6d, as written, it appears that Meloxicam will be administered twice, please clarify to indicate that Meloxicam will be injected once.
m. In Form B, item 6d, please uncheck box for surgeon scrub.
n. In Form B, item 7, please include acute heat and cold stress procedures.
o. Appendix 1: Please revise the breeding tables for numbers and reconcile numbers table A4.
p. General comment: please correct the typos and spelling mistakes.

20-172

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

COI: Please submit the test results from testing fibrosarcoma cells to OACIB for review and approval prior to initiation of studies involving the fibrosarcoma cells.

a. In Form A, item 3, please provide appropriate number assigned by funding agency. Also, provide Proposal Approval Form number for this grant.
b. In Form A, item 5c, please specify room number and procedures to be performed in [redacted] and remove listing of hazard rooms.

c. In Form A, item 7b, please specify that test results from fibrosarcoma cells must be submitted to, and approved by, a BRL veterinarian prior to their use.
d. In Form A, item 8d, please elaborate as to why animal models are specifically necessary to achieve the project goals.
e. In Form A, item 8e, please expand/ explain why CH3 animals are the most appropriate strain for this study.
f. In Form A, item 8g, please address the following:
    i. As written, it seems that a tumor biopsy from calf muscle will be performed to obtain cells for subsequent reinjection. However, few details are performed as to the biopsy process. Please describe in more detail how tumor tissue will be dissected from the animal legs. If the same animals will be used for imaging, then this is a survival surgery and should be described in detail and include additional changes to several parts of Form B. If not, then tumor growth and imaging should be described separately and accounted for in section 8.h. Please modify protocol elsewhere as appropriate.
    ii. Please remove passage "Tumors set up in the calves are less invasive and not painful to set up for the animal" from paragraph 2 on page 14. Please note that tumor grown to the desired size in calf is likely to be extremely invasive and painful and will require more frequent monitoring than is described.
    iii. Pursuant to previous point, please adjust monitoring frequency to 3x week, and daily thereafter with supportive care (e.g.: moistened food, hydrating gels) if any reduced mobility is observed. These changes should also be reflected in Form B9.
    iv. Under endpoints, veterinarians will not prescribe treatment for an ulcerated tumor; please remove that language and clarify that tumor ulceration tumor is humane endpoint criteria and animals should be euthanized appropriately.
    v. Under transportation of animals, please remove the reference to "conceal the items from the general public" and replace with "maintain the wellbeing of the experimental subjects prior to experiment". Also, it is not necessary to use a second bag, please remove.
g. In Form A, item 8h, please address the following:
    i. Please specify the source of the animals to be used.
    ii. How will the success of the pilot study be determined to justify a full size follow up? Please specify statistical tests to be performed to assess the results from these animals.
h. In Form A, item 10b and c, please remove thoracotomy as a secondary method of euthanasia or else discuss when it will be used in lieu of dislocation.
i. In Form A, item 12a, please check "NO" box for second part.
j. In Form A, item 13a, the justification lacks detail; growing a tumor to the desired size in the relatively small rodent calf is not a preferred method and per veterinary staff and thus likely to be very painful. This requires strong justification to be permissible. Please specify why this specific tumor approach is appropriate over other less painful approaches.
k. In Form A, item 13b, the period for literature search should be narrowed and be focused more on the alternative models; please redo search and update accordingly.
l. In Form A, item 14, please remove animal experience not relevant to the procedures in this protocol.
m. In Form A, item 15, mentor, departmental head, or BRL director signature required. Also, remove past affiliation with UIC.
n. In Form B, item 3, please address the following:
    i. Please complete section for methods and/or substance to be used or else uncheck boxes.
    ii. Add IM or SC injections of purified tumor tissue as well as IV injections before imaging.

n. In Form B, item 5a, please uncheck "non-survival surgery" as it relates to the imaging procedure. Pending replies to previous clarifications in A8g above, this box or box for survival surgery may need to be checked to describe tumor biopsy process.
o. In Form B, item B.9, top two paragraphs (above the heading "Tumor Pilot Study") are redundant and can be removed. Also, see comments on monitoring frequency in A8g above.
p. PI should complete Biologic material appendix and submit with revisions. (COI: Result of testing for cell line)

20-178

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:
a. In Form A, item 4, please indicate that both male and female mice will be used for breeding.
b. In Form A, item 5b, please list specific room in [redacted] that will be used for AOM administration.
c. In Form A, item 5c, please indicate location of exsanguination procedure.
d. In Form A, item 7d2, please address the following:
    i. Please indicate storage conditions for all compounds and if freshly prepared please indicate so.
    ii. Please indicate method of sterilization for AOM or whether it is obtained sterile.
    iii. According to A.8g, Ganciclovir will be obtained from Invivo Gen, however, according to 7d2 it will be obtained from Sigma; please clarify for consistency.
    iv. For sterility purposes, corn oil should be obtained from Sigma-Aldrich and not from whole foods store.
    v. Please use appropriate number designations as described in 7d2 legend for scientific justification.
e. In Form A, item 8c, please indicate the injury models, mouse strains, and any treatments that will be administered and include a summary of key findings and manuscripts published.
f. In Form A, item 8d, PI should address why computer models and *in vitro* explant models cannot be used.
g. In Form A, item 8g, please address the following:
    i. Under study, clarify that mice will be euthanized by CO_2 inhalation followed by cervical dislocation.
    ii. Under Study 4, please indicate that DT treatment will be given following induction of colitis.
    iii. Under Study 8, clarify the number of DSS cycles that will be administered for this study.
    iv. Under Study 9, indicate injection volume for AOM injection. Also, clarify that mice will be euthanized by CO_2 inhalation followed by cervical dislocation.
h. In Form A, item 8h, power calculations should not be identical for all experimental groups, please redo power calculations for each experimental group.
i. In Form A, item 10a, please specify dose to be used for ketamine/xylazine anesthesia.
h. In Form A, item 10b, uncheck box for "incision of the chest cavity…"
i. In Form A, item 13b, limit the years searched to decrease the relevant references to a number that can be reasonably reviewed for alternatives.
j. In Form A, item 15, PI assurance signature is required.
k. In Form B, item 4, confirm that Xylazine will be administered at 10 mg/kg rather than the recommended dose of 5 mg/kg.

l. In Appendix 2, items 2 & 7, please remove references regarding notification of veterinary staff after AOM administration

20-184

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, the assigned ACC Protocol number should be 184.
b. In Form A, item 3, please provide number assigned by funding agency and proposal approval number for all matched grants.
c. In Form A, item 4, please address the following:
    i. Reconcile final animal numbers with sections A8g and A8h.
    ii. In A8e, several mouse strains and transgenic lines including Sprague Dawley rats are listed but are not accounted for in A4, please remove or reconcile with sections A.4, A.8g, and A.8h and include appropriate justification where applicable.
    iii. Shiverer MBP -/- and shiverer Tg MBP -/- are listed in the breeding appendix but only the experimental animal number are reported here. All animals in appendix 1 should be accounted for here.
d. In Form A, item 5c, please indicate applicable [redacted] and [redacted] room numbers.
e. In Form A, item 7d2, Freund's incomplete adjuvant and keyhole limpet hemocyanin listed in study I should be added including scientific justification, source, method of preparation and sterilization.
f. In Form A, item 8e, see "C" concerning comments on Sprague Dawley rats, R6/2 mice, and APPswe/PS1deltaE9 mice.
g. In Form A, item 8f, please remove JNK-/- and MLK2/MLK3-/- mice since there are no phenotypes.
h. In Form A, item 8g, please address the following:
    i. Under study I, please reconcile animal numbers with A.4 and A.8h.
    ii. Under study II, please indicate the maximum duration that mice will be used for ascites collection before euthanasia.
    iii. For tapping during ascites production, PI should consider using fentanyl as anesthetic instead of ketamine/xylazine. PI should consult veterinary staff for anesthetic dose of fentanyl.
    iv. Please note that there is no study IV.
    v. Under Study VI and VII, please indicate the age of the embryos.
    vi. Under Study VII, change "mice" to "rats"
i. In Form A, item 8h, please address the following:
    i. Provide power analysis and sample size calculations and justification.
    ii. Considering that sex is a biological variable, include justification and reconcile all animal numbers with A.4 and A.8g.
j. Form A, item 10 please address the following:
    i. PI should use decapitation (method 4) without cold anesthesia for embryos euthanasia.
    ii. Please answer 10f for method 9.
    iii. Indicate [redacted] locations for CO_2 euthanasia.
    iv. Please use applicable numbers as listed below table for method of euthanasia.
    v. According to A8g, Ketamine/xylazine will be used for exsanguination of rats but in the table, pentobarbital is listed; please clarify.
k. In Form A, item 10c, please select "exsanguination" as indicated in A10a.

l. In Form A, item 10d, please select "Verify the absence…" as indicated in A.10a.
m. In Form A, item 14, please indicate the specific procedures that are relevant to the experiments described in this protocol for personnel.
n. In Form B, item 4 - indicate that standard buprenorphine will be used.
o. Appendix 1, item 3c, indicate number of female breeders, duration of breeding in years or months, and reconcile the number of experimental animals with number justified in A.8h and those listed in A.4.

20-185

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 2, please indicate role for co-investigators in the protocol.
b. In Form A, item 4, please add numbers from the breeding table and correct use codes to reflect those requested in appendix 1.
c. In Form A, item 5a, please remove [redacted].
d. In Form A, item 5c, please specify [redacted]
e. In Form A, item 7a, note that initiation of the studies described in this protocol is contingent on IBC protocol approval.
f. In Form A, item 7c, please indicate room number [redacted] for isoflurane.
g. In Form A, item 7d, for clarity, please distinguish between "vehicle 1" and "vehicle 2" in the table Also, [redacted] is listed twice, please consolidate.
h. In Form A, item 8g, please address the following:
  i. Under Study 2, three dosages are listed for [redacted] delivery, but is proposing six doses for "EC50". Is this referring to LD50? The 6 doses seem to represent separate experiments from the ones listed in the previous paragraph, so please elaborate on the rationale for testing these doses and clarify duration of treatment and experimental endpoints for the LD50 animals.
  ii. Under Study 4, please define efficacious dose (e.g.: optimal dose established in study 2)
  iii. Under Technique 1, please elucidate how severity of respiratory distress will be assessed/measured to indicate humane endpoint criteria.
  iv. Under Technique 1, please expand description of how virus will be delivered intranasally.
  v. Under technique 3, please define restraint device more clearly. Is this a commercially available device?
  vi. Under technique 8, the experimental description states "after termination of experiment". Does this refer to one of the previous techniques? Or is technique 8 always used after techniques 7? Please clarify here and in Form 8h as to whether these techniques employ the same animals in Study 2.
  vii. Under technique 8, procedure lists K/X injection as method of anesthesia, but continuation of anesthesia using a nose cone. Please confirm and specify that isoflurane will be used for maintenance of anesthesia and indicate dose.
i. In Form A, item 8h, please address the following:
  i. Please include a page break and label to indicate the beginning of this section.
  ii. Indicate how pilot numbers were estimated.
  iii. Please specify how values and variance were estimated for power analysis in all studies.
  iv. Please consolidate tables listed as study 4, Technique 8-9.

i. In Form A, item 10a, please add method 2 to this list to account for animals anesthetized under isoflurane in technique 4. Please also uncheck cervical dislocation (this does not appear to be appropriate for any animals euthanized this way, and is not discussed in section 8.g) or else specify in the experimental details which animals are to be cervical dislocated under isoflurane anesthesia. Please also add [redacted] here.

j. In Form A, item 12a & b, BAL is considered a terminal surgical procedure, so check appropriate boxes here.

k. In Form A, item 13a, please use this section to justify use of painful procedures. As written, this section only recapitulates the justification for the hACE2 strain already given in A8.e.

l. In Form A, item 13.b, please remove "the studies in non-human primates will be serviced at IIT-RI"

m. In Form A, item 13c, please add verbiage to specify that none of the known alternative models represent less sentient animal species than mice.

n. In Form A, item 14, please indicate personnel with nasal inoculation, nasal and throat swab experiences.

o. In Form B, item 3, if performed with anesthesia, tail snips are likely done with a topical cream. Please add this to section 4 if true. However, if tail snips will be done in pups, check "No"

p. In Form B, item 5b, check box for non-survival terminal surgical procedure (BAL surgeries).

q. Answer Form B, item 6a, b & c for terminal BAL surgery.

r. In Form B, item 9, please add "BCS score <2" as a humane endpoint.

s. In Appendix 1, please address the following:

i. Under item 2, please specify background strain and zygosity.

ii. Under item 3c, please remove question marks or explain their meaning. If these are meant to convey uncertainty as to whether this breeding is to be pursued, PI should note that approval of animal numbers cannot be made conditional upon success in obtaining them elsewhere: please either confirm plans to breed these animals or remove breeding table from document.

iii. Under item 3c, breeder males and females in top box should represent total numbers of breeders used, not just numbers breeding simultaneously, and should probably read 42 and 84, respectively. Also, 6 pups/litter * 3 litters per female * 84 breeding females would result in an estimate of 1512 pups. If these numbers are retained in upper box, please ensure that the number in box labeled "disposition" equals 1512, designate additional animals as "surplus" and indicate method of disposition. Please also correct elsewhere in the document as needed (i.e.: Form A items 4 and 8h) so that all numbers exactly match the values entered in this breeding table.

s. Please attach Appendix 2 for BSL3 agents.

20-188

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 2a, please add mailing address and work phone number for PI if available.

b. In Form A, item 2b, please add work phone number and email address for Co-Investigator if available.

c. In Form A, item 4, please clarify if mice listed in rows "i" and "j" are from different sources and whether the littermates are from C57 mice.

d. In Form A, item 5a, please check [redacted] and for location indicate TBD.
e. In Form A, item 5c, please list all procedures and for locations indicate TBD.
f. In Form A, item 7c, please indicate if the method is active or passive.
g. In Form A, item 7d2, please address the following:
  i. Please specify the type of "sterile condition" that will be applied. For sterile preparations, all solutions should be filtered through 0.22-micron filter.
  ii. PI should consider using commercial euthanasia solution (pharmaceutical grade) instead of pentobarbital.
  iii. The scientific justification for Nicotine should be something other 1.
  iv. Please indicate if nicotine salt or free base will be used.
  v. Select only one applicable scientific justification for succinylcholine and caffeine.
h. In Form A, item 8a, please define TNNT and TNNI the first time used.
i. In Form A, item 8c, if this protocol is a new submission, this should not be completed.
j. In Form A, item 8e, please address the following:
  i. Please justify the use of strains listed in table A4.
  ii. In 7d2, PI indicated that succinylcholine will be used but it is not clear when or during which procedure it will be used. Also, the dose, route of administration and injection volume are not provided.
  iii. Only ANM-sTnT KO and WT mice are currently proposed for functional studies in item 8g. Please remove all unnecessary strains or provide details of studies that will be performed with each listed strain in item 8g.
  iv. Please justify the use of Balb/c mice for mouse immunization and production of hybridoma ascites fluid in 8e 2).
  v. Please include a brief description for ANM-sTnT mean; is it a global knockout of TnT or tissue specific or same type of TnT loss as ANM patients? Please clarify.
  vi. Please add brief explanations on the type of mutation in ssTnL-R14C KI and cTnl-KO+cTnl-ND mice.
k. Form A, item 8g, please address the following:
  i. Please indicate the specific WT mice that will be used in each experiment.
  ii. Please indicate the approximate age of mice to be used in each study.
  iii. Under experiment 2b, please indicate injection volumes for all substances to be administered.
  iv. Under experiment 3, please indicate the type/nature of immunization to be administered. Also, indicate injection volumes that will be administered.
  v. Under experiment 4, according to guidelines, the injection for pristane should not more than 0.2ml, please clarify.
  vi. Under experiment 4, please indicate the dose/ number of cells, volume, and frequency of administration for hybridoma cells. Also, include a brief description of how "production of ascites" will be determined.
  vii. Under experiment 6, please spell out EDL the first time used.
  viii. Please include details regarding how analgesics or euthanasia will be used in 8g.
  ix. Description for toe clipping procedure (listed in Form B item 3) should be added here.
  x. A summary table for all experiments will be useful. Also, indicate how many BABL/C mice will be needed for antibody production.
l. In Form A, item 8h, please include power analysis and justification for group size. Also indicate if the same proportion of male and female mice will be used in all experiments. Also, all species that will not be used in this protocol should be removed.
m. In Form A, item 10a, please address the following:
  i. Please add location (building/room number) for all methods of euthanasia.

ii. According to guidelines the pentobarbital dose for euthanasia should be 5x the anesthetic dose, please reconcile or change to method 3.

n. In Form A, item 12a & b, please check "yes" for all boxes.

o. In Form A, item 13a, please list procedures that might cause pain or distress for mice and include justification for why each procedure is necessary. Also add toe clipping and include justification for this procedure.

p. In Form A, item 13b, please use combination of search terms including "troponin + myopathies" and/or "animal model +troponin+ myopathies" and update literature search accordingly.

q. In Form A, item14, please address the following:

i. Please complete required training (ACC regulatory training date, mouse/rat training date) and list training and expertise for all personnel listed in this section.

ii. Please add email (if available) for personnel.

r. In Form B, item 3, there are no developmental studies proposed in A8g, please remove toe clipping or include a strong justification for this procedure.

s. In Form B, item 5a, check box for non-survival for terminal muscle contractility studies.

t. In Form B, item 6a, b, & c, please complete this section for the muscle contractility studies.

s. In Form B, item 8, the information provided here should be moved to B7 and include monitoring and humane endpoint for the ascites tumor model.

t. In Form B, item 9, please add monitoring and humane endpoint.

u. Please re-do Appendix 1 based on the changes in Form A item 8e.

20-189

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 2a, please add mailing address and work phone number for PI if available.

b. In Form A, item 2b, please add work phone number and email address for Co-Investigator if available.

c. In Form A, item 4, please consolidate SD rats in row a and b in the same row.

d. In Form A, item 5a, please check [redacted] and for location indicate TBD.

e. In Form A, item 5c, please list all procedures and for locations indicate TBD.

f. In Form A, item 7d, please address the following:

i. Please indicate that all preparations will be performed in a certified sterile biosafety cabinet.

ii. In A8g PI indicated that heparin will be used, if non-pharmaceutical or pharmaceutical grade heparin will be used indicate so in A8g.

iii. PI should only use one of the representative numbers for scientific justification of all compounds listed.

h. In Form A, item 8b, please spell or define HFpEF the first time used.

i. In Form A, item 8c, the information provided here should be moved to 8b (the scientific background). Also, this section should not be completed if the protocol is new to UIC.

j. In Form A, item 8e, please address the following:

i. Please clarify what embryonic splice form mean in the strain Emb-TnT mouse.

ii. Please provide better description of each strain (type of mutation for each strain) and include appropriate justification for each strain.

iii. Please include appropriate justification for using both male and female animals.

k. In Form A, item 8g, please address the following:

i. Under item 1, please specify the "genetically matching wild type control mice" that will be purchased, and if it is a strain other than C57 wildtype mice, please add to A4 and where appropriate throughout the protocol.
ii. PI needs to provide strong scientific justification for toe or tail clipping.
iii. Under item, please include a detail description of the procedure to be performed and indicate dose and volume of heparin to be administered. Also, indicate if heart will be collected right after heparin injection and clarify the dose of pentobarbital to be used.
iv. Please add justification for using different analgesics.
v. Under item 6, please indicate duration for osmotic pump implantation procedure.
vi. Under item 7, please indicate the dose of isoflurane to be used.
vii. Please clarify if pharmaceutical grade bupivacaine and 0.2% ascorbic acid will be used.
viii. Under detailed of procedures, PI should contact veterinary staff if breeder diet will be used.
ix. Under detailed of procedures and mouse genotyping, there are no developmental studies proposed, are all experiments done in adult mice?
x. Under detailed of procedure 2, PI should note that the hood in the animal room is not appropriate for use of isoflurane for tails clips. PI should consider using EMLA cream for toe clipping.

l. In Form A, item 8h, please provide power analysis better justification for group size determination; a summary table with appropriate numbers might be helpful.

m. In Form A, item 10a, please address the following:
i. Please add CO_2.
ii. According to guidelines the pentobarbital dose for euthanasia should be 5x the anesthetic dose, please reconcile or change to method 3.
iii. Please use the representative numbers (see legend below the table) instead a full description for method of euthanasia.
iv. The committee suggest that PI should consider administration of anesthetic or analgesics to toads and frogs prior to decapitation.

n. In Form A, item 12a & b, please check "yes" for all boxes.

n. In Form A, item 13a, please list procedures that might cause pain or distress for mice and include justification for why each procedure is necessary. Also add toe clipping and include justification for this procedure.

o. In Form A, item 13b, please use combination of search terms including "troponin + myopathies" and/or "animal model +troponin+ myopathies" and update literature search accordingly.

q. Form A, item14, please address the following:
i. Please complete required training (ACC regulatory training date, mouse/rat training date) and list training and expertise for all personnel listed in this section.
ii. Please add email (if available) for personnel.

u. Form B, item 3, please remove toe clipping and replace with appropriate method used in adult mice.

s. Form B, item 5b, please indicate the type of procedures and frequency since multiple survival is checked in item 5a.

t. Form B, item 6b, PI should consider using Meloxicam instead of Carprofen.

u. Form B, item 6e, osmotic pump implantation should be listed under class 1 surgery and transverse aortic restriction a class 4 surgery.

v. Form B, item 9, please include a detailed description for monitoring procedure and indicate monitoring frequency.

w. General comment, please correct typographical errors prior to resubmission.

7. **Review from Subcommittee #2**

20-181
The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 6 and 9 for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 4, please clarify the age or weight range for the animals.
b. In Form A, item 5c, please list all the procedures and list locations (i.e., craniotomy surgery to remove scalp).
c. In Form A, item 5d, please clarify why the consequent imaging will take more than 12 hours? This needs to be justified.
d. In Form A, item 8d, please delete 2nd paragraph.
e. In Form A, item 8e, please justify why this needs to be done in two different rodent species, mice and rats.
f. In Form A, item 8g, please address the following:
    i. Please change Day -2 to Day -3, animals need at least 3 days of quarantine when they arrive at the facility.
    ii. Please provide detail regarding the animals going through surgical procedure and then imaging. The only information provided is related to non-surgical procedures and imaging.
    iii. Please provide rational behind repeated imaging of animals and is there any evidence that repeated imaging may have any effects on animals' well-being of animals.
    iv. Please clarify how long would each imaging session last/per animal and why is indicated in item 5d, that some imaging sessions will be longer than 12 hrs.
    v. Under "non-surgical procedures", please address the following:
        1. Under #4, please clarify what is thin plastic membrane and the purpose of it and why animals fur is not shaved prior to imaging?
        2. It is indicated that "In the case of scalp & skull-removed animals, PI will pull whiskers of the animals and perform paw.
        stimulation for evaluation of the functional imaging capability of the system". Please clarify if this is the method used to assess anesthetic depth? Animals should not respond to these stimuli under appropriate depth. Please use appropriate methods to measure the depth of anesthesia, such as respond to toe pinch.
    vi. Under "Schedule of non-surgical procedures", please address the following:
        1. Change Day -2 to Day -3.
        2. Please clarify the statement regarding "on day 7-up to 3 years, scalp-opened rodents are imaged and after imaging are euthanized before they awaken from anesthesia", it is not clear that if the same animals is being imaged for 3 years or just this experiments will continue with new animals for 3 years. Please revise your statement accordingly.
        3. It is indicated that "In the case of scalp & skull-removed animals, we will pull whiskers of the animals and perform paw.
        stimulation for evaluation of the functional imaging capability of the system". Please clarify if this is the method used to assess anesthetic depth? Animals should not respond to these stimuli under appropriate depth. Please use appropriate methods to measure the depth of anesthesia, such as respond to toe pinch.

vii. Under humane end points, please move the current answer under pervious paragraph "post-procedure care". Please provide humane endpoint criteria (i.e. 20% weight loss, loss of appetite, hunched pasture, rough coat…).
viii. Please remove the following statement "CO2, will be used as a secondary method for both".

g. In Form A, item 8h, PI should justify n=6/group and clarify as pilot study what are some of the main outcome measure being evaluated and what would be the definition of success. the study should be followed up by a full study.
h. In Form A, item 10a, the method should 1 and 2, remove "secondary".
i. In Form A, item 10b and 10c, please check cervical dislocation.
j. In Form A, item 10e, please remove the answer.
k. In Form A, item 12a, please check "yes" for both questions.
l. In Form A, item 13, please justify the craniotomy and removing skull.
m. In Form A, item 13b, please conduct lit search for craniotomy.
n. In Form B, item 4a, please under "species", indicate mice and rats.
o. In Form B, item 6a, the detail about shaving the head should be added to Form A, item 8g.
p. In Form B, item 6c, please address the following:
    i. Clarify if both mice and rats will go through the same surgical procedure since only "Rats" are mentioned in the writeup.
    ii. the last sentence "The rat…." Should be moved to item B6b.
    iii. Please indicate the approximate duration of the procedure.
q. In Form B, item 7, please delete the answer.

20-186

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 7d2, please identify the two different formulation of compound and vehicle differently, so could be easily identified which one is being used for which study.
b. In Form A, item 8A, please add the first paragraph from 8b to this section.
c. In From A, item 8d, please remove the word "Justification".
d. In Form A, item 8g, please address the following:
    i. Please clarify specifically for each study which vehicle and formation of [redacted] is being used.
    ii. Please define "MTD".
    iii. Please clarify what kind of catheter will be used and why is important that animals get dosed approximately the same time for 28 days?
    iv. Please clarify why animals with VAP, are not being use for 28 day studies.
e. In Form A, item 13b, please conduct a lit search for alternatives to Retro orbital (RO) sinus blood collection, which is listed in 13a, as painful procedure.
f. In Form B, item 8, please remove the answer.

20-182

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

COI: PI must validate the system first in rodents and large animal model prior to initiating studies with specific disease model in large animals.

a. In Form A, item 4, Since this is a neonatal model, committee suggests PI consider younger pigs, since 8-week-old pigs have thick skulls, much thicker than a child and also thicker skull will be harder to surgically remove.
b. In Form A, item 6g, please uncheck both boxes, this is for field studies only.
c. In Form A, item 8e, Justify the age, since 8-week old pig is not equivalent to human neonate.
d. In Form A, item 8f, please uncheck the box.
e. In Form A, item 8g, please address the following:
    i. Under Anesthetic Procedures (pre-study), please address the following:
        1. Please change cephalic or saphenous vein to auricular vein.
        2. Please change "Iso will be administered using" to "animals will be intubated".
        3. Please delete the sentence about pre-op bupivacaine.
        4. Please indicate arterial catheter will be placed to run blood gas analyses.
    ii. Under overall procedure please address the following:
        1. Please change animal will be sedated to anesthetized and clarify how oxygen is delivered, nose cone or intubated?
        2. Please clarify if there will be any will be any adverse effects due to low level of oxygen being tested (range: 10 -100%).
        3. Please remove the last paragraph.
    iii. Under Scheduled procedures, please address the following:
        1. Under task #1, please change sedated to anesthetized.
        2. Under Task 2, please remove "if the surgery goes well".
        3. Please clarify the number of imaging sessions/animal, is it 3 or 5?
        4. Hemorrhage induction process needs to be described in Overall procedure section. Please provide reference for the model and the large volumes that will be injected. Please also clarify the rest period between each hemorrhage sessions, since it is indicated 3 time/week in 8h but 8g indicates one week rest between sessions. Please reconcile.
    iv. Under humane endpoints, please add weight loss or failure to gain weight as humane end criteria.
    v. Please indicate study end point. Is it 2 months after fontanelle surgery?
f. In Form A, item 8h, only 6 animals are accounted for but A4 indicates 7 animals, please clarify.
g. In Form A, item 10b, please uncheck decapitation.
h. In Form A, item 10e, remove the answer.
i. In Form A, item 13a, please add hypoxia and provide a justification for performing painful procedures.
j. In Form A, item 13b, please conduct lit search for painful procedures (i.e. craniotomy surgery, hemorrhage induction and hypoxia induction).
k. In Form A, item 14, please address the following:
    i. Please change the Sheep to pigs under procedures to be done for personnel.
    ii. Please clarify who will be perform the surgical procedures, and their level of experience with the surgeries. Please list personnel in this section.
l. In Form B, item 4a, b, and c, under "species" please indicate pigs

m. In Form B, item 5a, please mark "multiple survival" and justify repeated induction of hemorrhage.
n. In Form B, item 6b, please change sedated to anesthetized. Please delete bupivacaine.
o. In Form B, item 6c, please address the following:
    i. Under surgery # 1, please address the following:
        1. Please indicate total size of craniotomy.
        2. Please indicate the size of the incision.
        3. Please clarify the methods used to monitor the state/depth of anesthesia.
    ii. Under surgery # 2, please reconcile how often hemorrhage will be induced and imaging will be done and the interval between each session, please reconcile between Form A, items 8g and 8h and Form B, item 6c.
p. In Form B, item 6d, please mark: Cap, Drape and also check Ethylene Oxide Sterilization.
q. In Form B, item 7 needs to be answered for Hypoxia induction.
r. In Form B, item 9 needs to be answered for induction of hemorrhage.

20-190
The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:
s. In Form A, item 7d2, please identify the two different formulation of compounds and and the vehicle differently, so they can be easily identified as to which one is being used for which study.
t. In Form A, item 8A, please add the first paragraph from 8b to this section.
u. In From A, item 8d, please remove the word "Justification".
v. In Form A, item 8g, please address the following:
    i. In Study 1, please clarify if the same animals will be used for testing both formulations.
    ii. Please clarify if blood and body weights will be collected every day of the study? How many blood samples in total for each study?
    iii. In Study 2, Please clarify why animals have to be dosed once a day at approximately the same time for 7 days? What is the significance of timing of dosing?
    iv. Under humane endpoint Criteria; PI indicates that "The following signs of illness, alone or in combination, that may indicate moribundity include but are not limited to: Rough coat, hunching, distended abdomen, inability to remain upright, or lack of purposeful movement when stimulated, abnormal coloration such as jaundice, pallor, or cyanosis, coughing, rales, or respiratory distress, weight loss ≥ 20% or prolonged inappetence, marked dehydration, chronic diarrhea or constipation or central nervous system disturbance - head tilt, seizures, tremors, circling, spasticity, paresis/paralysis. Scheduled Euthanasia", please note that some of signs such as rough coat, distended abdomen, or constipation alone do not warrant as humane endpoint criteria and should just be listed as general signs compare to some other signs such as hunching, inability to remain upright, or lack of purposeful movement when stimulated, abnormal coloration such as jaundice, pallor, or cyanosis, coughing, rales, or respiratory distress, weight loss ≥ 20% or

prolonged inappetence, central nervous system disturbance - head tilt, seizures, tremors, circling, spasticity, paresis/paralysis are criteria for humane endpoint.

v. Under Study 3, please clarify at what days PK samples will be collected.

vi. Please provide more description of Draize scoring and the scoring chart any why is being done. Also remove veterinarian from list of responsible personnel to do Draize scoring.

w. In Form A, item 8h, please provide statistical analysis for group sizes for each study. Study 2 should be N=6/ sex, total of 12 animals/sex. Also, PI is not requesting any extra animals, committee recommends that PI should request 1 or 2 animals extra/sex.

8. Review from Subcommittee #3

20-177

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 7a, please remove the chemical hazards as these compounds are not considered hazardous under the condition used in this study.

b. In Form A, item 7d2, please identify the type of filter that will be used to sterilize (e.g., 0.2 or 0.5 micron).

c. In Form A, item 8b, and 8g, please include a rationale for examining the effect of an inhibitor of the IGF1 receptor and the proposed combination treatments with this inhibitor and mTOR inhibitors.

d. In Form A, item 8g, please delete the duplicate of the first paragraph and clarify how the duration of the experiment (2-4 weeks) will be determined.

e. In Form A, item 8g, please move the justification for the number of animals to the missing item 8h and add the statistical methods that will be used. Also, there seems to be words missing in the description of the power calculation: the standard deviation is unlikely to be 0.05 which probably is the alpha-value.

f. In Form A, item 10a, please replace 100% with either "CO2" or "according to the BRL euthanasia SOP".

g. In Form A, item 13b, please redo the searches focusing on alternatives of the mouse xenograft models used and provide the precise number of relevant references.

h. In Form B, item 9, please reconcile the maximum tumor size indicated here (20 mm diameter) with that indicated in Form A, item 8.g. (15 mm).

i. In Appendix 2, please remove the information for the chemicals and add information about the origin of the human tumor cell lines and whether they have been passaged in rodents. If these cells have been passaged in rodents, provide documentation that they have been screened for rodent pathogens and are free of those.

20-183

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via member 6 for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 7b, please uncheck the no box and provide information whether the cells/ tumor line has been screened for and are free of murine pathogens.
b. In Form A, item 7d2, please provide information about how and by whom the Neohybrids compounds will be sterilized and whether they are provided injection-ready or need dilution or reconstitution in a vehicle as suggested in item 8.g.
c. In Form A, items 8a and 8b, appear identical; please put item 8.a. in layperson's language and provide the scientific details in item 8.b.
d. In Form A, item 8g, please provide the following clarifications:
    i. In the second line of the response, please replace the word "housed" with "placed".
    ii. The duration of the Nair treatment of the mouse skin is too long; please reduce it to < 2 minutes.
    iii. The number of melanoma cells per injection should be 1x105, not 1x105.
    iv. Please provide a literature reference for the expectation that the tumors will not ulcerate or metastasize before the end of the study and at what point in time ulceration would be expected to develop.
    v. Please provide details about the dye and gold particle preparations and their injections (vehicle, concentration, injection volume). Also explain what DPBS is.
    vi. Throughout the protocol there is mention of intradermal and subcutaneous injection and transdermal administration; please reconcile this. Also note that 100ul is too large of a volume to be administered intradermally.
    vii. It is not entirely clear how many imaging sessions will be carried out on a single animal; will this be just one followed by euthanasia or more than one. It is also not clear what imaging schedule will be applied to the rats. It is recommended that a table be provided, that lays out the experimental design and timeline for both the mouse and rat studies.
    viii. In item 10a, cervical dislocation under anesthesia is listed as euthanasia method, but in item 8.g. under Schedule of Procedure, it is stated that the animals will be cervically dislocated followed by CO2 inhalation as secondary method. The latter is not allowed or appropriate. Animals should be euthanized by CO2 inhalation followed by cervical dislocation as secondary method to assure death. Please correct this and reconcile the euthanasia methods in items 8.g. and 10.a.
    ix. The animals should be euthanized before tumor or skin biopsy samples are taken. If this is done immediately after cervical dislocation, collection of high-quality samples will be possible.
    x. In the first sentence under Schedule of Procedure, there mention of transfer of animals to new housing; please clarify what is meant here.
    xi. Under Post-procedure Care, there is mention of an attachment, but this was not provided. Please do so or remove reference to the attachment.
    xii. There is hardly any detail about the experiments with rats. Please provide a more substantial rationale for these studies and details about their experimental design. Also clarify why 48 rats are needed for a penetrance study. Could this study be done with fewer animals? It appears the rats will not have tumors and therefore it is not clear how the contrast agents (IV and transdermal administration) will be distributed to the skin for penetrance analysis as they target melanoma cells.
e. In Form A, item 10a, please identify the anesthetic and its dose and reconcile the euthanasia method with that indicated in item 8.g. (CO2 followed by cervical dislocation) which should be listed here as method 1.
f. In Form A, item 10e, please delete the word "guillotine".

g. In Form A, item 12.b., please check the no box and uncheck the yes box as no surgery is proposed.
h. In Form A, item 13a, please remove current text and list xenograft tumor as the potentially painful procedure and justify the use of the tumor model.
i. In From A, item 13b, please redo the searches with a focus on subcutaneous tumor growth as a model.
j. In Form B, item 3, please reconcile the transdermal route of administration with the intradermal administration listed in Form A, item 8.g.; transdermal suggests topical application and diffusion through the skin whereas intradermal suggests an injection.
k. In Form B, items 5 and 7, please delete all text and checked boxes as the collection of tissue biopsy samples should be done after death and not before.
l. In Form B, item 9, please add tumor size $\geq$ 2 cm in largest diameter as humane endpoint.

20-174

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a) In Form A, item 2a, please provide the mailing address of the PI rather that the building and room number.
b) In Form A, item 7d2, please change the scientific justification for lithium chloride and NCO from 1 to 2.
c) In Form A, item 8b, please define DREADD at the first mention of this abbreviation.
d) In Form A, item 9, under sick animals, please check a box.
e) In Form A, item 10d, please check the box for "Removal of Vital Organ.
f) In Form A, item 13b, please redo the searches for conditioned taste aversion and taste neophobia focusing on alternatives.

20-187

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

COI: veterinary staff must be notified two weeks prior to initiation of the studies.

a) In Form A, item 3, please provide the PAF number.
b) In Form A, item 4 and 8g, please clarify why only males will be studied.
c) In Form A, item 8b, please check whether 30-35 g rats were used (second line from bottom of first paragraph) or whether this is a mistake that needs to be corrected, i.e. 300-350 g rats.
d) In Form A, item 8g, in the second paragraph of the rationale please identify which mouse strain was used to establish the dose range curve. In the second paragraph of the Total Body Radiation section, please delete "until they awaken" as the mice will not be anesthetized according to the description of the use of restrainers.
e) In From A, item 8g. and Form B, item 10, please add CNS symptoms that interfere with mobilization, feeding, and drinking.

f) In Form A, item 8h., please display the number of animals to be used in the various experiments in the last paragraph of each of the three types of studies in a table to facilitate visualization of those numbers by experiment.
g) In Form A, item 9, please correct the omission of information for dead animals and duplication of sick ones, i.e. somehow the PI has 2 sections on how to address sick animals and nothing on dead animals
h) In Form A, item 10a, please replace 100% with either "CO2" or "according to the BRL euthanasia SOP".
i) In Form A, item 13c, please describe the alternatives that were identified and why they can't be used
j) In Form A, item 14, please request (re)training by [redacted] in humane endpoint assessment of high-dose irradiated mice for all staff that will be involved in this.
k) In Form B, items 3 and 4, please uncheck the anesthesia box in 3 and delete the anesthesia information in 4 as the animals will not be anesthetized during irradiation, unless anesthesia will be used in which case this need to be made explicit in Form A, item 8.g. (see comment d above).
l) In Form B, item 11, please provide the requested information.

20-191
The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Clarifications:

a. In Form A, item 7d2, please add Matrigel
b. In Form A, item 8g, in the last line of page 1 of 6, please remove "10-" as only 30% is appropriate under the current BRL SOP.
c. In Form A, item 8h, please display the number of animals to be used in the various experiments in the last paragraph of each of the three types of studies in a table to facilitate visualization of those numbers by experiment.
d. In Form A, item 14, please update the ACC training Per personnel # 3.
e. In Biological Material Testing Appendix, please add Matrigel.

9. Designated Review(s), Exemptions, and Lab Visits

a) **Protocols**

Member 6 updated the Committee on the review of protocols 20-171, 20-173, 20-175, 20-179 and 20-180 by DMR process and that protocols 20-175, 20-179 and 20-180 were approved and protocols 20-171 and 20-173 required following clarifications to secure approval.

20-171
a. In Form A, item 4, please note that the number of animals for all strains requested is the same as the previous protocol. PI should review lines and numbers as it would It seem like there should be some change based on work that was completed on the experimental protocols.
b. In Form A, item 5c, 8g, 14 and Appendix 1: PI refers to ear clipping. Should this be ear punching? Please clarify.
c. In Form A, item 8b, along with the experiments already listed, PI should include the associated

protocol numbers that are supported by this breeding protocol.

d. In Form A, item 11, please remove entry.
e. In Form A, item 14, PI should be removed as she will not be handling animals. Training and expertise included for other members should be specifically related to maintaining the breeding colony.

20-173

a. In Form A, item 8g, immature rat study; please justify 150 rats in text (5 animals/experiment x 10 experiments:50/year x 3 years =’s 150 rats; however, in table PI justifies 180 rats over 3 years. PI needs to reconcile the numbers in this section and if needed correct numbers in A,4.
b. In Form A, item 8g, CYP19Cre-IGF1R mouse study, please clarify what is done with the mouse ovaries at 300 days, i.e. in the text PI only accounts for them at 21, 60 and 120 days.

Exemptions

There were none

b) **Lab Visits**

Member 6 informed the Committee that the following labs were visited as part of the post-approval monitoring program.

The following labs/investigators were visited during the last month:

Lab	**ACC**
[redacted]	18-067 17-230 18-031, 18-247 18-200 19-094, 19-170 19-126, 19-215 19-100, 20-066, 20-042 18-005, 19-203 17-185 20-057, 20-060 18-029, 18-136 19-019, 19-050 18-024, 19-132 18-232

10. New Business

a. Triennial training announcement for Mouse/Rat Training

The Committee reviewed the edited version of triennial training announcement and following discussion it was decided that the announcement will be sent to Vice Chancellor for final review and approval, prior to being send to all PIs conducting animal research at UIC.

b. Policy 0393: Noncompliance policy

The Committee reviewed and discussed the following that there were minor editorial changes needed to this policy. Following review, a motion to approve the policy were passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Guideline 0394: Working with Human and Non-human Primate Cells and Tissues in Animals

The Committee reviewed the guideline and discussed the following that there were only minor editorial changes required to this guideline. Following review, a motion to approve the guideline was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Modification of Protocol 19-108 (10)

The Committee reviewed PI's request to evaluate a novel lipid LPC in mice with STZ induced Type 1 diabetes. Committee discussed the following 1) that this protocol is not approved for STZ induced diabetes and 2) that the addition of an STZ diabetic induction model would require a detailed description in the modification. Following discussion, a motion that significant clarifications are needed prior to rereview by the full committee and to defer this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form D, item 4, PI indicates that this modification is to evaluate a novel lipid LPC in mice with STZ induced Type 1 diabetes. **Note:** PI is not approved in this protocol for STZ induced diabetes and it would need to be added to the protocol as a modification.
b. In Form D, item 5c, the addition of an STZ diabetic induction model would require a detailed description in Form D, item 5c; including dose, what constitutes diabetes, monitoring endpoint criteria and how the animals will be used in terms of group of animals receiving LPC
c. In Form D, item5d, this section needs to be completed for the STZ and induction of diabetes.
d. In Form D, item 5i, need to be completed for the STZ model.
e. In Addition, please clarify if this modification will require additional animals and if so include them in the modification

e. Modification of Protocol 19-055 (04)

The Committee reviewed PI's request for additional 2520 mice to conduct a variety of acute lung injury models (LPS and CLP) for which the PI is already approved. As part of the modification the PI requested to study a highly selective SIRT2 inhibitor and an oncogenic protein (PML) to determine if they can stabilize pulmonary endothelium and mitigate pulmonary inflammation and pathology. Also request to conduct two survival studies in which the PI will administer an LD50 and LD 80 dose of LPS. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form D, Item 4, please define PML the first time used.
b. In Form D, item 5b, please address the following:

i. Please include a section for the respective survival studies that describes the animal monitoring program, humane endpoints and the duration of the study, i.e. how long will PI take out animals post LPS and CLP, is it 7 days?
ii. Please clarify the dose of LPS that will be given to the mice in the non-survival studies and also clarify that CLP will be performed in accordance with what is approved in the original protocol.
iii. Please provide statistical justification (Power calculations) for group sizes. Please indicate if same group sizes as originally approved protocol.

c. In Form D, item i, please justify conducting LD50 and LD80 studies and conduct a lit search.

f. Modification of Protocol 18-107 (05)

The Committee reviewed PI's request for 1) the addition of a gastric bypass surgery in a mouse model to alter the gastro physiologic/pathophysiologic environment, 2) PI's request to investigate the Wnt responsive cells in both the acinar and islets compartment by transplant of such cells into a diabetic nude mouse model and 3) PI's request to conduct a kidney capsule transplant followed 4 weeks later by a second major operative procedure a nephrectomy**.** Following discussion, a motion that significant clarifications are needed and that PI needs to contact member 6 and discuss the committee concerns prior to submitting a revised modification to be rereview by the full committee and to defer this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.

g. Modification of Protocol 20-017 (01)

The Committee reviewed PI's request to change the humane end point criteria from an endpoint of lung metastasis based upon bioluminescence levels to one based upon humane endpoint criteria. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form D, Items 5c is only section need to be answered. Please remove text from 5h.
b. In Form D, item 5c, please address the following:
    i. please clarify freq. of observation of mice between inoculation and 3 weeks post inoculation. Recommend that PI check mice daily after 3 weeks, twice daily does not seem necessary or appropriate for the model.
    ii. For Humane endpoint criteria list the following: signs of pulmonary distress, labored breathing, hunched posture, failure to groom, lethargy, and a body condition score less than 2 on a scale of 5.
c. In Form D, Item 5f can be left blank. Attrition of animals resulting in a single animal in a cage due to experimental studies is covered in the institutional policy on single housed animals and need not be justified in this section.

h. Policies and Guideline Review

The Committee reviewed the following policies: policy on Sanitation of Behavioral and Specialized Research Equipment and Euthanasia Policy. The Committee discussed the following: 1) that there was no change required for Sanitation of Behavioral and Specialized Research Equipment Policy and 2) that there were minor changes required to Euthanasia Policy. Following review, a motion to approve the Sanitation of Behavioral and Specialized Research Equipment Policy and a motion that the revised Euthanasia Policy would be sent for designated review determination was passed by the following vote: 9 in favor, 0 opposed, 0 abstentions, and 0 recusals.