University of Kentucky
Institutional Biosafety Committee (IBC) Meeting

Date: 03DEC2025
Time: 12:02PM – 1:32PM
Location: Virtual Meeting via Zoom - https://uky.zoom.us/j/82694753461

Minutes

Call to Order

The meeting was called to order by Douglas Harrison at 12:02PM EST.

Attendance

IBC Members Present

Maria Landron (Local, Non-Affiliated Member)

Thomas Chambers (Local, Non-Affiliated Member)

Doug Harrison (Chairperson)

Cheryl Haughton (Animal Containment Expert)

Carrie Shaffer (Institutional Member)

Delena Mazzetti (Biological Safety Officer)

Mike Mendenhall (Local, Non-Affiliated Member)

Brandy Nelson (Institutional Member)

Amelia Pinto (Institutional Member)

Carol Pickett (Local, Non-Affiliated Member)

Arthur Hunt (Plant Containment Expert)

Yadi Wu (Institutional Member)

Regrets

Jan Smalle (Plant Containment Expert)

Delphine Malherbe (Laboratory Staff Representative)

Guests

Elizabeth Brooks (Administrative Support Associate I)

Robert Hayman (Assistant Biological Safety Officer)

Jeff Howell (IBC Administrative Professional II)

Audra Strahl (IBC Administrative Professional II)

Melissa Hollifield (Animal Compliance Manager)

Quorum

Per the University of Kentucky Institutional Biosafety Committee By-Laws, at least 6 voting members shall constitute a quorum.

Approval of Previous Month's Meeting Minutes

2025.11.05 IBC Meeting Minutes DRAFT.pdf

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The previous month's minutes were approved. Thomas Chambers initiated the motion. Cheryl Haughton seconded the motion. All members present (12) voted in favor.

Old Business

None.

New Business

Request for extension of IBC protocol approval for IBC-24-301, PI Dr. Michael Flythe, due to recent Federal Government shut down. Dr. Flythe is employed by the USDA and was unable to complete the IBC renewal in time. IBC-24-301 will expire on December 6, 2025.

The motion for a three-month extension of IBC protocol IBC-24-301 approval period was approved. Delena Mazzetti initiated the motion. Carrie Shaffer seconded the motion. All members present (12) voted in favor.

Protocol Review

Amendments

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PI: Ioannis Papazoglou
IBC Protocol Number: IBC-24-35
Protocol Title: Neuronal response to hypoglycemia
Protocol Type: Amendment
Amendment To: Personnel
Applicable Guidelines & Regulations: NIH Guidelines Section III-E-1, NIH Guidelines Section III-F-1, NIH Guidelines Section III-D-4, NIH Guidelines Section IV-B-7, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, OSHA Act of 1970 Clause 5(a)(1)
Maximum Containment Level: Biological Safety Level 1 (BSL1), Animal Biological Safety Level 1 (ABSL1)
Primary Reviewers: C. Haughton, C. Shaffer, A. Hunt

Brief Project Overview:

Hypoglycemia is the most prevalent consequence in the treatment of diabetes. It can lead to brain damage and even death and thus it is a significant hurdle to achieving and maintaining ideal blood sugar levels. Normally, a drop of blood sugars below physiological levels triggers the counterregulatory response, a series of events orchestrated by the brain causing several tissues to react in order to restore blood sugars back to normal. However, some diabetic individuals lose this function due to the brain's failure to respond appropriately. Our research focuses on the brain's response to hypoglycemia and how it operates to bring blood glucose levels back to normal. We aim to identify the brain regions that respond to hypoglycemia and how each one of them controls on or more counterregulatory actions. We also investigate why these brain regions fail to respond in some patients. The findings from these studies will lead to better understanding of these mechanisms and help improve the therapies for diabetes.

Summary of Biohazard Materials & Manipulations:

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Manipulations Planned: Animal work (breeding, surgeries, etc.), Imaging/Microscopy, Immunohistochemistry, Use of Viral Vectors

Transport: Yes

Materials Transported: Biohazardous Materials, Animals

Infectious Agent(s)/Natural Host(s): N/A

Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: EGFP/ Aequorea victoria/ tracking gene/ expression/ mice/ AAV;mCherry/ Aequorea victoria/ tracking gene/ expression/ mice/ AAV;mCitrine/ Aequorea victoria/ tracking gene/ expression/ mice/ AAV;hM3D (Gq)/ H. sapiens/ membrane protein/ expression/ mice/ AAV;hM4D (Gi)/ H. sapiens/ membrane protein/ expression/ mice/ AAV;Kir2.1/ M. musculus/ membrane protein/ expression/ mice/ AAV;ChETA/ M. musculus/ optogenetic stimulation/ expression/ mice/ AAV;Synaptophysin/ M. musculus/ synaptic labeling/ expression/ mice/ AAV;mRuby/ Aequorea victoria/ tracking gene/ expression/ mice/ AAV;EYFP/ Aequorea victoria/ tracking gene/ expression/ mice/ AAV

Vector(s) [Vector Category/Vector Technical Name]: Adeno-Associated Virus (AAV)/AAV8-hSyn-DIO-EGFP/; Adeno-Associated Virus (AAV)/AAV8-hSyn-DIO-mCherry/; Adeno-Associated Virus (AAV)/AAV8-hSyn-DIO-hM3D(Gq)-mCherry/; Adeno-Associated Virus (AAV)/AAV8-hSyn-DIO-hM4D(Gi)-mCherry/; Adeno-Associated Virus (AAV)/AAV8-hSyn-DIO-HA-hM3D(Gq)-IRES-mCitrine/; Adeno-Associated Virus (AAV)/AAV8-hSyn-DIO-HA-hM4D(Gi)-IRES-mCitrine/; Adeno-Associated Virus (AAV)/AAV9-EF1a-DIO-Kir2.1-P2A-EGFP/; Adeno-Associated Virus (AAV)/AAV-mDlx-jGCaMP8m-WPRE/; Adeno-Associated Virus (AAV)/AAV-Ef1a-DIO ChETA-EYFP/; Adeno-Associated Virus (AAV)/AAV hSyn FLEx mGFP-2A-Synaptophysin-mRuby/; Adeno-Associated Virus (AAV)/AAV-CamKIIa-jGCaMP8m-WPRE

Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: N/A

Animal Use: Yes

Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Viral Vector - Adeno-Associated Virus (AAV)/Intracranial injection/Isoflurane Anesthesia /ABSL1/lab coat, disposable gloves, and eye protection/ABSL1/No//

Risk Assessment/Discussion:

Dr. Papazoglou has submitted an amendment to his current IBC protocol entitled Neuronal response to hypoglycemia. In this amendment, they have updated personnel and adeno-associated virus (AAV) vector constructs. The two new AAV constructs will be administered to mice via intracranial injection to express ChETA and Synaptophsin. Dr. Papazoglou is currently approved for work with several different AAV constructs in mice. All AAVs will be purchased from commercial vendors. After two weeks of recovery, mice will undergo trapping during hypoglycemia. Work with the new AAV constructs will be completed at ABSL1 containment and housing, as previously approved. Personnel will wear lab coats, disposable gloves, and eye protection for the work described. The addition of these new AAV constructs does not significantly alter the biohazardous risks associated with Dr. Papazoglou's IBC protocol.

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IBC Discussion & Vote:

The amendment to IBC-24-35 (version 43.0) was approved.

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Arthur Hunt initiated the motion. Carrie Shaffer seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Caroline Geisler
IBC Protocol Number: IBC-24-445
Protocol Title: Neuroendocrine Control of Systemic Metabolism and Energy Balance
Protocol Type: Amendment
Amendment To: Genetic constructs
Applicable Guidelines & Regulations: NIH Guidelines Section III-E-3, NIH Guidelines Section III-D-4, NIH Guidelines Section III-F-1, NIH Guidelines Section IV-B-7, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, OSHA Act of 1970 Clause 5(a)(1), NIH Guidelines Section III-E-1
Maximum Containment Level: Animal Biological Safety Level 1 (ABSL1), Biological Safety Level 1 (BSL1)
Primary Reviewers: C. Haughton, A. Hunt, J. Smalle

Brief Project Overview:

Almost 75% of US Adults are obese or overweight, a condition that puts individuals at an elevated risk of all major mortality-linked diseases including type 2 diabetes, cardiovascular disease, cancer, and Alzheimer's. While cancer and Alzheimer's are not typically thought of as metabolic diseases, research over the last decade shows that they are based in metabolic dysfunction. Thus, improving metabolic health is paramount to fighting against all these obesity-associated diseases. Metabolism and energy balance are coordinated between the brain and body by sensing signals from nutrients, hormones, and neurotransmitters that communicate the fuel needs of our organs. Our understanding of how these neuroendocrine signals are integrated to regulate behaviors (eating) and metabolism (storage and use of the nutrients we eat) are incompletely understood. We hypothesize that obesity alters the brain's ability to accurately sense the signals indicating stored and available fuel in the body, contributing to overeating and dysregulated metabolism. Our research will investigate mechanisms of how the brain senses and responds to circulating nutrients (glucose, lipids, amino acids) and hormones indicative of metabolic status (fed or fasted state), and how this in turn regulates metabolic activity in the body. Through studying these mechanisms, we aim to develop new therapeutic targets that will improve whole-body metabolic homeostasis to mitigate the risk of obesity-associated diseases.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Cell culture, DNA/RNA isolation/purification, Genetics, Histology, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Transfection, Use of viral vectors

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Transport: Yes
Materials Transported: Animals, Biohazardous Materials
Infectious Agent(s)/Natural Host(s): N/A
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: Diazepam Binding Inhibitor (DBI)/Acyl-CoA Binding Protein (ACBP)/ Mouse/ Lipid Binding Protein/ Overexpression in astrocytes/ Mouse/ AAV;Diazepam Binding Inhibitor (DBI)/Acyl-CoA Binding Protein (ACBP)/ Mouse/ Lipid Binding Protein/ Overexpression in astrocytes/ Mouse/ plasmid;Diazepam Binding Inhibitor (DBI)/Acyl-CoA Binding Protein (ACBP)/ Mouse/Rat/ Lipid Binding Protein/ siRNA Knockdown/ Mouse/Rat/ AAV;Cre Recombinase/ P1 Bacteriophage/ Recombinase Enzyme/ Introduce Cre expression for genetic manipulation strategies/ Mouse/Rat/ AAV;Gq-coupled hM3D Designer Receptors Exclusively Activated by Designer Drugs (DREADD)/ Synthetic construct - modified human muscarinic 3 receptor to recognize exogenous ligand CNO/ G-Protein Coupled Receptor/ Express hM3D excitatory DREADD/ Mouse/Rat/ AAV;Green Fluorescent Protein (GFP)/ Crystal Jellyfish Aequorea Victoria/ Fluorophor/ Express GFP for labeling/ Mouse/Rat/ AAV;mCherry/ Discosoma sea anemones/ Fluorophor/ Express mCherry for labeling/ Mouse/Rat/ AAV;NaChBac/ Synthetic Construct of Bacterial Sodium Channel/ Membrane Ion Channel/ Chronically depolarize neurons/ mouse/rat/ AAV;GCaMP/ Synthetic construct from fusion of green fluorescent protein (GFP), calmodulin (CaM), and M13, a peptide sequence from myosin light-chain kinase/ Fluorescent Calcium Indicator/ Express GCaMP to visualize calcium signaling/ Mouse/Rat/ AAV;Gi-coupled hM4D Designer Receptors Exclusively Activated by Designer Drugs (DREADD)/ Synthetic construct - modified human muscarinic 4 receptor to recognize the exogenous ligand CNO/ G-Protein Coupled Receptor/ Express inhibitory DREADD/ Mouse/Rat/ AAV;Diazepam Binding Inhibitor (DBI)/Acyl-CoA Binding Protein (ACBP)/ Human/ Lipid Binding Protein/ Overexpression in astrocytes/ Mouse/ AAV
Vector(s) [Vector Category/Vector Technical Name]: Adeno-Assocaited Virus (AAV)/See list of viral vectors below in table; Plasmid/ pAAV-GFAP(0.7)-mACBP-IRES-GFP-WPRE
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Animal/Primary Cortical Neuronal Culture/; Animal/Brain organoid type slice culture/; Animal/Brain organoid type slice culture/; Animal/Liver organoid type slice culture/; Animal/Primary Cortical Astrocyte Culture/
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Rat/Viral Vector - Adeno-Associated Virus (AAV)/Intracerebroventricular, into brain parenchymal tissue, IV/KAX or isoflurane/ABSL1/gloves, gown, shoe covers./ABSL1/No//; Mouse/Viral Vector - Adeno-Associated Virus (AAV)/Intracerebroventricular, into brain parenchymal tissue, IV, into pancreas/KAX or isoflurane/ABSL1/gloves, gown, shoe covers./ABSL1/No//

Risk Assessment/Discussion:
Dr. Geisler has submitted an IBC amendment to her current protocol entitled *Neuroendocrine Control of Systemic Metabolism and Energy Balance*. In this amendment, Dr. Geisler seeks to add two new adeno-associated virus (AAV) vector constructs that express wildtype and mutant Diazepam Binding Inhibitor (DBI)/Acyl-CoA Binding Protein (ACBP), a lipid-binding protein, and GCaMP6, a fluorescent calcium indicator. Both AAVs will be administered to animals as previously described and approved for other AAV constructs. Work with AAVs in animals will be completed

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using ABSL1 containment and housing. Personnel will wear gloves, gown, shoes cover, and eye protection. The addition of these two new AAV vectors does not significantly alter the biohazardous risks associated with Dr. Geisler's current IBC protocol. There is a hold on the corresponding IACUC protocol 2024-4486.

IBC Discussion & Vote:

The amendment to IBC-24-445 (version 32.0) was approved.
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Arthur Hunt initiated the motion. Cheryl Haughton seconded the motion. All IBC members present (12) voted in favor of the motion.
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Conflicts of Interest: None
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New Protocols

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PI: Michael C. Tackenberg
IBC Protocol Number: IBC-25-130
Protocol Title: Genetic, molecular, and environmental determinants of circadian period length and output phase.
Protocol Type: New
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-4, NIH Guidelines Section III-E-1, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, OSHA 29 CFR 1910.1030, NIH Guidelines Section III-D-2, NIH Guidelines Section III-F-3
Maximum Containment Level: Biological Safety Level 2 (BSL2), Animal Biological Safety Level 1 (ABSL1)
Primary Reviewers: C. Haughton, A. Hunt, M. Mendenhall

Brief Project Overview:

Biological rhythms (like the sleep/wake cycle) are controlled by biological clocks inside of the body. These biological clocks can be influenced by internal factors (like genetics) and external factors (like diet, exercise, and light exposure). This project looks to investigate how internal and external factors, together and separately, impact the timing of biological clocks.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Bacterial culture, Cell culture, Creation of viral vectors, DNA/RNA isolation/purification, Genetics, Histology, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Transfection, Transformation, Use of viral vectors, Viral culture, Use of infectious agents
Transport: Yes
Materials Transported: Animals, Biohazardous Materials
Infectious Agent(s)/Natural Host(s):

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Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: Npas2/ Mouse/ Transcription factor/ Overexpression/ Mouse/ AAV(PHP.eB), AAV8;Clock/ Mouse/ Transcription factor/ Overexpression/ Mouse/ AAV(PHP.eB), AAV8;Bmal1/ Mouse/ Transcription factor/ Overexpression/ Mouse/ AAV(PHP.eB), AAV8;Per2/ Mouse/ Transcription repressor/ Overexpression/ Mouse/ AAV(PHP.eB), AAV8;Cre/ P1 bacteriophage/ Recombinase/ Recombination/ Mouse/ AAV(PHP.eB), AAV8;Gfp/ multiple sources/ Reporter/ Reporter/ Mouse/ AAV(PHP.eB), AAV8;GCaMP/ synthetic/ Reporter/ Reporter/ Mouse/ AAV(PHP.eB), AAV8;dCas9/ Streptococcus pyogenes or Staphylococcus aureus / RNA-guided (dead) endonuclease/ Transcription factor delivery/ Mouse/ AAV(PHP.eB), AAV8;pMag/nMag/ synthetic/ light-sensitive protein/ light-inducible elements/ Mouse/ AAV(PHP.eB), AAV8;Npas2 shRNA/ synthetic/ shRNA/ Gene knockdown/ Mouse/ pAAV(PHP.eB)/AAV8;Clock shRNA/ synthetic/ shRNA/ Gene knockdown/ Mouse/ pAAV(PHP.eB)/AAV8;Clock shRNA/ synthetic/ shRNA/ gene knockdown/ Mouse/ pAAV(PHP.eB)/AAV8;Nr1d1 shRNA/ synthetic/ shRNA/ gene knockdown/ mouse/ AAV(PHP.eB)/AAV8;Nr1d2 shRNA/ synthetic/ shRNA/ gene knockdown/ mouse/ AAV(PHP.eB)/AAV8
Vector(s) [Vector Category/Vector Technical Name]: Adeno-Associated Virus (AAV)/pAAV (AAV2 ITR); Plasmi/pcDNA3
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/U2OS; Human/HEK293
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Viral Vector - Adeno-Associated Virus (AAV)/i.v. (tail vein injection)/Rotating tail injector platform/ABSL1/Gloves, gown, eye protection/ABSL1/No/Performed in BSC/

Risk Assessment/Discussion:

Dr. Tackenberg is a new PI to UK and has submitted an IBC protocol for his work studying circadian rhythms. Dr. Tackenberg's lab seeks to understand how the external environment, nearby cells/tissues, and molecular composition of a cell alter the molecular mechanisms regulating circadian rhythm. Mice will be utilized to prepare ex vivo brain slices for AAV delivery. Alternatively, AAV will be delivered via tail-vein injection into mice. Mice will be restrained in a tail-vein injection platform, greatly minimizing the risk of accidental needlestick during injections. Animal work will be conducted using ABSL1 containment and housing. AAVs will be purchased commercially or prepared in Dr. Tackenberg's laboratory using a 3-plasmid packaging system in HEK293 cells. AAV preparation will be done using BSL2 containment practices, including use of a Biological Safety Cabinet and lab coat, disposable gloves, and protective eyewear. The gene targets for AAV expression or silencing include reporting genes such as GFP, transcription factors or repressors, calcium sensors, Cre recombinase and dCas9.

IBC Discussion & Vote:

The protocol IBC-25-130 (version 9.0) was approved pending minor modifications as listed below:
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SCIENTIFIC SUMMARY -

1. Please clearly describe the “appropriate PPE” that will be used for each procedure.
2. Provide a brief description of the AAV gene targets for overexpression/knockdown. Specifically, what risk(s) are there to personnel should they be exposed to these specific

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AAV vectors? Is it possible that these AAV vectors could also target human gene sequences?

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Michael Mendenhall initiated the motion. Arthur Hunt seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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Amendments

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PI: Andrew Stewart
IBC Protocol Number: IBC-24-333
Protocol Title: Gene Therapy Approaches to Induce and Control Neuronal Growth in Rodents With Spinal Cord Injuries
Protocol Type: Amendment
Amendment To: Genetic constructs, Laboratory or Greenhouse procedures
Applicable Guidelines & Regulations: NIH Guidelines Section III-F, NIH Guidelines Section III-D-4, NIH Guidelines Section III-E-1, NIH Guidelines Section III-F-1, NIH Guidelines Section IV-B-7, UK Administrative Regulation 6.9, UK Administrative Regulation 6.3, OSHA Act of 1970 Clause 5(a)(1), NIH Guidelines Section III-D-1, OSHA 29 CFR 1910.1030, NIH Guidelines Section III-D-2
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+), Animal Biological Safety Level 2 (ABSL2)
Primary Reviewers: C. Haughton, D. Harrison, Y. Wu

Brief Project Overview:

I seek to regenerate the spinal cord after it has been damaged. My past work has deleted a gene (PTEN) from the mouse genome that inhibits regeneration of the spinal cord. Our results worked far better than anticipated. This was made possible due to mouse lines that are transgenic and interact with proteins (Cre) that are delivered using gene therapies. This approach can only work in these specific transgenic mice and will not work in any other organism. The aim of this project is to make a similar gene therapy strategy that will work in non-transgenic animals, or in other words, be able to work in any species or organism.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Bacterial culture, Cell culture, Creation of Viral Vectors, DNA/RNA isolation/purification, Genetics, Histology, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Transfection, Transformation, Use of Viral Vectors, Use of Infectious Agents
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: AKT3/Human/Oncogene and cell growth/induce regeneration in a

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neuron specific manner/bacteria, human cell line, mouse and rat spinal cord/AAV retro/; rTA/Bacteria/Regulatory/Make inducible expression of AKT3/bacteria, human cell line, mouse and rat spinal cord/AAV retro/; rtTA and TET-ON 3G/Bacteria/Regulatory/Make inducible expression of AKT3/bacteria, human cell line, mouse and rat spinal cord/AAV retro/; eGFP/dTomato/mCherry/tdTomato/Jelly Fish/Tracking/Label Neurons/bacteria, human cell line, mouse and rat spinal cord/AAV retro / Lentivirus/; Cre/Bacteria/Regulatory/KO PTEN from transgenic mouse line. Make a stable cell line of neuronal stem cells that express cre recombinase to test Syn1-DIO constructs in vitro./Mouse and Rat Spinal Cord, human neuronal stem cells and packaging cells/AAV retro/; Flp/Bacteria/Regulatory/expression of genes in a Flp dependent manner/Mouse and Rat Spinal Cord/AAV retro/; Cre/Bacteria/Regulatory/create stable cell line producing cre recombinase to test other cre-dependent constructs./Neural Stem cell line/Lenti-Cre-IRES-PuroR/; miR30-shRNA(Kv1.2 murine)/shRNA/Translation/knockdown the expression of the potassium channel Kv1.2./Neural Stem Cell Line/AAV-Retro/; Crispr Cas9 and Guide arms against REST/NRSF/Bacteria/Translation/Knockout of the DNA binding domain of gene REST/NRSF/HEK293/Expression Plasmid/; ApoA1/Human/Lipid Trafficking/Study of HDL and Dysfunctional HDL/HEK293/AAV plasmid/; ApoA1(milano)/Human/Lipid Trafficking/Study of HDL and Dysfunctional HDL/HEK293/AAV Plasmid/; PKA (PRKACA)/Human/Regulatory/Catalytic domain of PKA to study effects on neural excitability./Hek293, Mouse and Rat Spinal Cord/AAV-Retro/; PKA (L 206 -> R) (PRKACA)/Mouse/Regulatory/Mutant catalytic domain of PKA to confer constitutive activity via interference with regulatory domain./Hek293, Mouse and Rat Spinal Cord/AAV-Retro/; 3xHA-eGFP-OMP25(C' 170-206)/Mouse/Mitochondria Reporter/Mitochondrial targeted reporter with HA tag for neuron-specific pull down studies./Hek293, Mouse and Rat Spinal Cord/AAV Retro/; DDR2/Human/Receptor/Study of collagen receptor for axon growth over collagen/Hek293, hNPC/AAV Plasmid/; EPAC1 (VLVLE to AAAAA)/Mouse/Regulatory/Expression of constitutivley active EPAC1 in vitro and in spinal-projecting neurons in vivo to study regeneration/Mouse and Rat Spinal Cord, HEK293s, Mouse Primary Neuron Culture/AAV retro/; miR30(CXCL12/shRNA/Translation/Knockdown of Mouse CXCL12 in vitro and in vivo/Mouse and Rat Spinal Cord and Hek293/AAV2/; miR30(CXCR4)/shRNA/Translation/Knockdown of Mouse CXCR4 in vitro and in vivo/Mouse and Rat spinal cord, Hek293/AAV retro/; BFP (Blue Fluorescent Protein)/Aequorea victoria/Reporter/Reporter Gene/Mouse and Rat Spinal Cord, HEK293/AAV2/; L1CAM/RAT/Cell Adhesion Molecule/Express in Stem Cells for Transplantation/Mesenchymal Stem Cells/pLenti-EF1a-L1CAM-CMV-BFP/PuroR/; NCAM1/Rat/Cell Adhesion Molecule/Expression Stem Cells for Transplantation/Mesenchymal Stem Cells/pLenti-EF1a-NCAM1-CMV-BFP/NeoR/; CNTN1/Rat/Cell Adhesion Molecule/Express in Stem Cells for Transplantation/Mesenchymal Stem Cells/pLenti-EF1a-CNTN1-CMV-BFP/HygroR/; miRFP670 Nano/Nostoc punctiforme/Reporter Gene/Reporter Gene for Vector Transduction/Rat and Mouse/pAAV-(Antisense) WPRE3-myrAKT3-TRE3G (SENSE) Syn1-TETON3G-2a-miRFP670 Nano WPRE3/; pAAV-(Antisense) WPRE3-dTomato-TRE3G (SENSE) Syn1-TETON3G-2a-miRFP670 Nano WPRE3/; pAAV-(Antisense) WPRE3-3' beta Actin-myrAKT3-TRE3G (SENSE) Syn1-TETON3G-2a-miRFP670 Nano WPRE3/; Kir2.1/synthetic/Ion Channel/Establish Stable Cell Line/HEK293/Lentivirus/; PGC1alpha/Mouse/Transcription Factor/Co-activator/Gene Expression in neurons in mice/Mouse, Rat, HEK293, mouse Neural Stem Cells /AAV retro/; HA_eGFP-MitoTag/Jelly Fish/Reporter Gene/Label Mitochondria and Pull Down/Mouse, Rat, HEK293, Mouse Neural Stem Cells/AAV Retro/; shRNA (Kv1.2)/shRNA/Regulatory/Knockdown Kv1.2/Mouse/AAV Retro/; HA-eGFP-MitoOMM/Jelly Fish/Tracking/Identification and isolation of neuron-specific

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mitochondria/Hek293, Mouse and Rat Spinal COrd/pAAV-CamKIIa-HA-eGFP-MitoOMM/; 3xFlag-BFP-MitoOMM/Jelly Fish/Tracking/Tracking and isolation of Astrocyte-specific mitochondria/Hek293, Rat and Mouse Spinal Cord/pAAV-GFAP-3xFlag-BFP-MitoOMM/; Myc-RFP-MitoOMM/Jelly Fish/Tracking/Tracking and Isolation of Oligodendrocyte-specific mitochondria/Hek293, Mouse and Rat spinal cords/pAAV-MAG2.2-Myc-RFP-MitoOMM/; Pink1/Mouse/Regulatory/Overexpression of Pink1 in spinal projecting neurons within mouse and Rat spinal cords after injury./Hek293, Mouse and Rat spinal cords/pAAV-Syn1-Pink1-p2a-HA-eGFP-MitoOMM/; Firefly Luciferase/Firefly/Reporter/In vivo bioluminescence reporter/Hek293, Mouse spinal cord/pcDNA-Axolotl Enhancer- Hsp68 min- eGFP-p2a-ffLuc/; pLenti-Axolotl Enhancer- Hsp68 min- eGFP-p2a-ffLuc/; pcDNA-Hsp68 min- eGFP-p2a-ffLuc/; pLenti-Hsp68 min-eGFP-p2a-ffLuc/; pLenti-Axolotl Enhancer- Hsp68 min- RunX1-p2a-ffLuc/; pLenti-Axolotl Enhancer- Hsp68 min- ffLuc/; pLenti-CMV-eGFP-p2a-ffLuc-wpre/; pLenti-CMV-Runx1-p2a-ffLuc-wpre/; Runx1/Mouse/Transcription Factor/Transcription Modification/Hek293, Mouse Spinal Cords/pLenti-Axolotl Enhancer- Hsp68 min- RunX1-p2a-ffLuc/; pLenti-CMV-Runx1-p2a-ffLuc-wpre/; CD44/Mouse/Cell Adhesion Molecule/Express CD44 to determine role in growth in spinal cord lesions/Hek293, mouse spinal cord/pAAV-Syn1-CD44-HA-WPRE3/; Pink1 reporter split-luciferase/Synthetic/Reporter/Measure Pink1 activity in vivo in a cell-specific manner/Hek293, mouse spinal cord/pAAV-(CMV/Syn1/GFAP/CamK2a)-Pink1 reporter split-Luciferace/; CRISPR-CAS9 U6-Guide Arms (Pink1)/Bacteria/Translation/Knockout of the Pink1 protein in Hek293 cells/Hek293/CMV-CRISPR-CAS9 U6-Guide Arms (Pink1)
Vector(s) [Vector Category/Vector Technical Name]: Plasmid/PHR-EF1alpha-TET-On 3G/; Adeno-Associated Virus (AAV)/pAAV-Thy1PS-rTA/; Lentivirus/PHRIG-AKT3-IRES-eGFP/; Adeno-Associated Virus (AAV)/pAAV-hSyn1-Cre-P2A-dTomato/; Adeno-Associated Virus (AAV)/pAAV-TRE3G-tdTomato/; Adeno-Associated Virus (AAV)/AAV-hSyn1-rtTAV16/; Adeno-Associated Virus (AAV)/AAV-hSyn1-TET-ON 3G/; Adeno-Associated Virus (AAV)/AAV-hSyn1-rTA/; Adeno-Associated Virus (AAV)/pAAV-TRE3G-AKT-IRES-eGFP/; Adeno-Associated Virus (AAV)/pAAV-TRE3G-eGFP/; Adeno-Associated Virus (AAV)/pAAV-ihSYN1-DIO-tTA/; Adeno-Associated Virus (AAV)/pAAV-ihSYN1-DIO-AKT-IRES-dTomato/; Adeno-Associated Virus (AAV)/pAAV-ihSYN1-DIO-dTomato/; Adeno-Associated Virus (AAV)/pAAV-EF1a-fDIO-Cre/; Adeno-Associated Virus (AAV)/AAV phSyn1(S)-FlpO-bGHpA/; Lentivirus/pMD2.G VSV-G/; Lentivirus/Lenti-Cre-IRES-Puro/; Adeno-Associated Virus (AAV)/pAAV-CAG-Flex-tdTomato/; Adeno-Associated Virus (AAV)/pAAV-CMV-eGFP-mir30-shRNA(Kv1.2 murine)/; Plasmid/CMV-CRISPR-CAS9 U6-Guide Arms (REST/NRSF)/; Adeno-Associated Virus (AAV)/pAAV-Ef1a-ApoA1-IRES-eGFP/; Adeno-Associated Virus (AAV)/pAAV-Ef1a-ApoA1(milano)-IRES-eGFP/; Plasmid/pcDNA-CMV-PKA/; Adeno-Associated Virus (AAV)/AAV-Syn1-eGFP-2a-mKv1.2/; Adeno-Associated Virus (AAV)/AAV-TRE-eGFP-2a-PKA/; Adeno-Associated Virus (AAV)/AAV-TRE--eGFP-2a-PKA(L 206-> R)/; Plasmid/pMXs-3xHA-eGFP-OMP25/; Plasmid/Syn1-3xHA-eGFP-OMP25/; Adeno-Associated Virus (AAV)/Syn1-3xHA-eGFP-OMP25(c'170-206)/; Plasmid/pAAV-CamK2a-RFP/; Plasmid/pCDNA-Hb9-eGFP/; Plasmid/pDONR223-DDR2/; Adeno-Associated Virus (AAV)/pAAV-hSyn1-DDR2-2a-eGFP/; Adeno-Associated Virus (AAV)/pAAV-Syn1-eGFP-2a-PKA (L 206 R)/; Adeno-Associated Virus (AAV)/pAAV-Syn1-HA-EPAC1 (VLVLE to AAAAA)/; Adeno-Associated Virus (AAV)/pAAV-CMV-BFP-mir30(CXCL12)/; Adeno-Associated Virus (AAV)/pAAV-Syn1-eGFP-mir30(CXCR4)/; Lentivirus/pLenti-EF1a-L1CAM-CMV-BFP/PuroR/; Lentivirus/pLenti-EF1a-NCAM1-CMV-BFP/NeoR/; Lentivirus/pLenti-EF1a-CNTN1-CMV-BFP/HygroR/; Adeno-Associated Virus (AAV)/pAAV-(Antisense) WPRE3-myrAKT3-TRE3G (SENSE) Syn1-TETON3G-2a-miRFP670 Nano

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WPRE3/; Adeno-Associated Virus (AAV)/pAAV-(Antisense) WPRE3-dTomato-TRE3G (SENSE) Syn1-TETON3G-2a-miRFP670 Nano WPRE3/; Adeno-Associated Virus (AAV)/pAAV-(Antisense) WPRE3-3' beta Actin-myrAKT3-TRE3G (SENSE) Syn1-TETON3G-2a-miRFP670 Nano WPRE3/; Adeno-Associated Virus (AAV)/pAAV-Syn1-EPAC1 (VLVLE to AAAAA) - 3' Beta Actin/; Lentivirus/pRSV-REV/; Lentivirus/pMDLg/pRRE/; Lentivirus/HK_13_BLA_Lenti_KIR2.1/; Adeno-Associated Virus (AAV)/pAAV-CMV-eGFP-U6-shRNA(Kv1.2)/; Adeno-Associated Virus (AAV)/pAAV-Syn1-PGC1alpha-HA_eGFP_MitoTag/; Adeno-Associated Virus (AAV)/pAAV-Syn1-HA_eGFP_MitoTag/; Adeno-Associated Virus (AAV)/pAAV-CamKIIa-HA-eGFP-MitoOMM/; Adeno-Associated Virus (AAV)/pAAV-GFAP-3xFlag-BFP-MitoOMM/; Adeno-Associated Virus (AAV)/pAAV-MAG2.2-Myc-RFP-MitoOMM/; Adeno-Associated Virus (AAV)/pAAV-Syn1-Pink1-p2a-HA-eGFP-MitoOMM/; Plasmid/pcDNA-Axolotl Enhancer- Hsp68 min- eGFP-p2a-ffLuc/; Lentivirus/pLenti-Axolotl Enhancer- Hsp68 min-eGFP-p2a-ffLuc/; Plasmid/pcDNA-Hsp68 min- eGFP-p2a-ffLuc/; Lentivirus/pLenti-Hsp68 min-eGFP-p2a-ffLuc/; Lentivirus/pLenti-Axolotl Enhancer- Hsp68 min- RunX1-p2a-ffLuc/; Lentivirus/pLenti-Axolotl Enhancer- Hsp68 min- ffLuc/; Lentivirus/pLenti-CMV-eGFP-p2a-ffLuc-wpre/; Lentivirus/pLenti-CMV-Runx1-p2a-ffLuc-wpre/; Adeno-Associated Virus (AAV)/pAAV-Syn1-CD44-HA-WPRE3/; Adeno-Associated Virus (AAV)/pAAV-(CMV/Syn1/GFAP/CamK2a)-Pink1 reporter split-Luciferace/; Plasmid/CMV-CRISPR-CAS9 U6-Guide Arms (Pink1)/; Plasmid/pCAGGS-FuG-B2
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/Hek 293; Human/hNPC (Human Neural Progenitor Cell) ATC-5004; Human/hiPSC (Human Induced Pluripotent Stem Cells); Human/Hek 293-REST-KO; Animal/Mouse Neural Stem Cell; Human/Hek 293-Pink1-Knockout
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Viral Vector - Adeno-Associated Virus (AAV)/Spinal Cord Injection/Anesthesia/Vertebral Clips/ABSL1/Mask/Gloves/Eye Protection/Lab Coat/Hair Bonet/ABSL1/No/Sterile technique, We use a BSC for injection although not required. Mice will be housed in ABSL2 containment for 24 hours after treatment until the wound has closed. Some AAVs contain the use of antisense oligonucleotides/; Mouse/Viral Vector - Lentivirus/Spinal Cord Injection/Anesthesia/Vertebral Clips/ABSL2/Mask/Gloves/Eye Protection/Lab Coat/Hair ABonet/ABSL2/No/Sterile technique. Perform spinal cord injections in BSL2 certified biosafety cabinet. House mice in ABSL2 containment for 72 hours post-injection. Disinfect the area after use and dispose of all sharps into sharps containers.

Risk Assessment/Discussion:

Dr. Stewart has submitted an amendment to update personnel and add a new adeno-associated virus (AAV) vector construct to an already long list of approved viral vectors. The new AAV construct will be packaged in Dr. Stewart's laboratory, whereas previous AAV constructs were purchased ready-made from outside vendors. PAAV-Crym1-DIO-eGFP will be injected into mice or rats along with Syn1-cre-p2a-dTomato (previously approved AAV vector) to restrict eGFP expression to the corticospinal tract. AAVs will be packaged in Hek293 cells using a three-plasmid system. AAV preparation will take place using BSL2 containment wearing lab coat, disposable gloves, and eye protection. Spinal cord injections will be done as previously described and approved. Although the

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addition of AAV packaging does increase the containment level of AAV work from BSL1 to BSL2, the overall increase in risk is minimal given other work already approved.

IBC Discussion & Vote:

The amendment to IBC-24-333 (version 86.0) was approved pending minor modifications as listed below:

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SCIENTIFIC SUMMARY – Please clearly describe the specific PPE that will be utilized for each procedure.

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Douglas Harrison initiated the motion. Yadi Wu seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Paramarajan Piranavan
IBC Protocol Number: IBC-24-422
Protocol Title: A Phase 2, open-label study to evaluate the efficacy and safety of rapcabtagene autoleucel in patients with active, refractory systemic lupus erythematosus (SLE) or active, refractory lupus nephritis (LN)
Protocol Type: Amendment
Amendment To: Administrative Information, Project Title
Applicable Guidelines & Regulations: UK Administrative Regulation 6.9, UK Administrative Regulation 6.3, OSHA 29 CFR 1910.1030, NIH Guidelines Section III-C-1, OSHA Act of 1970 Clause 5(a)(1), NIH Guidelines Section IV-B-7
Maximum Containment Level: Biological Safety Level 2 (BSL2)
Primary Reviewers: D. Harrison, T. Chambers, B. Nelson

Brief Project Overview:

This is a research study about to find out if rapcabtagene autoleucel (herein referred to as YTB323),. an investigational new therapy, is safe and effective (can help) for people who have systemic lupus erythematosus (SLE) with active lupus nephritis (LN). YTB323 is a CAR-T cell therapy, which is a type of gene therapy/immunotherapy. CAR-T involves collecting and using a patient's own immune cells, specifically their T cells, to treat their condition. The patient's T cells are sent off to the manufacturer's (Novartis) laboratory, where the T cells are genetically "modified" to fight and destroy immune cells such as B cells. B cells contribute to lupus disease.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Human Clinical Trial, Use of Human Source Material(s)
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids,

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organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: CAR-19 Transgene/Chimeric, murine & human sequences synthetically generated/Chimeric Antigen Receptor/Expression/Autologous Cells/Transduce primary T-cells to express chimeric anti-CD19 scFv
Vector(s) [Vector Category/Vector Technical Name]: Lentivirus/ CTL019 (murine) HIV-1 Vector
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: N/A
Animal Use: No
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: N/A

Risk Assessment/Discussion:

Dr. Piranavan has submitted an amendment to his clinical IBC protocol to include the potential for administration of out-of-specification (OOS) rapcabtagene autoleucel to study participants and to update study elements, including the addition of a Systemic Lupus Erythematosus (SLE) cohort. All of aspects of this clinical study (ex. Genetic targets, product formulation, administration, etc.) remain the same as previously approved. The amendment specifies that OOS product will not be released in the event of detection of replication-competent lentivirus, endotoxin, mycoplasma, or other non-sterility. The administration of OOS product to study participants may increase their risk, however the risk to healthcare personnel and others handling the OOS product remains relatively the same.

IBC Discussion & Vote:

The amendment to IBC-24-422 (version 34.0) was approved pending minor modifications as listed below:

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SCIENTIFIC SUMMARY – Please clarify if this amendment affects the overall expected patient enrollment at the UK study site.

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Douglas Harrison initiated the motion. Thomas Chambers seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Rina Plattner
IBC Protocol Number: IBC-24-474
Protocol Title: Role of Abl Family Kinases in Solid Tumors
Protocol Type: Amendment
Amendment To: Cells or tissues used in research, Genetic constructs
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-1, NIH Guidelines Section III-F, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), OSHA 29 CFR 1910.1030, UK

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Administrative Regulation 6.9, NIH Guidelines Section III-F-1, NIH Guidelines Section III-F-7, UK Administrative Regulation 6.3
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+), Animal Biological Safety Level 2 (ABSL2)
Primary Reviewers: C. Haughton, A. Pinto, M. Landron

Brief Project Overview:

Our laboratory studies the Abl family of non-receptor tyrosine kinases (c-Abl, Arg) and their involvement in the development and progression of solid tumors such as melanoma and breast cancer. We are currently focusing on how these proteins are activated in these diseases; identifying biological processes that they mediate (e.g. invasion, migration, proliferation, survival, tumor growth, metastasis); and defining downstream signaling pathways that are activated by Abl kinases to promote the above biological processes. The biological safety issues associated with our research include the use of established human cancer cell lines, ecotropic retrovirus, lentivirus, recombinant DNA, use of radioactivity in conjunction with biohazardous materials, injection of human cancer cell lines into animals, and breeding of transgenic animals.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Bacterial culture, Cell culture, DNA/RNA isolation/purification, Flow cytometry/Cell sorting, Immunohistochemistry, PCR/qRT-PCR, Transformation, Transfection, Use of viral vectors, Creation of viral vectors, Use of Human Source Material(s), Imaging/Microscopy
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: ABL1, ABL2/ mouse, human/ proto-oncogene-enzyme, proliferation/ expression in cell culture, silencing in cell culture, also utilizing constitutively active (PP) and kinase-dead forms (K>R)/ mammalian cell culture/ MIGR1, PK1, pcDNA3;BRAF/ human/ proto-oncogene-enzyme/ expression in cell culture/ mammalian cell culture/ pBabePuro;IkB kinase/ human/ enzyme/ expression in cell culture/ mammalian cell culture/ pcDNA3;EGFP, EYFP, dsRed, mCherry/ jellyfish/ tag, cell tracking/ expression in cell culture/ mammalian cell culture/ various;STAT3/ human/ cell growth, survival/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;luciferase/ firefly/ cell tracking/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;beclin-1/ human/ autophagy protein/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;Src/ human/ cell growth and survival/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;cathepsins-B, L, D/ human/ protein degradation, autophagy/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;NF-kB, Sp1, Ets1/ human/ transcription factors/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;ATG proteins/ human/ autophagy/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;Rab5, Rab7/ human/ vesicular trafficking/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1,

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pBabepuro, pIRES-DsRed;NM23/ human/ metastasis suppressor/ silencing in cell culture/ mammalian cell culture/ lentivirus;Fus1/Tusc2/ human/ tumor suppressor/ expression in cell culture/ mammalian cell culture/ pGEX2T, pcDNA3, MIGR1, pBabepuro, pIRES-DsRed;ERK2/ human/ proliferation/ expression in cell culture/ mammalian cell culture/ pBabepuro;beta-catenin/ human/ proliferation/ expression in cell culture/ mammalian cell culture/ pcDNA3, EGFP-tag;MYC/ human/ proliferation/ expression in cell culture/ mammalian cell culture/ MSCV-IRES-GFP;ETS1/ human/ proliferation/ expression in cell culture/ mammalian cell culture/ pCMV-IRES-GFP;CCL2, CCL5, CXCL1, CXCL5, CXCL8, IL6/ human or mouse/ cytokine/ expression into mouse or human melanoma cells/ mammalian cell culture/ LV-vectors from GeneCopoeia;ZEB1/ mouse or human/ transcription factor/ Make stable cell lines in human or mouse melanoma cells/ mammalian cell culture/ LV-230 from Genecopoeia.;ZEB1 shRNA/ human or mouse/ transcription factor/ Silence ZEB1 in human or mouse melanoma cells/ human or mouse/ PLK0.1 or PLK0.5 from Sigma;N-cadherin/ human or mouse/ E3 ligase/ over expression/ mammalian cell culture/ PLK0.5 from Sigma;N-cadherin/ Homo sapiens/ transmembrane protein/ shRNA for silencing the gene/ mammalian cell culture/ PLK0.5-viral vector from Sigma;NEDD4L/ Homo sapiens/ E3 ligase/ silencing in cell culture with shRNA/ mammalian cell culture/ PLK0.1 or PLK0.5 from Sigma;shNT (non-targeting shRNA)/ none/ none/ non-targeting shRNA/ mammalian cell culture/ PLK0.1 or PLK0.5 from Sigma;Div-DDR1 (constitutively active)/ homo sapiens/ receptor tyrosine kinase/ create stable melanoma cell lines/ mammalian cell culture/ pCDH from Dr. Ge

Vector(s) [Vector Category/Vector Technical Name]: Plasmid/pcDNA3/; Plasmid/Migr1/; Plasmid/pBabe Puro/; Plasmid/pEGFP-N1/; Plasmid/pGEX2T/; Plasmid/pIRES-dsRed2/; Plasmid/pKLO-IPTG-3XLacO/; Plasmid/Piggybac-cumate/; Plasmid/Piggybac-cum-shRNA/; Plasmid/pWZLblast/; Lentivirus/pLKO.1, PLK0.5/; Plasmid/PK1/; Plasmid/pCMV-mCherry/; Plasmid/pCMV-IRES-GFP/; Plasmid/MSCV-IRES-GFP/
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/293T HEK/; Animal/NIH3T3/; Human/MDA-MB-435s/M14, M14-BR, M14-BMR/; Human/BT-549/; Human/MDA-MB-231/; Human/MDA-MB-468/; Human/WM3248/; Human/MCF-7/; Human/A375/; Human/WM239,WM278,SBCL2, WM35, Mel1617, 451-Lu,WM164,UACC-903,WM9, WM1232,WM3211,WM793, 12050-Lu. WM3248 and WM164 expressing constitutively active ABL1 and ABL2 (WM164-ABL1/2-PP, WM3248-ABL1/2-PP)/; Human/melanocytes/; Human/mammary epithelial cells/; Human/BT-474/; Human/SUM1315/; Animal/melan-a/; Human/Hermes-1/; Human/LOX IVMI/; Human/SK-Mel-2, SK-Mel-5, SK-Mel-28, UACC-62, UACC-257, malme-3M, and SK-MEL-2 resistant to MEK inhibitor (SK-MEL-2MR)/; Human/SK-Mel-30, SK-Mel-147 and their BRAF and MEK inhibitor resistant counterparts (-BMR)/; Animal/OSUMMER.12, OSUMMER.13 and their MEK inhibitor resistant counterparts (-MR)/; Animal/Ma-NRAS1-1007, Ma-NRAS2-1014 and their MEK inhibitor resistant counterparts (MR)/; Animal/YUMM5.2, YUMM1.7, YUMM3.3, B16F10, and YUMM-.BMR (cell lines resistant to BRAF and MEK inhibitors)/
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Cells - Human, non-modified/subcutaneous injection/isoflurane/ABSL2/Gown, eye protection, gloves, mask or BSC/ABSL2/No/Excess cells will be autoclaved. Sharps use minimized. Cages only opened in changing station, BSC or chemical fume hood./; Mouse/Cells - Animal, genetically modified/subcutaneous injection/isofluorane/ABSL1/Gown, gloves, eye protection/ABSL1/No/Excess material will be

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autoclaved. Sharps will be minimized./; Mouse/Cells - Human, genetically modified/subcutaneous injection/isoflurane/ABSL2/Gown, eye protection, gloves/ABSL2/No/Excess material will be autoclaved. Sharps will be minimized. Cages will only be opened in changing stations, BSC, or chemical fume hood./; Mouse/Tissue - Human (ex. PDX tumor tissue)/subcutaneous/isoflurane anesthesia/ABSL2/Gown, eye protection, gloves, mask or BSL2 hood/ABSL2/No/Excess human tissue will be autoclaved. Use of sharp objects will be minimized. Cages will only be open in a cage changing station, BSC, or chemical fume hood.

Risk Assessment/Discussion:

Dr. Plattner has submitted an amendment to her IBC protocol to update lentiviral gene targets. Specifically, she has added new lentiviral vectors that will overexpress and silence N-cadherin, silence NEDD4L, and express Div-DDR1 in mammalian cells. These new lentiviral constructs will be produced and packaged as previously described and approved using BSL2+ containment. Lentivirus-transduced cells will be administered to mice via subcutaneous injection as previously described and approved. All other downstream assays/manipulations of animals and their tissues remain the same as previously approved. The new gene targets are not known oncogenes or otherwise known to be particularly hazardous. There is a hold on the corresponding IACUC protocol 2020-3426.

IBC Discussion & Vote:

The amendment to IBC-24-474 (version 21.0) was approved pending minor modifications as listed below:

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GENERAL INFORMATION -

1. Under Radiological Hazards, if your permit is currently inactive and you have no current plans or approval to work with radioactive materials, please select “No” in response to the question “Does your research involve the use of radiological hazards?”
2. In the Lay Description of the project, please remove the statement regarding radioactivity in conjunction with biohazards if your lab is not doing this work.

CELL LINES – Cells in Use table: The IACUC lists: MEL1617-BMR, SK-MEL-30MR, SK-MEL-147MR, YUMM5.2-BMR, OSUMMER.12, OSUMMER.12-BMR; however, the IBC Protocol lists MEL1617 but not MEL1617-BMR; SK-MEL-30-BMR and SK-MEL-147-BMR but not SK-MEL-30-MR and SK-MEL-147-MR; and OSUMMER.12-MR but not OSUMMER.12-BMR.

Please update the cell line entries to ensure the names of all cell lines are congruent between the IBC and IACUC.

SCIENTIFIC SUMMARY - If radioactivity work is not approved or planned for current experiments, please remove all descriptions of work associated with radioactive materials.

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Amelia Pinto initiated the motion. Maria Landron seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Bonnie Firestein
IBC Protocol Number: IBC-25-104
Protocol Title: Regulation of Dendritic Morphology and Function by Cypin, the Main Guanine Deaminase, and Other Proteins
Protocol Type: Amendment
Amendment To: Genetic constructs
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-1, NIH Guidelines Section III-D-4, NIH Guidelines Section III-E, NIH Guidelines Section III-E-1, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), OSHA 29 CFR 1910.1030, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, NIH Guidelines Section III-F-1
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+), Animal Biological Safety Level 2 (ABSL2)
Primary Reviewers: C. Haughton, B. Nelson, C. Pickett

Brief Project Overview:

The central goal of this research is to investigate how cypin (guanine deaminase, GDA) regulates synaptic protein composition, cellular metabolism, and neuronal recovery after traumatic brain injury (TBI), while also testing therapeutic strategies that include viral vectors, exosome-mediated RNA delivery, and small-molecule modulators. Our studies use both in vitro systems (primary rodent neurons, HEK293T, SH-SY5Y cells) and in vivo rodent models (mice and rats). Because these experiments involve replication-deficient viral vectors, plasmids, and biohazardous manipulations, we provide here a stepwise description of procedures, biosafety levels (BSL), and inactivation practices in compliance with UKY IBC policies.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Cell culture, DNA/RNA isolation/purification, Histology, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Proteomics, Transfection, Use of viral vectors, Use of Human Source Material(s), Bacterial culture, Creation of viral vectors, Transformation
Transport: Yes
Materials Transported: Animals, Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: Guanine Deaminase (GDA or Cypin)/Homo sapiens / Mus musculus/Cytoskeletal remodeling / Guanine metabolism/Overexpression, knockdown, fluorescent tagging/Human cells, rat, mouse, neurons/Lentivirus (pHUUG-Cypin-shRNA, FG12.Cypin-EGFP), AAV (pAAV[Exp]-CMV>mGda:IRES:EGFP:WPRE, pAAV[Exp]-Syn1>mGda:IRES:EGFP:WPRE, pAAV[Exp]-CBh>mGda:IRES:EGFP:WPRE, AAV-CamKII-Cypin, AAV-PHP.eB-Cypin)/; AHCYL1/Homo sapiens / Mus musculus/Metabolic enzyme complex / protein interactor/Expression, region mapping, interaction assays/HEK293T cells for packaging, Mouse/rat for delivery /AAV (AAV-PHP.eB), Lentivirus (pLV-CMV, pLV-U6)/; PSD-95 (DLG4)/Homo sapiens / Mus musculus/Synaptic scaffolding protein/Overexpression and tagging/E. coli, HEK 293,

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neurons/Plasmids (pSuper-GFP)/; Klotho/Homo sapiens / Mus musculus/Aging-associated factor/Overexpression/Mouse, rat, neurons, cell lines/Lentivirus (FGF12.Cypin-EGFP)/; CamKII (a-subunit)/Mus musculus/Kinase (signaling pathway)/Neuronal promoter (for targeting excitatory neurons)/Mouse (in vivo), neurons/AAV1.CamKII.eGFP, AAV-CamKII-Cre/; Protein kinase sensors (e.g., AKAR4a, AKAR4?)/Synthetic / engineered/Kinase activity biosensors/FRET-based live imaging of kinase activity/HEK293T, neurons/Lentivirus (pRK5 series), plasmid transfection/; GNSTM-3-RVG-10-Lamp2b-HA/Synthetic/Fusion protein for exosome targeting/Exosome modification (capsid targeting)/HEK293T for packaging; Mouse/Rat for delivery/AAV (PHP.eB, rh10 capsids)/; Vinculin/Homo sapiens/Cytoskeletal protein/Fluorescent tagging (VinTi, VinTS, VinVenus, etc.)/Neurons, HEK293T, SH-SY5Y/Lentivirus (pRRL series: VinTi, VinTS, VinVi, VinVenus, etc.)/; nNOS (NOS1, Nitric Oxide Synthase)/Homo Sapiens / Mus musculus/Neuronal Constitutive - Nitric oxide synthase regulator/Fluorescent tagging/E. coli, HEK 293, COS-7 cells, rats (in-utero electroporation)/Plasmid (pEGFP-C1, pEGFP-N1, pIRES-GFP, pCAG-GFP, pGE2hrGFPII, pSuper-GFP)/; CPE (Carboxipeptidase)/Homo sapiens / Mus musculus/Protein-coding gene/Fluorescent tagging/E. coli, HEK 293, COS-7 cells, Neuro2A cells, mice (in utero electroporation)/Plasmid (pEGFP-C1, pEGFP-C1-CPE, pEGFP-C1-CPE-H114A,E117A); monomeric Red Flourescent Protein (mRFP)/Dscosoma/Flourescent tagging, Fused or not fused to cypin (mRFP, cypin-mRFP or cypin H84A-RFP); Flourescent Tagging/Human cells, rat, mouse, neurons/ pAAV-hSyn-mRFP-WPRE (AAV9 or PHP.eB); pAAV-hSyn-mGDA-mRFP-WPRE (AAV9 or PHP-eB), pAAV-hSyn-cypinH84A-mRFP-WPRE (AAV9 or PHP-eB)
Vector(s) [Vector Category/Vector Technical Name]: Adeno-Associated Virus (AAV)/pAAV[Exp]-CBh>EGFP:WPRE/; Adeno-Associated Virus (AAV)/pAAV[Exp]-CBh>mGda[NM_010266.2]:IRES:EGFP:WPRE/; Adeno-Associated Virus (AAV)/pAAV[Exp]-CMV>mGda[NM_010266.2]:IRES:EGFP:WPRE/; Adeno-Associated Virus (AAV)/pAAV[Exp]CMV>EGFP:WPRE/; Adeno-Associated Virus (AAV)/pAAV[Exp]-Syn1>mGda[NM_010266.2]:IRES:EGFP:WPRE/;Adeno-Associated Virus (AAV)/pAAV[Exp]-Syn1>EGFP:WPRE/; Plasmid/pEGFP-C1, pEGFP-N1, pIRES-GFP, pCAG-GFP, pGE2hrGFPII, pSuper-GFP/; Lentivirus/pLV-CMV, pLV-U6/; Adeno-Associated Virus (AAV)/AAV hSyn1-WRPE-HGHpA/; Plasmid/pGEXT-1/; Lentivirus/pHUUG-GST-shRNA, pHUUG-Cypin-shRNA/; Lentivirus/pRRL-VinTi, pRRL-VinVi, pRRL-VinTS, pRRL-TSMod, pRRL-VinVenus, pRRL-empty/; Plasmid/pRK5-tAKAR4alpha, pRK5-tAKAR4alpha T391A, pRK5-tAKARalpha, pRK5-tAKARalpha T391A, pRK5tAKAR4-gamma/; Adeno-Associated Virus (AAV)/GNSTM-3-RVG-10-Lamp2b-HA/; Plasmid/All pEGFP, pIRES, pSuper, pGEXT vectors/; Plasmid/pMAL/; Plasmid/pET28a/; Adeno-Associated Virus (AAV)/AAV1.CamKII.eGFP/; Adeno-Associated Virus (AAV)/CamKII.HI.eGFP-Cre/; Lentivirus/FG12.EGFP, FG12.Cypin-EGFP/
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/Embryonic Kidney 293 cells/; Human/SH-SY5Y human neuroblastoma/; Animal/Rat Hippocampal and Cortical Neurons /; Animal/Rat spinal cord neurons/; Animal/Mouse hippocampal and cortical neurons/; Animal/Mouse spinal cord neurons/; Animal/Cos7 cells/; Animal/PC12 cells/; Animal/Neuro-2A/
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Viral Vector – Adeno-Associated Virus (AAV)/Intra-Cranial Injections/Isoflurane-anesthesia/ABSL1/Lab coat, gloves and eye protection/ABSL1/No/None/; Mouse/Viral Vector - Adeno-Associated Virus

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(AAV)/Intracerebroventricular (ICV)/Stereotaxic frame (surgery under anesthesia)/ABSL1/Lab coat, disposable surgical gown, disposable gloves, surgical mask/ABSL1/No//; Mouse/Viral Vector - Adeno-Associated Virus (AAV)/Intravenous (IV)/Tail vein injection restrainer device/ABSL1/Lab coat, disposable surgical gown, disposable gloves, surgical mask/ABSL1/No//; Mouse/Viral Vector - Adeno-Associated Virus (AAV)/Intrahippocampal stereotaxic injection (surgery under anesthesia)/Stereotaxic frame/ABSL1/Lab coat, disposable surgical gown, disposable gloves, surgical mask/ABSL1/No//; Mouse/Viral Vector - Lentivirus/Intracerebroventricular (ICV)/Stereotaxic frame (surgery under anesthesia)/ABSL2/Lab coat, disposable surgical gown, disposable gloves, surgical mask/ABSL2/No//; Mouse/Plasmid/In-utero electroporation/Isoflurane Anesthesia/ABSL1/Lab coat, disposable surgical gown, disposable gloves, surgical mask/ABSL1/No//; Rat/Plasmid/In-utero electroporation/Isoflurane Anesthesia/ABSL1/Lab coat, disposable surgical gown, disposable gloves, surgical mask/ABSL1/No/

Risk Assessment/Discussion:

Dr. Firestein has submitted an amendment to add a new adeno-associated virus (AAV) vector construct expressing mRFP for use in animals. All work with the new AAV construct will be conducted as previously described and approved using ABSL1 containment and practices. mRGP is a fluorescent tag and does not present any enhanced risk to personnel should they be accidentally exposed. All downstream assays and manipulations remain the same. This addition does not significantly alter the biohazardous risks associated with Dr. Firestein's IBC protocol. There is a hold on corresponding IACUC 2024-4486.

IBC Discussion & Vote:

The amendment to IBC-25-104 (version 15.0) was approved.

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Carol Pickett initiated the motion. Brandy Nelson seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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New Protocols

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PI: Anthony Gerber
IBC Protocol Number: IBC-25-143
Protocol Title: Epigenetic and transcriptional and mechanisms in ex vivo and cultured cell models of lung disease airway
Protocol Type: New
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-1, NIH Guidelines Section III-D-3, NIH Guidelines Section III-E, NIH Guidelines Section III-E-1, NIH Guidelines Section III-F, NIH Guidelines Section III-F-1, NIH Guidelines Section III-F-2, NIH Guidelines Section III-F-3, NIH Guidelines Section III-F-8, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), OSHA

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29 CFR 1910.1030, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, NIH Guidelines Section III-F-6
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+)
Primary Reviewers: Y. Wu, C. Pickett, C. Shaffer

Brief Project Overview:

Our goal is to use human and animal cells and tissues to study lung inflammation and disease. To accomplish this, we use recombinant RNA, DNA and viruses to modify specific pathways that are relevant to disease. In our cellular model systems, this means that we generate fragments of recombinant DNA that we deliver into cells and bacteria using standard approaches. We also use new techniques called "genome editing" to make specific genetic changes in cultured human cells. Through these techniques, we will get better understanding of lung inflammation and disease.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Bacterial culture, Cell culture, Creation of viral vectors, DNA/RNA isolation/purification, Flow cytometry/Cell sorting, Histology, Genetics, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Transfection, Use of Human Source Material(s), Use of viral vectors, Viral culture
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: ELF3/Human/Transcription factor/transfection and transduction/Human cells/pCDNA, siRNA, CRISPR TARGETING; GRHL2/Human/Transcription factor/Trnsfection and transduction/Human/pCDNA, siRNA, CRISPR TARGETING; NR3C1/Human/Transcription factor/transfection/Human cells/pcDNA, CRISPR, siRNA; EHF/Human/Transcription factor/Transfection and transduction/Human/pCDNA, siRNA, CRISPR TARGETING; TP63/Human/Transcription factor/Transfection and transduction/Human/pCDNA, siRNA, CRISPR TARGETING; AHR/Human/transcription factor/Transfection/Human cells/pcDNA, CRISPR
Vector(s) [Vector Category/Vector Technical Name]: Plasmid/pcDNA3; Plasmid/PGL3; Plasmid/PRL; Plasmid/dCas9; Retrovirus/pBABE
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/BEAS-2B; Human/Primary Human Airway Smooth Muscle; Human/Primary Human Airway Epithelial cells; Animal/3T3; Human/HK293; Human/Lenti-Pac™ 293Ta packaging cell line; Human/A549
Animal Use: No
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: N/A

Risk Assessment/Discussion:

Dr. Gerber is a new PI to UK and has submitted an IBC protocol entitled *Epigenetic and transcriptional and mechanisms in ex vivo and cultured cell models of lung disease airway*. Dr. Gerber's laboratory studies lung inflammation and disease and seeks to understand the function of

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transcription factors in regulating downstream pathways and how genetic variant impact these processes. They will utilize a number of viral and non-viral methods to modify expression of transcription factors such as ELF3, EHF, N3RC1, GRHL2, FOXA1, FOXA2 and TP63. Lentivirus and Retrovirus vectors will be packaged using a 2nd generation packaging system at BSL2+ containment. They will not be concentrating lentivirus or retrovirus. Adenovirus, obtained pre-packaged from an outside vendor, will also be utilized to transduce cells. All viral vector work will be done using BSL2+ containment. Target genes will also be knocked out via Cas9 or overexpressed via pCDNA based plasmid. Dr. Gerber's laboratory will also obtain tissues from patients with lung diseases or healthy controls to establish primary cell cultures. Genetically modified cells will be utilized for flow cytometry or sorting in the Flow Cytometry and Cell Sorting Facility in HKRB.

IBC Discussion & Vote:

The protocol IBC-25-143 (version 8.0) was approved pending minor modifications as listed below:

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RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Vector Information Table: Please ensure all vectors in use are listed in this table. For instance, adenovirus, lentivirus, and retrovirus vectors are all in use, but the only viral vector entry in this table is for retrovirus.

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Viral Vector Information table: An entry for each viral vector in use must be made in this table. Only adenovirus is listed here, but there is no entry for lentivirus or retrovirus. Additionally, all fields must be completed. Only one entry per distinct viral vector backbone is necessary in this table.

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Gene Information table: Please add FOXA1 and FOXA2 to the table. Ensure the table entries are congruent with the information discussed in the SCIENTIFIC SUMMARY.

SCIENTIFIC SUMMARY: Please add secondary containment for live cell line transport to and from the lab and flow cytometry core facility.

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Carol Pickett initiated the motion. Yadi Wu seconded the motion. All IBC members present (12) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Douglas Katz
IBC Protocol Number: IBC-25-150
Protocol Title: KB801-01: A Phase 1/2, Multicenter, Double-Masked, Placebo-Controlled Study of KB801 in Subjects with Stage 2 or 3 Neurotrophic Keratitis
Protocol Type: New
Amendment To: N/A

APPROVED

Applicable Guidelines & Regulations: NIH Guidelines Section III-C-1, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), OSHA 29 CFR 1910.1030, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9
Maximum Containment Level: Biological Safety Level 2 (BSL2)
Primary Reviewers: D. Harrison, T. Chambers, B. Nelson

Brief Project Overview:

This research study is being sponsored Krystal Biotech, Inc. (the "Sponsor"), to learn about the safety (to see if there are side effects) and efficacy (to see if there are signs that the study drug is working) of KB801, an investigational gene therapy for the treatment of corneal (eye) damage due to Neurotrophic Keratitis (NK). KB801 works by delivering two copies of a gene to the body so that specific proteins can be made. The genes will be carried and delivered by a genetically modified herpes simplex virus type 1 (HSV-1). It simply acts as a vehicle to deliver genes to your cells. Additionally, the genes that are delivered do not affect or change a person's own DNA or cause disease. The goal of such therapy is to heal corneal damage in people with NK. An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA). This study is the first use of the study drug in human study participants.Unmodified HSV-1 is the virus that causes cold sores and can lead to NK. About two out of every three people have HSV-1, but many are unaware of it because it does not typically cause any symptoms. In KB801, the parts of the virus that cause cold sores and NK are taken out. This means the virus cannot harm cells and spread to other parts of the body by making copies of itself. It simply acts as a vehicle to deliver copies of NGF genes to the cells. Other drugs using the same HSV-1 viral delivery vehicle have been used in previous investigational studies with no concerning side effects. One of these drugs, called B-VEC (Vyjuvek®), has been approved by the FDA to treat a skin disorder called Dysmorphic Epidermolysis Bullosa (DEB). Additionally, one patient under a compassionate use program received an ophthalmic (eye drop) form of B-VEC after eye surgery and has had no bad side effects associated with the drug after weekly long-term use.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Use of viral vectors, Human Clinical Trial, Use of Human Source Material(s)
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: NGF (beta Nerve Growth Factor)/Human/Growth Factor/Expression/Human Research Participants/KB801; proNGF (precursor Nerve Growth Factor)/Human/Growth Factor/Expression/Human Research Participants/KB801
Vector(s) [Vector Category/Vector Technical Name]: Herpes Simplex Virus (HSV)/KB801 (herpes simplex virus type 1 based vector)
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: N/A
Animal Use: No
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of

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Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: N/A

Risk Assessment/Discussion:

Dr. Katz has submitted a new IBC protocol for a clinical study for safety and efficacy of KB801, an investigational gene therapy for the treatment of corneal damage due to Neurotrophic Keratitis (NK). KB801 is a genetically modified herpes simplex virus type 1 vector designed to deliver functional, full-length human nerve growth factor (NGF). KB801 is designed to be directly applied to the corneal surface via topical administration. The HSV-1 vector backbone has been rendered replication-incompetent via deletion of both copies of the essential viral Immediate Early (IE) gene ICP4. In addition, IE gene ICP22 was also deleted to further diminish potential for cytotoxic effect. The HSV-1 backbone of KB801 is the same used for an FDA approved product, beremagene geperpavec-svdt. Manufacturing for KB801 is based on the same platform. Enrolled study participants or their delegate will be trained to self-administer KB801 at home after the first study visit for a duration of 8 weeks. Study participants are also provided with disposable gloves, biohazardous waste container, disinfectant, alcohol pads, sterile gauze, and other materials used to safely administer KB801 at home and clean and disinfect surfaces after use and in the event of a spill. Biohazardous waste collected at home will be brought back to the study site clinic for disposal. Investigational product is tested for replication-competent virus in a non-complementing cell line prior to release, as well as sterility, titer, identify, and other parameters. Blood and urine samples will be collected from study participants, packaged and shipped back to the study sponsor for further processing. At UK, 3 patients will be enrolled over 2 years.

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IBC Discussion & Vote:

Arthur Hunt and Maria Landron left the meeting at 12:50pm during discussion of Dr. Katz's IBC protocol

The protocol IBC-25-150 (version 6.0) was approved pending resubmission and review by primary reviewers, requested modifications listed below:

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RECOMBINANT and/or SYNTHETIC NUCLEIC ACIDS – Source/Nature of Nucleic Acid: Please make a selection under "The following apply to this research:".

DISINFECTANTS, EMERGENCY RESPONSE, TRANSPORT, WASTE – Off Campus Work: Please select "Yes" when asked "Will any work with biohazardous materials described in this registration take place off of University of Kentucky owned properties?" to reflect home administration of study agent.

DISINFECTANTS, EMERGENCY RESPONSE, TRANSPORT, WASTE – Waste: Please update this section to reflect waste returned to study site for disposal.

SCIENTIFIC SUMMARY-

1. Please provide a few sentences discussing the potential effects of over expressed NGF in unintended tissues and recipients. What risks are posed to immunocompromised individuals, children, and the elderly in case of accidental exposure to the study agent?

2. Please clarify if waste containers will be shipped for disposal, or if they will be returned to the study site by the patient?
3. Patient Administration Guide - The verbiage "a virucidal agent such as 70% isopropyl alcohol (provided), 6% hydrogen peroxide or <0.4% ammonium chloride" is used in the guide and summary. Please specifically state the disinfectant to be used during patient/delegate training, and what will be provided at the UK study site.
4. Patient Administration Guide – Please clarify at what specific steps PPE disposal and handwashing will be conducted in the Patient Administration Guide.
5. Please specify what information will be documented for patient/delegate training and approval, to qualify for home administration. Will this documentation include the date, time, and acknowledgement of understanding for this training?
6. The committee suggests a training video be offered in addition to written instructions for patient/delegate self-administration. Alternatively, administration for the small number of patients enrolled at the UK study site could be conducted on campus in the UK Advanced Eye Care Clinic, negating the need for self-administration off campus.

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Douglas Harrison initiated the motion. Thomas Chambers seconded the motion. All IBC members present (10) voted in favor of the motion.

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Conflicts of Interest: None

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Renewals

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PI: Olivier Thibault
IBC Protocol Number: IBC-25-141
Protocol Title: Constitutively active insulin receptors in the brain of rodents
Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-4, NIH Guidelines Section III-E-1, NIH Guidelines Section III-F-8, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), OSHA 29 CFR 1910.1030, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, NIH Guidelines Section III-D-1
Maximum Containment Level: Animal Biological Safety Level 1 (ABSL1), Biological Safety Level 2 - Enhanced (BSL2+)
Primary Reviewers: C. Haughton, B. Nelson, Y. Wu

Brief Project Overview:

Our lab investigates the role of insulin receptors in different cell types in the brain of mice. Clinical data indicate insulin delivery to the brain (e.g., intranasal) improves cognition in aging and Alzheimer's disease patients, however, the mechanisms underlying these benefits are not yet clear. The role of reducing insulin receptors (knock out) in different cell types will also be studied for impact on several cognitive and gait functions. Our overall goal is to better understand the links

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between diabetes, insulin signaling, obesity and brain aging and AD with a focus on ameliorating cognition and gait.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Creation of viral vectors, DNA/RNA isolation/purification, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Use of viral vectors, Bacterial culture, Cell culture, Use of Human Source Material(s)
Transport: Yes
Materials Transported: Animals, Biohazardous Materials
Infectious Agent(s)/Natural Host(s): N/A
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: Insulin receptor Beta Subunit/Human/Hormone receptor/Expression in cells and animals/Rodents; cultured cells/AAV; GFP/Synthetic/tracking/Expression in cells and animals/Rodents; cultured cells/AAV; PercevalHR, ATP:ADP nanosensor/Synthetic/Reporter/Expression in cells and animals/Rodents - AAV; Cultured cells – lentivirus/AAV , lenti; GFAP/Synthetic/Restriction/Expression in cells and animals/Rodents; cultured cells/AAV; Cre-recombinase/Synthetic/Knockout of floxed insulin receptor gene/Expression in cells and animals/Rodents; cultured cells/AAV; GCaMP8f/Synthetic/Reporter for calcium (green)/Expression in cells and animals/Rodents; cultured cells/AAV; Peredox, NAD:NADH nanosensor/Synthetic/Reporter/Expression in cells and animals/Rodents; cultured cells/AAV; jRCaMP/Synthetic/Reporter for calcium (red)/Expression in cells and animals/Rodents; cultured cells/AAV; PHP.eB/Synthetic/Tracking/Targeting/Expression in cells and animals/Rodents; cultured cells/AAV; Luciferase/Synthetic/Reporter/Expression in cells and animals/Rodents; cultured cells/AAV; nLightG, nanosensor (green)/Synthetic/Reporter/Expression in cells and animals/Rodents; cultured cells/AAV; ChRmine/Synthetic/Reporter/ activator/Expression in cells and animals/Rodents; cultured cells/AAV
Vector(s) [Vector Category/Vector Technical Name]: Adeno-Associated Virus (AAV)/pZac2.1 gfaABC1D-cyto-GCaMP6f/; Adeno-Associated Virus (AAV)/AAV5.GfaABC1D.LCK.GCaMP6f.SV40/; Lentivirus/Lentivirus-PercevalHR Plasmid-HumanUbiquitinC Promotor/; Adeno-Associated Virus (AAV)/AAV-plasmid.PercevalHR-GFAP promotor/; Adeno-Associated Virus (AAV)/pAAV.GFAP.ER-GCaMP6f/; Adeno-Associated Virus (AAV)/AAV-Gfa104-hIRbeta-HA/; Adeno-Associated Virus (AAV)/AAV-Gfa104-Cl-6xHIS-GCaMP8f-WPRE-SV40/; Adeno-Associated Virus (AAV)/pAAV-GfaABC1D-Peredox-mCherry/; Adeno-Associated Virus (AAV)/AAV-GfaABC1D-Cre-4x6T/; Adeno-Associated Virus (AAV)/pAAV-Syn-NES-jRCaMP1a-WPRE-SV40 /; Adeno-Associated Virus (AAV)/PHP.eB/; Adeno-Associated Virus (AAV)/pAAV-hSyn1-nLightG/; Adeno-Associated Virus (AAV)/AAV-Gfa104-Luc-SV40/; Adeno-Associated Virus (AAV)/pAAV-Gfa104-ChRmine-mScarlet
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Animal/PC12 cells; Animal/Hippocampal cell cultures; Animal/Dorsal Root Ganglion cultures (DRGs)
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Viral Vector - Adeno-Associated Virus (AAV)/intracranial injection/anesthesia/ABSL1 /Lab coat, Disposable gloves, Eye protection, Surgical mask, Head cover, Surgical gown/ABSL1/No; Mouse/Viral Vector - Adeno-Associated Virus (AAV)/fat pad injection/anesthesia/ABSL1/Lab coat, Disposable gloves, Eye protection, Surgical

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mask, Head cover, Surgical gown/ABSL1/No; Mouse/Viral Vector - Adeno-Associated Virus (AAV)/retro-orbital/anesthesia/ABSL1/Lab coat, Disposable gloves, Eye protection, Surgical mask, Head cover, Surgical gown/ABSL1/No

Risk Assessment/Discussion:

Dr. Thibault has submitted a renewal of his IBC protocol entitled *Constitutively active insulin receptors in the brain of rodents*. Dr. Thibault's laboratory studies the role of calcium dysregulation in brain aging and Alzheimer's disease models. In this renewal, Dr. Thibault proposes to investigate the actions of overactive insulin receptors in the brain. Adeno-Associated Virus (AAV) vectors expressing calcium sensors, insulin receptors, GFP, Cre, PercevalHR, GAFP, Peredox, PHHP.eb, luciferase, nLightG, and ChRmine will be delivered into the brains of anesthetized mice. After administration of AAV, mice will be used for electrophysiology studies. There is brief reference to lentiviral work that is "not currently active" which should be removed. Dr. Thibault's laboratory also collaborates with Dr. Chris Norris to develop new AAV delivery methods using retro-orbital delivery of PHP.eb AAV. Three different AAVs expressing GCaMP8f, IR-beta, and Cre-recombinase will be delivered to mice via retro-orbital injection during craniotomy procedure. 4-6 weeks after, mice will undergo imaging. Animal work with AAV will be done using ABSL1 containment and housing. Personnel will wear lab coats, disposable gloves, and eye protection. Most of the genes expressed via AAV are reporter genes, and none of the genes expressed are known oncogenes or otherwise known to be hazardous. Dr. Thibault's current IBC protocol will expire on January 23, 2026.

IBC Discussion & Vote:

The protocol renewal IBC-25-141 (version 8.0) was approved pending minor modifications as listed below:

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GENERAL INFORMATION - Maximum Biosafety Level Required for Research: Since lentivirus vector work has been removed from the protocol, the biosafety level for the protocol can be changed from BSL2+ to BSL2.

ANIMAL RESEARCH – ANIMAL IACUC: Please update the IACUC number listed from 2022-4131 to 2022-4031

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Vector Details table: Please remove line three, “Lentivirus,” from the table.

RECOMBINANT and/or SYNTHETIC NUCELIC ACID MATERIALS – Under “Does your research involve the use of retrovirus and/or lentivirus vectors?”, please select “No”.

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Viral Vector Information table: Please remove line four, “Lentivirus,” from the table.

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Retrovirus/Lentivirus Information table: Please remove Lentivirus from the table.

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – Gene Information table: Please edit the Vector column of the third line referencing lentivirus as a vector.

RECOMBINANT and/or SYNTHETIC NUCLEIC ACID MATERIALS – RG2, 3, 4 Agents as Host-Vector Systems: Please change the answer from YES to NO.

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DISINFECTANTS, EMERGENCY RESPONSE, TRANSPORT, WASTE – TRANSPORT – Biohazardous Materials Transport Description: Please clarify if AAVs are transported to DLAR for injections and if so, add the details of the transport and container(s) used to the textbox.

LOCATIONS – Research Locations: Please clarify whether lentivirus stocks are still stored in the Medical Science Building, room MS-304. If no, please update.

SCIENTIFIC SUMMARY: Please remove all references to lentivirus.

NIH GUILDINES and OTHER APPLICABLE REGULATIONS: Please UNCHECK NIH Guidelines Section III-D-1.

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Brandy Nelson initiated the motion. Yadi Wu seconded the motion. All IBC members present (10) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Xia Liu
IBC Protocol Number: IBC-25-144
Protocol Title: The mechanism of cancer metastasis
Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-1, NIH Guidelines Section III-F-1, NIH Guidelines Section III-F-2, NIH Guidelines Section IV-B-7, OSHA Act of 1970 Clause 5(a)(1), OSHA 29 CFR 1910.1030, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+), Animal Biological Safety Level 2 (ABSL2)
Primary Reviewers: C. Haughton, Y. Wu, M. Landron

Brief Project Overview:

Breast cancer is the most frequent cancer among women in the United States. Among all the types of breast cancers, triple-negative breast cancers (TNBC), which are not stimulated to grow from exposure to hormones estrogen and progesterone and protein Her2, are more aggressive than other breast cancers and have fewer treatment options. Metastases, a stage of breast cancer where the tumor cells have released from the breast and travel to other organs in the body, are the cause of 90% of breast cancer deaths. Hence, there is an urgent need to better understand the mechanisms underlying TNBC metastasis, discover novel therapeutic targets, and develop novel effective treatments for this lethal disease. It's known that metastasis is a very inefficient process. One mechanism to explain this inefficiency is provided by the cancer stem cell (CSC) theory, which propose that only cells with CSC properties can establish metastasis. However, molecular mechanisms driving CSCs metastasize remain poorly understood, which has hampered the development of effective CSC-targeted anti-metastatic treatments. The goal of our research is to understand the mechanisms of TNBN metastasis and develop novel CSC-targeted therapeutic strategies to treat metastatic TNBC.

APPROVED

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Animal work (breeding, surgeries, etc.), Bacterial culture, Cell culture, Creation of viral vectors, DNA/RNA isolation/purification, Flow cytometry/Cell sorting, Genetics, Histology, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Proteomics, Transfection, Transformation, Use of Human Source Material(s), Use of viral vectors
Transport: Yes
Materials Transported: Animals, Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/ Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: eGFP/ Jellyfish/ tracking gene/ expression/ mouse and human cells/ lentiviral pFu-Luc2-eGFP;tdTomato/ Discosoma/ tracking gene/ expression/ mouse and human cells/ lentiviral pFU-Luc2-tdTomato;luciferase/ Firefly/ tracking gene/ expression/ mouse and human cells/ lentiviral pFU-Luc2-eGFP and pFu-Luc2-tdTOmato;ICAM1/ human and mouse/ membrane-bound protein/ knockdown/ mouse and human cells/ lentiCRISPR v2;CD36/ human and mouse/ membrane-bound protein/ knockdown/ mouse and human cells/ lentiCRISPR v2 and expression vector pcDNA3.1;CSF3/ mouse and human/ cytokine/ knockdown/ mouse and human cells/ lentiCRISPR V2;uPAR/ human and mouse/ membrane-bound protein/ knockdown/ mouse and human cells/ lentiCRISPR v2
Vector(s) [Vector Category/Vector Technical Name]: Plasmid/pcDNA3.1-eGFP/; Lentivirus/pFU-Luc2-eGFP/; Lentivirus/pFU-Luc2-tdTomato/; Lentivirus/lentiCRISPR V2/;

Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Animal/4T1/; Human/MDA-MB-231/; Animal/E0771/; Human/Primary breast cancer cells from established PDXs/; Human/HEK293/; Animal/G-CSF Overexpressing E0771/
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Cells - Human, genetically modified/Subcutaneous, Intravenous /Isoflurane anesthesia/ABSL2/Dedicated lab coat, disposable gloves, shoe covers, eye protection,etc/ABSL1/No/Animals administered cells transduced with 2nd generation lentivirus will be housed at ABSL2 housing for 72 hours post administration, after which they will be moved to ABSL1 housing; for cells transduced with 3rd generation lentivirus, cells will be washed a minimum of 3 times prior to administration to animals and then housed at ABSL1 housing. /; Mouse/Cells - Human, non-modified/Subcutaneous, Intravenous/Isoflurane anesthesia/ABSL2/Dedicated lab coat, disposable gloves, shoe covers, eye protection,etc/ABSL1/No/Animals administered cells transduced with 2nd generation lentivirus will be housed at ABSL2 housing for 72 hours post administration, after which they will be moved to ABSL1 housing; for cells transduced with 3rd generation lentivirus, cells will be washed a minimum of 3 times prior to administration to animals and then housed at ABSL1 housing. /; Mouse/Cells - Animal, genetically modified/Subcutaneous, Intravenous/Isoflurane anesthesia/ABSL2/Dedicated lab coat, disposable gloves, eye protection, etc/ABSL1/No/Animals administered cells transduced with 2nd generation lentivirus will be housed at ABSL2 housing for 72 hours post administration, after which they will be moved to ABSL1 housing; for cells transduced with 3rd generation

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lentivirus, cells will be washed a minimum of 3 times prior to administration to animals and then housed at ABSL1 housing.

Risk Assessment/Discussion:

Dr. Liu has submitted a renewal of their IBC protocol entitled *The mechanism of cancer metastasis*. Dr. Liu's laboratory specifically focuses on the study of triple-negative breast cancer (TNBC) metastasis and seeks to develop novel cancer stem cell (CSC) targeted therapies to treat metastatic TNBC. 2nd or 3rd generation lentivirus will be used to transduce breast cancer cells. Lentivirus will be used to generate luciferase labelled breast cancer cells and ICAM-1 and uPAR knockout cells via CRISPR-Cas9 that will be sorted in the Flow Cytometry Core facility and expanded for future experiments. All lentivirus work will be conducted using BSL2+ containment. Lentivirus transduced cells will be administered to anesthetized mice within a BSC. RCV testing will be completed for cells transduced with 2nd generation lentivirus. Mice will be subjected to downstream imaging. Additionally, human blood samples obtained from the BPTP SRF will be used to isolate neutrophils for downstream analysis. Isolated cells will be lysed via lysis buffer within the BSC, after which samples will be moved outside of BSC for further downstream analysis. Lentiviral work will be conducted using BSL2+ practices, including use of dedicated lab coat, disposable gloves, eye protection, and exclusive use of BSC. Tumor cells will be administered to mice using ABSL2 containment, after which mice will be housed at ABSL1. Dr. Liu's current IBC protocol will expire on January 3, 2026.

IBC Discussion & Vote:

The protocol renewal IBC-25-144 (version 9.0) was approved pending minor modifications as listed below:

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ANIMAL RESEARCH – Animals with Biohazards table: The Special Practices / Procedures for non-modified cells in the Animals with Biohazards table should not include the language about lentivirally transduced cells. Please update.

RECOMBINANT AND/OR SYNTHETIC NUCLEIC ACIDS – Gene Information table: Please add CD44 and FASN to the Gene Information table for congruency with IACUC 2019-3367 renewal.

SCIENTIFIC SUMMARY – The target genes CD36 and CSF3 are listed in the Gene Information table but are not explicitly described in the Scientific Summary. Please briefly describe the function and role of these gene targets in your research.

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Yadi Wu initiated the motion. Cheryl Haughton seconded the motion. All IBC members present (10) voted in favor of the motion.

*

Conflicts of Interest: None

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PI: Meifan Chen
IBC Protocol Number: IBC-25-149

APPROVED

Protocol Title: Neural repair after injury to the central nervous system
Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-4, NIH Guidelines Section III-E-1, NIH Guidelines Section III-F, UK Administrative Regulation 6.9, UK Administrative Regulation 6.3, OSHA Act of 1970 Clause 5(a)(1)
Maximum Containment Level: Biological Safety Level 1 (BSL1), Animal Biological Safety Level 1 (ABSL1)
Primary Reviewers: C. Haughton, M. Mendenhall, J. Smalle

Brief Project Overview:

Survivors of central nervous system (CNS) injury suffer from permanent disability largely due to the inability of injured CNS neurons to reconnect with their original targets. Our research seeks to identify genes that control the growth of nerve fibers (or axons) that form neural connections, with the eventual goal to design molecular therapy for neural repair. In order to test which genes control axon growth, we modify genes of interest using genetically-modified mice or virus-mediated gene manipulation in mice, then observe their effects on axon dynamics after CNS injury. Another use of AAV in our research is to visualize axons by virus-mediated expression of fluorescent proteins such as the green fluorescent protein.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Use of viral vectors, Transfection, PCR/qRT-PCR, Immunohistochemistry, Imaging/Microscopy, Histology, Flow cytometry/Cell sorting, DNA/RNA isolation/purification, Creation of viral vectors, Cell culture, Bacterial culture, Animal work (breeding, surgeries, etc.)
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): N/A
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: eGFP/ Aequorea victoria (jellyfish)fore/ fluorescence protein/ to fluorescently label transduced cells green/ Mouse, cells/ AAV;Cre/ P1 bacteriophage/ enzyme/ to delete or induce gene of interest in transduced cells/ Mouse, cells/ AAV;mCherry/ Discosoma sea anemones/ fluorescence protein/ to fluorescently label transduced cells red./ Mouse, cells/ AAV;MCT2/ Mus musculus/ transporter/ expression/ Mouse, cells/ AAV;PYGB/ Mus musculus/ enzyme/ expression/ Mouse, cells/ AAV;EYFP/ derived from GFP isolated from Aequorea victoria./ fluorescence protein/ to fluorescently label transduced cells / Mouse, cells/ AAV
Vector(s) [Vector Category/Vector Technical Name]: Adeno-Associated Virus (AAV)/pAAV.GFAP.eGFP.WPRE.hGH/; Adeno-Associated Virus (AAV)/pAAV.GFAP.Cre.WPRE.hGH/; Adeno-Associated Virus (AAV)/pAAV.CAG.ChR2.mCherry/; Adeno-Associated Virus (AAV)/pAAV.Syn.ChR2.EYFP/; Adeno-Associated Virus (AAV)/pAAV-hIBA1a-GFP-miR124T/; Adeno-Associated Virus (AAV)/pZac2.1-GfaABC1D-MCT2-Flag-mCherry/; Adeno-Associated Virus (AAV)/pZac2.1-GfaABC1D-PYGB-Flag/
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Animal/ primary neurons; Animal/primary astrocytes
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of

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Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Viral Vector - Adeno-Associated Virus (AAV)/intra-cortical injection, intra-spinal injection, or intravenous injection/under anesthesia or tail-vein restrainer/ABSL1/lab coat, double layers of gloves, goggles/ABSL1/No/AAV will be delivered into mice by one of the following routes: i) injection into cerebral cortex of the brain (intra-cortical) with animal under anesthesia, ii) injection into the spinal cord with animal under anesthesia, or iii) intravenous injection with animal in a tail vein restrainer.

Risk Assessment/Discussion:

Dr. Chen has submitted a renewal of her IBC protocol entitled *Neural repair after injury to the central nervous system*. Dr. Chen's laboratory seeks to identify the genes that control the growth of nerve fibers (or axons) that form neural connections. Their goal is to design molecular therapies for neural repair after CNS injury. Towards that aim, Dr. Chen's laboratory will induce gene deletion or expression in mice, perform CNS injury model surgery, and later label axons and follow their growth. Adeno-Associated Virus (AAV) vectors will be used to induce gene deletion/expression via Cre and label cells of the CNS via expression of fluorescent proteins. Dr. Chen's laboratory does not package AAV, but purchases ready to use AAV vectors from outside vendors. Work with AAV will be done at BSL1/ABSL1. AAV will be administered to mice via the brain or spinal cord of anesthetized mice or intravenously while the animal is securely held in a restraint device. Mouse tissues will be utilized for histological analysis. Cells transduced with AAVs will be used for flow cytometry and other downstream analysis after cell fixation or inactivation via lysis. Dr. Chen's current IBC protocol will expire on December 19, 2026.

IBC Discussion & Vote:

The protocol renewal IBC-25-149 (version 9.0) was approved pending minor modifications as listed below:

*

SCIENTIFIC SUMMARY –

1. Please correct the name of E. coli strain from “5-alpha E. coli strain” to “DH5alpha E. coli strain.”
2. Briefly describe the function of the AAV transgenes being used in this study and potential risks of accidental exposure to personnel.

*

Michael Mendenhall initiated the motion. Cheryl Haughton seconded the motion. All IBC members present (11) voted in favor of the motion.

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Conflicts of Interest: None

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PI: David Burgess
IBC Protocol Number: IBC-25-153
Protocol Title: B22-4115: Evaluation of gram negative and gram positive bacterial resistance mechanisms

APPROVED

Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: UK Administrative Regulation 6.9, UK Administrative Regulation 6.3, OSHA Act of 1970 Clause 5(a)(1), NIH Guidelines Section IV-B-7
Maximum Containment Level: Biological Safety Level 2 (BSL2)
Primary Reviewers: C. Pickett, C. Shaffer, M. Landron

Brief Project Overview:

Antimicrobial resistance is a growing problem in every community and healthcare facility. Our laboratory evaluates antibiotics ability to inhibit or kill gram-positive (e.g. Staphylococcus aureus) and gram-negative bacteria (e.g., Acinetobacter spp., Escherichia coli, Enterobacter spp., Klebsiella spp., and Pseudomonas aeruginosa) that has been isolated from patients utilizing standard microbiology techniques. We will perform in vitro susceptibility testing according to national guidelines outlined by the Clinical Laboratory Standards Institute. These tests can be performed using traditional microbiology assays such as broth microdilution, agar dilution, and agar diffusion.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Bacterial culture, Use of Human Source Material(s), Use of infectious agents, PCR/qRT-PCR, DNA/RNA isolation/purification, Propagation of infectious agents
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human; Staphylococcus aureus (RG2-bacteria)/Mammals; Pseudomonas aeruginosa (RG2-bacteria)/Mammals; Listeria spp. (RG2-bacteria),(Listeriosis)/Mammals, birds, fish, crustaceans and insects; Klebsiella spp. (RG2-bacteria)/Mammals; Escherichia coli (RG2-bacteria)/ Humans; Enterococcus faecalis (RG2-bacteria)/ Mammals, Birds; Enterococcus faecium (RG2-bacteria)/Mammals, Birds; Enterobacter spp. (RG2-bacteria)/plants, humans and animals (most common in lower GI tract of humans and animals); Campylobacter jejuni (RG2-bacteria)/Humans, animals and birds; Acinetobacter spp. (RG2-bacteria)/Humans
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: N/A
Vector(s) [Vector Category/Vector Technical Name]: N/A
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: N/A
Animal Use: No
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: N/A

Risk Assessment/Discussion:

Dr. Burgess has submitted a renewal of his IBC protocol entitled *Evaluation of gram negative and gram-positive bacterial resistance mechanisms*. Dr. Burgess' laboratory studies the antimicrobial resistance of RG2 bacterial pathogens obtained from the UK Medical Center Microbiology Laboratory. Specifically, the following clinical patient isolates will be identified as resistant by the UK Medical Center Microbiology laboratory and send to our lab: Staphylococus aureus,

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Escherichia coli, Psuedomonas aeruginosa, Acinetobacter spp., Enterobacter spp., Klebsiella spp., Campylobacter jejuni, Enterococcus faecalis, Enterococcus faecium and Listeria Spp.. Dr. Burgess laboratory also purchases strains from ATCC to use as controls. Bacteria will be culture and propagated using BSL2 containment within a BSC. Personnel will wear a dedicated or disposable lab coat, safety glasses, and eye protection. They will evaluate the effectiveness of antimicrobial combinations on resistant bacteria using checkerboard and time-kill assays. Dr. Burgess' laboratory will also obtain human blood from UK clinical patients enrolled in a study to investigate fixed dosing of daptomycin. Plasma will be removed and aliquoted for later analysis by a collaborator at University of Michigan. Dr. Burgess maintains records of all bacterial pathogens received and their unique antibiotic resistant traits that will be made available to treating physicians in the event of an accidental exposure. The bacterial pathogens obtained are not genetically modified in any way. Dr. Burgess' current IBC protocol will expire on December 14, 2026.

IBC Discussion & Vote:

Maria Landron returned to the meeting at 1:11pm during discussion of Dr. Burgess' IBC protocol

The protocol renewal IBC-25-153 (version 8.0) was approved.

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Carrie Shaffer initiated the motion. Carol Pickett seconded the motion. All IBC members present (11) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Chintan Kikani
IBC Protocol Number: IBC-25-154
Protocol Title: Epigenetic control of muscle stem cell function by PASK-Wdr5 signaling
Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-1, NIH Guidelines Section III-F, NIH Guidelines Section III-F-1, NIH Guidelines Section III-F-2, NIH Guidelines Section III-F-3, NIH Guidelines Section III-F-4, NIH Guidelines Section III-F-5, NIH Guidelines Section III-F-6, OSHA Act of 1970 Clause 5(a)(1), OSHA 29 CFR 1910.1030, UK Administrative Regulation 6.3, UK Administrative Regulation 6.9, NIH Guidelines Section IV-B-7
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+), Animal Biological Safety Level 1 (ABSL1)
Primary Reviewers: C. Haughton, B. Nelson, T. Chambers

Brief Project Overview:

My laboratory investigates how stem cells communicate with their surrounding tissues. We are working on a hypothesis that stem cell function in the tissue context is governed by signaling cues that regulate transcriptional activities within the stem cells. As the quality and quantity of the

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signaling cues changes due to various factors, stem cell functions are also adjusted to maintain a proper tissue function.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Bacterial culture, Cell culture, Immunohistochemistry, Histology, Flow Cytometry/Cell Sorting, Proteomics, Imaging/Microscopy, Genetics, DNA/RNA isolation/purification, Transfection, Transformation, PCR/qRT-PCR, Use of Viral Vectors, Creation of Viral Vectors, Animal work (breeding, surgeries, etc.), Use of Human Source Material(s)
Transport: Yes
Materials Transported: Animals, Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: PASK/Human/Metabolic Enzyme, Cell Cycle/Expression/Human or Mouse Cells/Retroviral, Lentiviral/; GFP/A.victorius/tracking gene/tracking/human or mouse cells/retrovirus, Lentiviral/; Slc25a39/human, mouse/metabolic enzyme/expression/human or mouse cells/retrovirus/; Slc25a39/Synthesized/Metabolic enzyme/Targeted knock-down of Slc25a39 during muscle regeneration in mice. /mouse/siRNA-based delivery/
Vector(s) [Vector Category/Vector Technical Name]: Naked nucleic acid/siRNA duplex; Retrovirus/pBabe-Puro; Retrovirus/pQCXIP; Lentivirus/p-Lenti-Blast; Lentovirus/p-Lenti-Puro
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/HEK293T; Animal/C2C12; Animal/Muscle Stem Cells; Human/HCT119; Animal/MEF; Human/A431; Human/HepG2
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Mouse/Naked Nucleic Acid-r/sDNA/Intramuscular/Anesthesia/ABSL1/Gloves, Lab Coat, Eye Protection/ABSL1/No

Risk Assessment/Discussion:

Dr. Kikani has submitted a renewal of his IBC protocol entitled *Epigenetic control of muscle stem cell function by PASK-Wdr5 signaling*. Dr. Kikani's laboratory seeks to understand how stem cells communicate with surrounding tissues. Specifically, they are working to understand the role of PAS domain-containing Kinase (PASK) in regulating stem cell function in response to metabolic stimuli. 2nd generation retrovirus and 3rd generation lentivirus will be used for in vitro experiments for the overexpression of PASK, Slc25a39, or GFP (retrovirus) and overexpression or shRNA-mediated knockdown of PASK or Slc25a39. Retrovirus and lentivirus will be produced using BSL2+ containment practices and procedures. Transduced cells will be used for histology and immunohistochemistry, flow cytometry (both live and fixed), and proteomics. Recombinant proteins will be generated in E. coli BL21 cells, including PASK, Wdr5, Slc25a39, or MyoD, and purified using affinity chromatography for downstream assays including protein-protein interaction mapping, kinase assays, etc. Dr. Kikani's laboratory will also transfect mammalian cells to express PASK, Slc25a39, or GFP for localization studies. Short-term knockdown of PASK or Slc25a39 will be accomplished via siRNA. Mice will be used for transplantation of muscle stem cells and IM injection of siRNA targeting Slc25a39. siRNA will be obtained from commercial sources. Mice will undergo muscle injury, after which siRNA will be delivered to anesthetized mice. Animal work will

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be performed at ABSL1 containment and housing. Animals will be euthanized, and muscle tissues harvest for qRT-PCR, western blotting, histological analysis, etc. Dr. Kikani's current IBC protocol will expire January 9, 2026.

IBC Discussion & Vote:

The protocol renewal IBC-25-154 (version 9.0) was approved pending minor modifications as listed below:

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DISINFECTANTS, EMERGENCY RESPONSE, TRANSPORT, WASTE – Biohazardous Materials Transport Description: If recombinant/synthetic nucleic acids are being transported from the lab to animal facilities for administration, please update the biohazardous materials transport description to include these details.

LOCATIONS – Research Locations Table:

1. The Scientific Summary states that animals are euthanized in THM 314, but this space is not listed as a research location. Please update the Research Locations table to include this space if it is being used for your work.
2. The IACUC protocol lists BBSRB/BioPharm complex for animal housing and procedures. As this is a renewal protocol, please specifically list the room locations assigned for housing and the typical procedure room utilized in the Research Locations table.
3. Please ensure all descriptions of locations throughout the IBC protocol are congruent.

SCIENTIFIC SUMMARY -

1. It is unclear if recombinant/synthetic nucleic acids will be transported from the lab to animal facilities administration. Please clarify and include details on how these biohazards are transported, if applicable.
2. In Paragraph 5: the “gain-of-function" verbiage suggests that the expression of PASK is truly novel for these cell types. Please modify this statement to say “restoration of gene function” studies are being performed.
3. Biosafety considerations are outlined for inadvertent exposure to siRNA complexes but not described for retrovirus/lentivirus constructs. Please briefly describe potential risks of exposure to these viral vector constructs.
4. The statement “Employees who have not been vaccinated or received a recent HBV vaccination will be tested for immunological status against HBV and, if necessary, offered immunization and be evaluated by a healthcare professional following an exposure incident.” should be removed. UHS or other providers should be determining the exposure response protocol.
5. In the paragraph starting with “Procedure: No survival surgeries or virus work is planned on our experimental cohorts…”, there is not enough information in this section on locations, transplantation, or associated biohazards. Please include more information to convey a clear flow of materials or remove any procedures that do not explicitly include biohazardous materials.
6. It is unclear where animal studies take place and what procedures occur in the lab vs DLAR. Please specify.

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7. There is insufficient discussion of the human sourced material being used in these studies. For example, while some descriptions of HEK 293T cells are noted, there is no discussion of the human colon carcinoma (HCT119), human adenocarcinoma (A431), or human hepatocellular carcinoma (HepG2) cells listed in the Cell Lines section of the protocol. Please review and update to include descriptions of work with these human cells or tissues.

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Thomas Chambers initiated the motion. Brandy Nelson seconded the motion. All IBC members present (11) voted in favor of the motion.

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Conflicts of Interest: None

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PI: Yekaterina Zaytseva
IBC Protocol Number: IBC-25-156
Protocol Title: The role of fatty acid metabolism in colorectal cancer
Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-1, UK Administrative Regulation 6.9, UK Administrative Regulation 6.3, OSHA 29 CFR 1910.1030, OSHA Act of 1970 Clause 5(a)(1), NIH Guidelines Section IV-B-7
Maximum Containment Level: Biological Safety Level 2 - Enhanced (BSL2+), Animal Biological Safety Level 2 (ABSL2)
Primary Reviewers: C. Haughton, D. Harrison, C. Pickett

Brief Project Overview:

Metabolic reprogramming is a hallmark of cancer, controlling various aspects of malignant development and progression. Activation of de novo lipogenesis in cancer cells, which is increasingly recognized as one of the characteristics of aggressive cancers, correlates with a poorer prognosis and shorter disease-free survival in many tumor types including colorectal cancer (CRC). Fatty Acid Synthase (FASN), a key enzyme of de novo lipid synthesis, is upregulated in many cancers including CRC; increased FASN activity is associated with decreased survival and increased disease recurrence. Recently, a first-in-class, oral FASN inhibitor (TVB-2640) entered a Phase I clinical trial (3V2640-CLIN-002) in solid tumor patients demonstrating a favorable tolerability profile with no significant adverse events; however, tumor characteristics that would indicate responsiveness to FASN inhibition are not fully understood. The purpose of our studies is: (i) to determine the effect of novel, selective and reversible FASN inhibitors on tumor growth as a monotherapy and in combination with other therapeutic agents in CRC xenografts and CRC patient-derived xenografts (PDXs); (ii) to identify potential biomarkers associated with CRC responsiveness to FASN inhibition; (iii) investigate the effect of sphingolipid metabolism on metastasis in CRC; and (iv) delineate the role of FASN in initiation of CRC using transgenic mouse models and established from them organoid cultures.

Summary of Biohazard Materials & Manipulations:

APPROVED

Manipulations Planned: Animal work (breeding, surgeries, etc.), Cell culture, Histology, Imaging/Microscopy, Immunohistochemistry, PCR/qRT-PCR, Use of infectious agents, Use of viral vectors
Transport: Yes
Materials Transported: Biohazardous Materials
Infectious Agent(s)/Natural Host(s): Human Sourced Materials (RG2-cells, tissues, bodily fluids, organs, etc.)/Human
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: FASN (FAtty Acid Synthase)/ Human/ metabolic enzyme/ shRNA knockdown in cell culture/ Human cells/ lentivirus;SPHK1 (Sphingosine Kinase 1)/ Human/ metabolic enzyme/ shRNA knockdown in cell culture; expression in cell culture/ Human cells/ lentivirus;SPHK2 (Sphingosine Kinase 2)/ Human/ metabolic enzyme/ shRNA knockdown in cell culture; expression in cell culture/ Human cells/ lentivirus;CD36/ Human/ cell adhesion/ shRNA knockdown in cell culture; expression in cell culture/ Human cells/ lentivirus;GFP/ Jellyfish/ tracking/ expression/ human cells, mouse cells/ lentivirus;Luciferase/ Firefly/ tracking/ expression/ human cells, mouse cells/ lentivirus;GFPT-1/ Human/ Metabolic enzyme/ shRNA knockdown in cell culture/ Human cells/ lentivirus;OGT/ Human/ Metabolic enzyme/ shRNA knockdown in cell culture/ Human cells/ lentivirus
Vector(s) [Vector Category/Vector Technical Name]: Lentivirus/pLKO.1/; Lentivirus/pLKO.1 FASNshRNA/; Lentivirus/shRNA plasmid-SPHK1shRNA/; Lentivirus/shRNA plasmid-SPHK2shRNA/; Lentivirus/shRNA plasmid control/; Lentivirus/shRNA plasmid - CD36/; Lentivirus/pLX_TRC317 SPHK1 & SPHK2/; Lentivirus/pLenti-C-Myc-DDK-P2A-Puro - CD36 & control/; Lentivirus/Mission shRNA lentivirus - Human GFPT-1 & OGT/; Lentivirus/Mission shRNA lentivirus - Human CD166
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: Human/HCT116/; Human/HT29/; Human/pt 93/; Human/pt 130/; Human/pt 2387/; Human/pt 2377 PT/; Human/pt 2377LM/; Human/HCT116 NTC/; Human/HT29 NTC/; Human/HCT116 FASN shRNA/; Human/HT29 FASN shRNA/; Human/HCT116 CD36 shRNA/; Human/HT29 CD36 shRNA/; Animal/CT26/; Animal/MC38/; Human/HCT116 CD166sh RNA/; Animal/CT26 FASN shRNA/; Animal/CT26 CD36 shRNA/; Animal/CT26 SPHK1 shRNA/; Animal/CT26 SPHK2 shRNA/; Animal/MC38 FASN shRNA/; Animal/MC38 CD36 shRNA/; Animal/MC38 SPHK1 shRNA/; Animal/MC38 SPHK2 shRNA/; Human/HCT116 CD36 over expression
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Tissue - Human (ex. PDX tumor tissue)/xenografts/anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Tissues are transferred in a sealed secondary container to the animal facility and implanted subcutaneously into NSG mice which are anesthetized as described in IACUC protocol. Subcutaneous implantation of tumor tissue will be done in a designated BSC in DLAR ABSL2 procedure roomas described in IACUC protocol.//; Mouse/Cells - Human, genetically modified/xenografts /anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Cells are transferred in a sealed secondary container to the animal facility and implanted subcutaneously into Nu/Nu mice which are anesthetized as described in IACUC protocol. Cell injections will be done in a designated BSC in DLAR ABSL2 procedure room as described in IACUC protocol./; Mouse/Cells - Human,

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genetically modified/tail vein injections/anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Cells are transferred in a sealed secondary container to the animal facility and injected of tail vein of Nu/Nu mice which are anesthetized as described in IACUC protocol. Cell injections will be done in a designated BSC in DLAR ABSL2 procedure room as described in IACUC protocol./; Mouse/Cells - Human, genetically modified/splenic injections/anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Cells are transferred in a sealed secondary container to the animal facility and injected of tail vein of Nu/Nu mice which are anesthetized as described in IACUC protocol. Cell injections will be done in a designated BSC in DLAR ABSL2 procedure room as described in IACUC protocol./; Mouse/Cells - Animal, non-modified/xenografts/anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Mouse cells are transferred in a sealed secondary container to the animal facility and injected subcutaneously into BALB/c wild type mice which are anesthetized as described in IACUC protocol. Injections will be done in a designated BSC in DLAR ABSL2 procedure rooms described in IACUC protocol./; Mouse/Cells - Human, genetically modified/cecum injections/anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Cells are transferred in a sealed secondary container to the animal facility and injected in cecum of Nu/Nu mice which are anesthetized as described in IACUC protocol. Cell injections will be done in a designated BSC in DLAR ABSL2 procedure room as described in IACUC protocol./; Mouse/Cells - Animal, genetically modified/xenografts/anesthesia/ABSL2/gloves, cover, eye protection/ABSL2/No/Mouse cells are transferred in a sealed secondary container to the animal facility and injected subcutaneously into BALB/c wild type mice which are anesthetized as described in IACUC protocol.We will inject Balb/c mice with mouse cell lines CT26 and MC38 with Luciferase reporter and altered expression of FASN, CD36, SPHK1 and SPHK2 genes. Injections will be done in a designated BSC in DLAR ABSL2 procedure rooms described in IACUC protocol.

Risk Assessment/Discussion:

Dr. Zaytseva has submitted a renewal of her IBC protocol entitled *The role of fatty acid metabolism in colorectal cancer*. Dr. Zaytseva's lab is particularly interested in Fatty Acid Synthase (FASN) and its role in metastasis in colorectal cancer. Dr. Zaytseva's laboratory will utilize 3rd generation lentiviral constructs purchased from 3rd party vendors to establish overexpression and knockout cell lines for administration to animals. Many of the transgenes to be expressed are implicated in cancer cell survival and metastasis. All work with lentiviral vectors will be performed using BSL2+ containment practices. No sharps will be utilized with lentivirus, greatly minimizing the risk of accidental exposure. After selection and expansion of lentivirus transduced cells (minimum 4-weeks), cells are administered to mice within a BSC in DLAR ABSL2 procedure room. Cells will be injected via tail vein or into spleen or cecum for study of lung and liver metastasis. Mice are restrained in a restraint device or anesthetized, greatly minimizing the risk of accidental needlestick. Dr. Zaytseva's laboratory will also utilize human and mouse organoid cultures and PDX models. Human colon tissues obtained from CRC patients at UK hospital will be obtained from the Biospecimen Core for implantation into mice or biobanking. BSL2/ABSL2 containment practices will be utilized for work with human tissues. Anesthetized animals will be subcutaneously implanted with tumor tissues and randomized into different treatment groups. Implantation will be done within a BSC in DLAR ABSL2 procedure room. Mice will be observed, tumor measurements taken, and tissues collected for biobanking or protein/RNA analysis. Dr. Zaytseva's current IBC protocol will expire on January 3, 2026.

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IBC Discussion & Vote:

The protocol renewal IBC-25-156 (version 9.0) was approved pending minor modifications as listed below:

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ANIMALS WITH BIOHAZARDS TABLE – IACUC 2019-3236 lists ABSL1 housing for animals administered human tumor tissues and cells. Please update to ensure congruency.

SCIENTIFIC SUMMARY – Confocal microscopy is mentioned in the Scientific Summary, but it is unclear if this is being performed in the lab or a core facility on campus. Please indicate where confocal microscopy work takes place, whether the cells/tissues are fixed or unfixed, and describe how the materials are transported between locations.

*

Douglas Harrison initiated the motion. Carol Pickett seconded the motion. All IBC members present (11) voted in favor of the motion.

*

Conflicts of Interest: None

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PI: Warren Alilain
IBC Protocol Number: IBC-25-162
Protocol Title: Understanding the role of FGF receptors in recovery after spinal cord injury
Protocol Type: Renewal
Amendment To: N/A
Applicable Guidelines & Regulations: NIH Guidelines Section III-D-4, NIH Guidelines Section IV-B-7, UK Administrative Regulation 6.9, UK Administrative Regulation 6.3, OSHA Act of 1970 Clause 5(a)(1), NIH Guidelines Section III-E-1, NIH Guidelines Section III-F-1
Maximum Containment Level: Biological Safety Level 1 (BSL1), Animal Biological Safety Level 1 (ABSL1)
Primary Reviewers: C. Haughton, A. Pinto, M. Mendenhall

Brief Project Overview:

We have previously shown that activating FGF receptors can improve recovery after SCI and that inhibition slow recovery. However we do not know which cells are responsible for these responses. This protocol will utilize AAV vectors to perform cell specific knockdown.

Summary of Biohazard Materials & Manipulations:

Manipulations Planned: Use of viral vectors, Animal work (breeding, surgeries, etc.), Imaging/Microscopy, Immunohistochemistry, Histology
Transport: Yes
Materials Transported: Animals
Infectious Agent(s)/Natural Host(s): N/A
Source & Nature of Inserted Nucleic Acid(s) [Gene Information/Gene Source/Gene Category/Use of Construct/Host(s)/Vector(s)]: enhanced green fluorescent protein (EGFP)/ NEB Stable/ tracking

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gene/ expression/ rat/ AAV;mCherry/ NEB Stable/ tracking gene/ expression/ rat/ AAV;rat FGFR3/ NEB Stable/ growth factor receptor/ knockdown/ rat/ AAV;rat FGFR4/ NEB Stable/ growth factor receptor/ knockdown/ rat/ AAV
Vector(s) [Vector Category/Vector Technical Name]: Adeno-Associated Virus (AAV)/AAV2-hSyn-EGFP/; Adeno-Associated Virus (AAV)/AAV2-hSyn-mCherry/; Adeno-Associated Virus (AAV)/AAV9-MBP-ratFGFR3-shRNA/; Adeno-Associated Virus (AAV)/AAV9-GFAP-ratFGFR3-shRNA/; Adeno-Associated Virus (AAV)/AAV9-GFAP-ratFGFR4-shRNA/; Adeno-Associated Virus (AAV)/AAV9-VE-cadherin (CDH5)-ratFGFR3-shRNA/
Cell line(s) Used [Cell Line Type/Cell Line Technical Name]: N/A
Animal Use: Yes
Materials introduced into Animals [Animal Host Species/Biohazardous Material/Route of Administration/Restraint/Animal Experimental Procedures/PPE/Animal Housing/Agent Shedding/Special Practices & Procedures]: Rat/Viral Vector - Adeno-Associated Virus (AAV)/intraspinal microinjection/anesthesia/ABSL1/sterile surgerical gloves, mask, gown/ABSL1/No/

Risk Assessment/Discussion:

Dr. Alilain has submitted a renewal of his IBC protocol entitled *Understanding the role of FGF receptors in recovery after spinal cord injury*. Dr. Alilain's laboratory has previously shown that activating FGF receptors can improve recovery after spinal cord injury, however it is unclear which cells are responsible for this response. They seek to utilize Adeno-Associated Virus (AAV) vectors to perform cell specific knockdown. AAVs will be purchased from commercial sources. AAVs expressing a fluorescent reporter or shRNA targeted to knock down fibroblast growth factor receptor 3 or 4 will be administered to anesthetized rats via injection. 21-70 days following injections, rats will be euthanized and tissues obtained to assess innervation of spinal neurons using fluorescence and confocal microscopy. CNS and other organs will be harvested, fixed, and sectioned for histological staining and immunohistochemical reactions. All animal work will be completed using ABSL1 containment and housing. Personnel will wear disposable gloves, mask, gown, and eye protection. Dr. Alilain's current IBC will expire on December 16, 2025.

IBC Discussion & Vote:

The protocol renewal IBC-25-162 (version 8.0) was approved pending minor modifications as listed below:

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RECOMBINANT AND/OR SYNTHETIC NUCLEIC ACIDS – Vector Information table: In the “Will DNA Integrate into the host genome?” column of the Vector Information table, the entry for “AAV9-GFAP-ratFGFR3-shRNA” is marked “Yes”; however, all of the other AAV entries are marked “No.” Please update for consistency.

SCIENTIFIC SUMMARY - Briefly describe the function of the AAV transgenes being used in this study and potential risks of accidental exposure to personnel.

*

Michael Mendenhall initiated the motion. Amelia Pinto seconded the motion. All IBC members present (11) voted in favor of the motion.

APPROVED

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Conflicts of Interest: None

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Incident Review

Nothing to report.

Protocol Issued Registration Numbers

Protocols issued registration numbers, including minor amendments. These protocols are exempt from IBC review and are registered with the UK Biological Safety Officer (BSO).

Venditto, Vincent, Venditto Lab Biosafety, Amendment, BSO, 12/02/25, IBC-25-33 (v.26.0)

Lane, Andrew, B23-4168: Environmental Systems Biochemistry, Amendment, BSO, 12/01/25, IBC-24-72 (v.15.0)

Satin, Jonathan, IBC-24-423 (formerly B21-3780-M2): Long-term Regulation of Cardiac Ion Channels / Cardioprotection, Amendment, BSO, 11/26/25, IBC-24-423 (v.35.0)

Nelson, Peter, Role of miRNA in neurodegenerative diseases, Amendment, BSO, 11/26/25, IBC-24-436 (v.31.0)

Staton, Michele, STOP Study, New, BSO, 11/25/25, IBC-25-155 (v.6.0)

Famulski, Jakub, Epithelial sheet fusion and periocular mesenchyme migration during zebrafish retinal morphogenesis., Amendment, BSO, 11/24/25, IBC-24-99 (v.31.0)

Pendergast, Julie, Misalignment of Circadian Rhythms, Amendment, BSO, 11/24/25, IBC-24-225 (v.23.0)

Morgan, Melissa, General Operations of the Food Microbiology Laboratory, Amendment, BSO, 11/24/25, IBC-24-34 (v.29.0)

Evers, B. Mark, Signaling pathways in the regulation of colon cancer metastasis, intestine differentiation, gut endocrine cell secretion, hepatic lipogenesis and pancreatic acinar cell aging., Amendment, BSO, 11/24/25, IBC-24-472 (v.42.0)

Schock, Elizabeth, Schock Lab-Biochem-IBC-2024, Amendment, BSO, 11/24/25, IBC-24-462 (v.25.0)

Nair, Girish, Inflammation and Fibrosis across the spectrum of lung disease, New, BSO, 11/24/25, IBC-25-129 (v.10.0)

Shaddox, Luciana, 1. Analysis of Host-Biofilm Interactions: A Novel Polymicrobial model 2: Evaluation of different risk factors on periodontal disease and caries 3: COVID-19 testing using Saliva and Nasal swabs 4. Analyze and characterize the oral microbiome in the presence COVID-19 in the Saliva and Dental plaque samples 5. Understanding the association between buprenorphine and oral health outcomes 6. Advancing Salivary Biomarker Development and Utility in Periodontitis 7. Targeting Health Disparities: Engineering Antimicrobial and Remineralizing

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Dental Resins for Therapeutic and Preventive Care in Underserved Communities, Amendment, BSO, 11/21/25, IBC-24-349 (v.55.0)

Li, Xiangan, The role of SR-BI in sepsis and in therapy-induced immune activation, Amendment, BSO, 11/21/25, IBC-24-96 (Version 21.0)

Wilson, Thad, AHA: Menopause-related vasomotor symptoms, New, BSO, 11/20/25, IBC-25-98 (v.10.0)

Li, Zhiguo, Enhancing the efficacy of cancer immunotherapy, Amendment, BSO, 11/20/25, IBC-24-41 (v.41.0)

Lucero, Diego, New Modulators of Lipoprotein Metabolism: From the liver to the vascular wall., Amendment, BSO, 11/19/25, IBC-25-97 (v20.0)

Wang, Wangxia, Mitochondrial Function and microRNA Regulation in Traumatic Brain Injury and Alzheimer's Disease, Amendment, BSO, 11/19/25, IBC-24-63 (v.47.0)

Morford, Lorri, University of Kentucky (UK) Center for the Biologic Basis of Oral/Systemic Diseases (CBBO/SD): Hereditary Genetics/Genomics Core 1. Prospective Investigation of External Apical Root Resorption (EARR) and Genetic Markers (IRB 09-0181-F6G/E-IRB 45268) 2. Combined Genetic and Cephalometric Analysis to Study Class III Malocclusion in Families From Brazil and Colombia (IRB 09-0398-F1V/E-IRB 45272) 3. Analysis of Genetic Variations Associated With Both Hypodontia (Naturally Missing Teeth) and Other Medical Conditions (IRB 10-0499-F6A/E-IRB 44209) 4. Genetics of Class III Malocclusion in US Caucasians (IRB 14-0446-F6A//E-IRB 45270) 5. Biosignatures of periodontitis: Effects of Diabetes and Methotrexate Anti-inflammatory Therapy (IRB 17-0439-F6A/E-IRB 44558), Amendment, BSO, 11/19/25, IBC-24-78 (v.29.0)

Yalniz, Fevzi, Autolus-OOS-EAP: Expanded Access Program (EAP) for Obecabtagene Autoleucel (obe-cel) Out-of-specification (OOS) in Adult Patients with Acute Lymphoblastic Leukemia (AUTO1-OS1), Amendment, BSO, 11/18/25, IBC-25-57

Fry, Christopher, Cellular regulators of skeletal muscle plasticity, Amendment, BSO, 11/14/25, IBC-25-74 (v.22.0)

Norris, Christopher, Neurovascular pathology in Alzheimer's disease and vascular cognitive impairment, Amendment, BSO, 11/14/25, IBC-25-124 (v.15.0)

Pennypacker, Keith, Blood and Clot Thrombectomy Registry and Collaboration, Amendment, BSO, 11/13/25, IBC-25-16 (v.16.0)

Grady, Martha, Biological Film Adhesion and Deformaibility, Amendment, BSO, 11/10/25, IBC-24-465 (v.21.0)

Graf, Gregory, Lipid metabolism in obesity and its related diseases, Amendment, BSO, 11/10/25, IBC-24-93 (v. 37.0)

Zhu, Qingzhang, Adipocyte function in metabolism, inflammation and fibrosis during obesity, Amendment, BSO, 11/10/25, IBC-24-493 (v.36.0)

Campbell, Kenneth, Cellular level contractile function in human heart failure, Amendment, BSO, 11/06/25, IBC-24-482 (v.46.0)

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Morford, Lorri University of Kentucky (UK) Center for the Biologic Basis of Oral/Systemic Diseases (CBBO/SD): Hereditary Genetics/Genomics Core 1. Prospective Investigation of External Apical Root Resorption (EARR) and Genetic Markers (IRB 09-0181-F6G/E-IRB 45268) 2. Combined Genetic and Cephalometric Analysis to Study Class III Malocclusion in Families From Brazil and Colombia (IRB 09-0398-F1V/E-IRB 45272) 3. Analysis of Genetic Variations Associated With Both Hypodontia (Naturally Missing Teeth) and Other Medical Conditions (IRB 10-0499-F6A/E-IRB 44209) 4. Genetics of Class III Malocclusion in US Caucasians (IRB 14-0446-F6A//E-IRB 45270) 5. Biosignatures of periodontitis: Effects of Diabetes and Methotrexate Anti-inflammatory Therapy (IRB 17-0439-F6A/E-IRB 44558), Amendment, BSO, 11/05/25, IBC-24-78 (v.23.0)

Protocols Meeting Registration Requirements

Protocols that have been approved by the IBC pending minor modifications that have met approval requirements.

Alsiraj, Yasir, Role of the sex chromosome genes in aortopathies, Renewal, IBC, 12/02/25, IBC-25-135 (v.13.0)

Barrett, Terrence, Regulation of Intestinal Stem Cell Activation in Colitis, Renewal, IBC, 12/01/25, IBC-25-119 (v.12.0)

Gauthier, Nicole, B23-4118: Fusarium Disease Management on Hemp, Renewal, IBC, 11/25/25, IBC-25-127 (v.14.0)

Firestein, Bonnie, Regulation of Dendritic Morphology and Function by Cypin, the Main Guanine Deaminase, New, IBC, 11/19/25, IBC-25-104 (v.10.0)

Gensel, John, Lipid Biomarkers after Spinal Cord Injury, Amendment, IBC, 11/14/25, IBC-25-46 (v.24.0)

Cai, Weikang, Understanding astrocytes and microglia functions in neurological diseases., Amendment, IBC, 11/14/25, IBC-24-408 (v.70.0)

Miller, Anne-Frances, Enzymatic Redox Catalysis, Renewal, IBC, 11/12/25, IBC-25-134 (v.9.0)

Sullivan, Patrick, Platelet Bioenergetics after Traumatic Brain Injury, Amendment, IBC, 11/12/25, IBC-25-68 (v. 16.0)

Hao, Zhonglin 25-LUN-146-GPX (ONC-003): A Phase 1/2 Open-Label, Dose-Escalation and Clinical Response Study of Quaratusugene Ozeplasmid in Combination with Osimertinib in Patients with Advanced, EGFR-Mutant, Metastatic Non-Small Cell Lung Cancer who have Progressed after Treatment with Osimertinib, New, IBC, 11/10/25, IBC-25-109 (v.8.0)

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IBC Training

None. All current IBC members have completed training online via SciShield.

Adjournment

Douglas Harrison moved to adjourn the meeting at 1:32PM. Thomas Chambers seconded the motion. All members present [11] voted in favor.