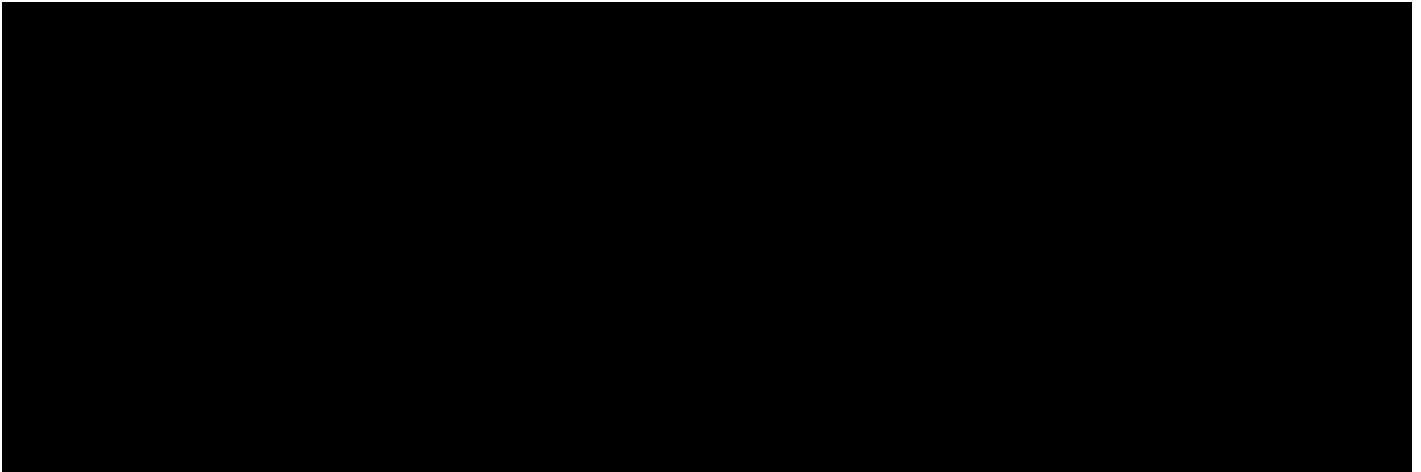


University at Buffalo
State University of New York
Office of Research Compliance

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE
MINUTES OF THE MEETING
September 20, 2021

ATTENDANCE:



CALL TO ORDER:

The IACUC Chair commenced the meeting at 12:31 PM.

If any member of the IACUC has submitted a protocol or amendment for review and approval, that member is not present during the discussion of and voting on their protocol or amendment. Quorum is maintained.

PRESENTATION OF THE MINUTES:

The minutes of the 2021 IACUC August meeting were presented. The August meeting minutes were voted on and unanimously approved.

BUSINESS:

RIA13095Y: The PI has been working with the IACUC to address the ongoing animal welfare concern regarding the vertical sleeve gastrectomy (VSG) procedure since 2019. On August 23, 2021 the suspension was lifted when the PI submitted an amendment removing experiment “2.13) Sleeve Gastrectomy Rat Model of Alcohol Intake in Alcohol Preferring and Non-Preferring Rats”, which includes the VSG procedure. On September 20, 2021, during the IACUC meeting the PI spoke to the committee via Zoom about the project, outlining their changes going forward. Subsequently, the committee discussed the VSG procedure and amendment requirements. The Committee Chair sent an email to the PI outlining the committee’s discussion and expectations regarding adding the VSG procedure back to the protocol. The departmental chair was also cc’d on this email. If the PI wishes to conduct any VSG procedure going forward they will need to submit an amendment adding the experiment back to the protocol with the following considerations: a very strong justification for why it

is necessary for the VSG surgery to be conducted by protocol staff, instead of being purchased from an institution that has consistently executed the procedure with trained surgeons and a stronger training program for protocol staff that will be performing the VSG procedure.

BME04112Y: On September 20, 2021 the suspension was lifted when the PI submitted an amendment removing the experiment “Anti-Tumor efficacy of topical cabazitaxel ointment”, which includes the application of the chemotherapy drug, cabazitaxel, along with DMSO. The committee reviewed the PI’s response regarding the suspension. The PI decided to halt all topical studies, as at this time, no further studies are needed. The committee has found no issue with the PI’s decision and will work closely with the PI if future topical studies are proposed.

PROTO20200027: The noncompliance occurred on October 10, 2020, where 3 pigs were injected with Indocyanine Green (ICG) dye during a procedure. The ICG dye is not approved for use. The incident was discovered when gathering information for a FOIL request and was reported by the IACUC Administrator. The committee reviewed the PI’s plan regarding appropriate supervision to ensure that all substances used in a procedure are IAUC approved. Additionally, the PI submitted an amendment adding contrasting agents to the protocol. The committee has accepted the PI’s plan to ensure that this noncompliance will not reoccur in the future.

APPROVALS:

A list of the submissions approved since the last meeting has been presented to the committee.

ANNUAL RENEWAL SUBMISSIONS:

Category E annual submissions:

AR202100056: Annual Review for MIC31107Y

The annual was unanimously approved.

AR202100063: Annual Review for PTE23087N

The annual was unanimously approved.

AR202100069: Annual Review for PROTO202000049

The annual was unanimously approved.

AR202100073: Annual Review for PROTO201800237

The annual was unanimously approved.

PROTOCOL REVIEW:

In addition to the IACUC review, Environment, Health & Safety (EHS) has also reviewed all protocols and amendments submitted this month. For protocols involving the use of hazardous agents in live animals, their use will be approved by the appropriate EHS authority and, as appropriate, laboratory SOPs will be placed as recommended by EHS prior to IACUC approval.

1. PROTO202100056

Protocol Summary: From PI’s non-scientific summary: Apelin and its receptor APJ play important roles in cancer and other diseases including diabetes. Overexpression of apelin and APJ is observed in

multiple cancer types (e.g., non-small cell lung cancer, cholangiocarcinoma, colon, ovarian cancer) and shown to promote tumor progression and metastasis. Recently we have shown that APJ promotes tumor progression and metastasis by two major mechanisms. First, APJ promotes formation of larger tumor spheroid formation. This makes chemotherapy less effective because the drug cannot reach enough to the center of large tumor spheroids, and thus reducing spheroid formation by APJ inhibition remarkably increased chemotherapeutic efficacy for paclitaxel and cisplatin. Second, apelin, an endogenous ligand for APJ is produced by fat cells and drives APJ-expressing cancer cells to migrate and invade into lipid-rich tissues. Bringing cancer cells close to the fat-rich environment makes easy for cancer cells to utilize lipids as fuel for their growth and survival. We have demonstrated that, when mice were injected with cancer cells genetically modified to have lower APJ expression, tumor progression and metastasis in those animals were significantly reduced, as compared to mice injected with unmodified cancer cells. Our goal of this proposed research is to demonstrate the therapeutic effects of blocking APJ function in cancers using small molecule APJ inhibitors. We will evaluate the pharmacokinetics and tolerability of APJ inhibitors in mice and the antitumor effects of APJ inhibitors alone or combining with chemotherapy, with aiming to further guide drug development of more effective APJ inhibitors.

Committee Discussion: Edits and clarification need to be made in Click. NPG forms need to be added. The type of imaging being performed needs clarifications. The spec sheet for the OVCAR-8 cells needs to be added and they need to be added as a substance administration. The request for sterile housing needs clarifications and an acclimation period needs to be added to the protocol. A monitoring chart needs to be created and added to Click. The “Intraperitoneal Injection (APJ)” and “Intraperitoneal Injection (Chemo)” need the need size, frequency and duration of the treatment and any side effects listed for the treatment added. The procedure “Oral gavage (APJ)” needs clarifications to the gavage procedure, weight ranges, and early removal from the experiment guidelines and if there will be any adverse side effects from the procedure. The procedure “Isoflurane (euthanasia/necropsy)” needs clarifications to the use of nosecone and edits to the procedure needs to be made. The procedure “Non-Surgical Procedure: Tumor Imaging – Bioluminescence” needs a supplemental heating source, imaging location, strain, and a timeline needs to be added. The procedure “IV Injection (APJ)” needs more information added regarding early removal from research. The experiment “PK/Biodistribution” needs clarifications. A scientific merit form needs to be added to the protocol.

Committee Action: The committee unanimously voted to require modifications to secure approval and to allow the revised protocol to be reviewed and approved by Designated Member Review.

2. TR202100037

Protocol Summary: From PI’s non-scientific summary: The objectives of this study are to (1) understand how changes in cardiac structure and function develop in various types of heart disease and (2) identify novel treatments to prevent or reverse adverse cardiac remodeling in these disease states.

Committee Discussion: Edits and clarification need to be made in Click. The radiation safety protocol needs to be updated. The experiment “Acutely instrumented Non-survival Studies” needs clarifications to single housing, analgesics need to be listed, and the experiment needs a stem cell administration. The procedure “Adenosine Administration” needs clarifications to the administration. The procedure “Analgesia Administration” needs clarifications to dosage. The experiment “Model 1- Chronic Coronary Stenosis Models and Respective Controls” needs clarifications to analgesics, splenectomy surgery and baseline physiological studies. The experiment “Model 2- Myocardial Infarction” needs clarifications to bone marrow collection and a flow chart needs to be added. The procedure “Closed chest- Myocardial Infarction Model” needs clarifications to the closure of the femoral artery. The procedure “Collection of Body Fluids” needs clarifications to blood collection volume and frequency. The procedure “Metoprolol Administration” needs clarifications to metformin.

The experiment “Model 3- Repetitive Pressure Overload Model” needs to have a flowchart added, clarifications to the splenectomy procedure and infusion drugs.

Committee Action: The committee unanimously agreed to approve the protocol pending that the personnel training requirements are meant.

3. TR202100041

Protocol Summary: Taken from the PI’s non-scientific summary: The objective of this submission is to provide fundamental insight on the role of fluid shear in regulating VWF structure, size and function; and also study a family of Synthetic Biomarkers called 'SynGlycans'. The binding of blood platelets to sites of plaque rupture/vascular injury via von Willebrand Factor (VWF) leads to the stoppage of blood flow during heart attack and stroke. This project aims to understand the role of fluid flow in regulating the structure and function of VWF. This understanding is necessary to find novel therapies that aim to modulate platelet adhesion rates in humans.

Committee Discussion: Minor edits and clarification need to be made in Click. An acclimation period needs to be added to the protocol. NPG forms need to be added. If CO2 is to be included as a euthanasia method option, scientific justification for why it is used over other methods is required. The procedure “Substance Administration: Stimulus administration - i.p.” needs clarifications to the time points. A procedure needs to be added for "Monitoring of Mice with Induced Peritonitis." Fatal Plus needs to be added to the protocol. A supplemental heating source needs to be added for all anesthetic procedures. Possible complications and humane endpoints needs to be added for the hydrodynamic tail vein injections. The procedure “stem cell, neutrophil and exosome admin.-ROinjections” needs more information regarding local anesthetic, needle size, volume and a monitoring chart needs to be added. The procedure “Blood collection –RO with anesthesia” needs clarifications to complications, general anesthesia, frequency and monitoring. The procedure “Submandibular blood collection” needs additional information regarding any adverse side effects and restraint. The experiment “Acute Inflammation” needs edits. A supplemental heating source needs to be added for anesthetic procedures. A stronger justification needs to be added for the use of CO2. The procedure “Tail clip assay” needs its classification changed and phenotype explanation needs to be added.

Committee Action: The committee unanimously agreed to approve the protocol pending that the personnel training requirements are meant.

The IACUC Chair adjourned the meeting at 2:27 PM.