

**COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION**

PROGRAM ANNOUNCEMENT/SOLICITATION NO./DUE DATE <b>NSF 21-506</b>		<input type="checkbox"/> Special Exception to Deadline Date Policy		FOR NSF USE ONLY	
FOR CONSIDERATION BY NSF ORGANIZATION UNIT(S) (Indicate the most specific unit known, i.e. program, division, etc.) <b>IOS - Physiol Mechs &amp; Biomechanics</b>				<b>NSF PROPOSAL NUMBER</b> <b>2114725</b>	
<b>DATE RECEIVED</b>	<b>NUMBER OF COPIES</b>	<b>DIVISION ASSIGNED</b>	<b>FUND CODE</b>	<b>UEI (Unique Entity Identifier)</b>	<b>FILE LOCATION</b>
01/04/2021	1	08090000 IOS	7658		
EMPLOYER IDENTIFICATION NUMBER (EIN) OR TAXPAYER IDENTIFICATION NUMBER (TIN) <b>150532082</b>		SHOW PREVIOUS AWARD NO. IF THIS IS <input type="checkbox"/> A RENEWAL <input type="checkbox"/> AN ACCOMPLISHMENT-BASED RENEWAL		IS THIS PROPOSAL BEING SUBMITTED TO ANOTHER FEDERAL AGENCY? (b) (4)	
NAME OF ORGANIZATION TO WHICH AWARD SHOULD BE MADE		ADDRESS OF AWARDEE ORGANIZATION, INCLUDING 9 DIGIT ZIP CODE			
AWARDEE ORGANIZATION CODE (IF KNOWN)					
NAME OF PRIMARY PLACE OF PERF <b>Cornell University</b>		ADDRESS OF PRIMARY PLACE OF PERF, INCLUDING 9 DIGIT ZIP CODE <b>373 Pine Tree Road, Ithaca, NY 14850-2820 US</b>			
IS AWARDEE ORGANIZATION (Check All That Apply)		<input type="checkbox"/> SMALL BUSINESS <input type="checkbox"/> FOR-PROFIT ORGANIZATION		<input type="checkbox"/> MINORITY BUSINESS <input type="checkbox"/> WOMAN-OWNED BUSINESS	
TITLE OF PROPOSED PROJECT <b>Collaborative Research: Revisiting the homeorhetic mechanisms of lactation: The role of ceramide</b>				<input type="checkbox"/> IF THIS IS A PRELIMINARY PROPOSAL THEN CHECK HERE	
REQUESTED AMOUNT \$ <b>1,021,609</b>		PROPOSED DURATION (1-60 MONTHS) <b>48</b> months		REQUESTED STARTING DATE <b>03/01/2021</b>	
				SHOW RELATED PRELIMINARY PROPOSAL NO. IF APPLICABLE	
THIS PROPOSAL INCLUDES ANY OF THE ITEMS LISTED BELOW					
<input checked="" type="checkbox"/> TYPE OF PROPOSAL <b>Research</b> <input checked="" type="checkbox"/> COLLABORATIVE STATUS <b>Collaborative from multiple organizations</b> <input type="checkbox"/> BEGINNING INVESTIGATOR <input type="checkbox"/> DISCLOSURE OF LOBBYING ACTIVITIES <input type="checkbox"/> PROPRIETARY & PRIVILEGED INFORMATION <input type="checkbox"/> HISTORIC PLACES <input checked="" type="checkbox"/> LIVE VERTEBRATE ANIMALS IACUC App. Date <b>PENDING</b> PHS Animal Welfare Assurance Number _____					
<input type="checkbox"/> HUMAN SUBJECTS Human Subjects Assurance Number _____ Exemption Subsection _____ or IRB App. Date _____ <input type="checkbox"/> FUNDING OF INT'L BRANCH CAMPUS OF U.S. IHE <input type="checkbox"/> FUNDING OF FOREIGN ORGANIZATION OR FOREIGN INDIVIDUAL <input type="checkbox"/> INTERNATIONAL ACTIVITIES: COUNTRY/COUNTRIES INVOLVED _____ <input type="checkbox"/> POTENTIAL LIFE SCIENCES DUAL USE RESEARCH OF CONCERN <input type="checkbox"/> OFF-CAMPUS OR OFF-SITE RESEARCH					
PI/DP DEPARTMENT <b>Animal Science</b>		PI/DP POSTAL ADDRESS <b>373 Pine Tree Road</b>			
PI/DP FAX NUMBER		<b>Ithaca, NY 148502820</b> <b>US</b>			
NAMES (TYPED)	High Degree	Yr of Degree	Telephone Number	EmailAddress	
PI/DP NAME <b>Joseph W McFadden</b>	<b>DPhil</b>	(b) (6)	<b>607-255-9941</b>	<b>jwm43@cornell.edu</b>	
CO-PI/DP					
CO-PI/DP					
CO-PI/DP					
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**CERTIFICATION PAGE****Certification for Authorized Organizational Representative(or Equivalent)**

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**Certification Regarding Conflict of Interest**

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**Certification Regarding Flood Hazard Insurance**

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- (1) community in which that area is located participates in the national flood insurance program; and
- (2) building (and any related equipment) is covered by adequate flood insurance.

By electronically signing the Certification Pages, the Authorized Organizational Representative (or equivalent) located in FEMA-designated special flood hazard areas is certifying that adequate flood insurance has been or will be obtained in the following situations:

- (1) for NSF awards for the construction of a building or facility, regardless of the dollar amount of the award; and
- (2) for other NSF awards when more than \$25,000 has been budgeted in the proposal for repair, alteration or improvement (construction) of a building or facility.

**Certification Regarding Responsible and Ethical Conduct of Research (RECR)**

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**Certification Regarding Organizational Support**

By electronically signing the Certification Pages, the Authorized Organizational Representative (or equivalent) is certifying that there is organizational support for the proposal as required by Section 526 of the America COMPETES Reauthorization Act of 2010. This support extends to the portion of the proposal developed to satisfy the Broader Impacts Review Criterion as well as the Intellectual Merit Review Criterion, and any additional review criteria specified in the solicitation. Organizational support will be made available, as described in the proposal, in order to address the broader impacts and intellectual merit activities to be undertaken.

**Certification Regarding Dual Use Research of Concern**

By electronically signing the certification pages, the Authorized Organizational Representative is certifying that the organization will be or is in compliance with all aspects of the United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern.

**Certification Requirement Specified in the William M.(Mac)Thornberry National Defense Authorization Act for Fiscal Year 2021, Section 223(a)(1) (42 USC 6605(a)(1))**

By electronically signing the Certification Pages, the Authorized Organizational Representative is certifying that each individual employed by the organization and identified on the proposal as senior personnel has been made aware of the certification requirements identified in the William M.( Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, Section 223(a)(1) (42 USC 6605(a)(1)).

**Certification Regarding Safe and Inclusive Working Environments for Off-Campus or Off-Site Research**

(This certification applies only to proposals in which data/information/samples are being collected off-campus or off-site, such as fieldwork and research activities on vessels and aircraft.)

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AUTHORIZED ORGANIZATIONAL REPRESENTATIVE		SIGNATURE		DATE	
NAME <b>Elizabeth Estabrook</b>		<b>Electronic Signature</b>		<b>Jan 04 2021 04:38 PM</b>	
TELEPHONE NUMBER <b>607-255-2782</b>	EMAIL ADDRESS <b>ee54@cornell.edu</b>		FAX NUMBER		

Submitted/PI: Amanda N Davis /Proposal No: 2114726

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DATE RECEIVED <b>01/04/2021</b>	NUMBER OF COPIES <b>1</b>	DIVISION ASSIGNED <b>08090000 IOS</b>	FUND CODE <b>7658</b>	UEI(Unique Entity Identifier)	FILE LOCATION
EMPLOYER IDENTIFICATION NUMBER (EIN) OR TAXPAYER IDENTIFICATION NUMBER (TIN) <b>146013200</b>		SHOW PREVIOUS AWARD NO. IF THIS IS <input type="checkbox"/> A RENEWAL <input type="checkbox"/> AN ACCOMPLISHMENT-BASED RENEWAL		IS THIS PROPOSAL BEING SUBMITTED TO ANOTHER FEDERAL AGENCY? <b>(b) (4)</b>	
NAME OF ORGANIZATION TO WHICH AWARD SHOULD BE MADE			ADDRESS OF AWARDEE ORGANIZATION, INCLUDING 9 DIGIT ZIP CODE		
AWARDEE ORGANIZATION CODE (IF KNOWN)					
NAME OF PRIMARY PLACE OF PERF <b>SUNY College at Cortland</b>			ADDRESS OF PRIMARY PLACE OF PERF, INCLUDING 9 DIGIT ZIP CODE <b>Research Foundation for SUNY, PO Box 2000 Cortland, NY 13045-2000 US</b>		
IS AWARDEE ORGANIZATION (Check All That Apply)		<input type="checkbox"/> SMALL BUSINESS <input type="checkbox"/> FOR-PROFIT ORGANIZATION		<input type="checkbox"/> MINORITY BUSINESS <input type="checkbox"/> WOMAN-OWNED BUSINESS	
TITLE OF PROPOSED PROJECT <b>Collaborative Research: Revisiting the homeorhetic mechanisms of lactation: The role of ceramide</b>					SHOW LETTER OF INTENT ID IF APPLICABLE
REQUESTED AMOUNT \$ <b>200,806</b>	PROPOSED DURATION (1-60 MONTHS) <b>48</b> months	REQUESTED STARTING DATE <b>08/01/2021</b>		SHOW RELATED PRELIMINARY PROPOSAL NO. IF APPLICABLE	
THIS PROPOSAL INCLUDES ANY OF THE ITEMS LISTED BELOW					
<input checked="" type="checkbox"/> TYPE OF PROPOSAL <b>Research</b> <input checked="" type="checkbox"/> COLLABORATIVE STATUS <b>Collaborative from multiple organizations</b> <input type="checkbox"/> BEGINNING INVESTIGATOR <input type="checkbox"/> DISCLOSURE OF LOBBYING ACTIVITIES <input type="checkbox"/> PROPRIETARY & PRIVILEGED INFORMATION <input type="checkbox"/> HISTORIC PLACES <input type="checkbox"/> LIVE VERTEBRATE ANIMALS IACUC App. Date _____ PHS Animal Welfare Assurance Number _____			<input type="checkbox"/> HUMAN SUBJECTS Human Subjects Assurance Number _____ Exemption Subsection _____ or IRB App. Date _____ <input type="checkbox"/> FUNDING OF INT'L BRANCH CAMPUS OF U.S. IHE <input type="checkbox"/> FUNDING OF FOREIGN ORGANIZATION OR FOREIGN INDIVIDUAL <input type="checkbox"/> INTERNATIONAL ACTIVITIES: COUNTRY/COUNTRIES INVOLVED _____ <input type="checkbox"/> POTENTIAL LIFE SCIENCES DUAL USE RESEARCH OF CONCERN <input type="checkbox"/> OFF-CAMPUS OR OFF-SITE RESEARCH		
PI/DP DEPARTMENT <b>Biological Sciences</b>		PI/DP POSTAL ADDRESS <b>10 SUNY Cortland 231 Bowers Hall Cortland, NY 13045 US</b>			
PI/DP FAX NUMBER					
NAMES( TYPED)	High Degree	Yr of Degree	Telephone Number	EmailAddress	
PI/DP NAME <b>Amanda N Davis</b>	<b>PhD</b>	<b>(b) (6)</b>	<b>607-753-2720</b>	<b>amanda.davis@cortland.edu</b>	
CO-PI/DP					
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AUTHORIZED ORGANIZATIONAL REPRESENTATIVE		SIGNATURE	DATE
NAME <b>Thomas Frank</b>		<b>Electronic Signature</b>	<b>Jan 04 2021 05:21 PM</b>
TELEPHONE NUMBER <b>607-753-2020</b>	EMAIL ADDRESS <b>thomas.frank@cortland.edu</b>	FAX NUMBER	



## PROJECT SUMMARY

### Overview:

Homeorhesis refers to chronic and coordinated adaptations that mammals utilize to support changing physiological states such as lactation. A fundamental homeorhetic mechanism that develops to support the onset of lactation is the reduction of insulin sensitivity in skeletal muscle, which spares glucose for the mammary synthesis of milk. This adaptation favors the survival of the neonate. Classic studies infer that maternal insulin resistance is mediated by pituitary somatotropin (ST) and uncoupling of the somatotrophic axis (i.e., reduced insulin-like growth factor-1 secretion from liver). We propose that this traditional view of homeorhesis is incomplete, and we have identified ceramide as a potential mediator of ST action, glucose partitioning, and lactation. McFadden and Davis have produced a large body of work to state the hypothesis that ceramide causes insulin resistance to support milk synthesis in mammals. The described work represents a new chapter in homeorhesis theory that challenges our understanding of ST and the synchronized metabolic adaptations that develop for mammals to produce milk. For Aim 1, we will determine whether the inhibition of ceramide synthesis increases insulin sensitivity to decrease milk production. The role of ST will be considered. For Aim 2, we will assess whether the induction of ceramide synthesis is a means to decrease insulin sensitivity to sustain milk production. For Aim 3, the mechanisms of insulin antagonism that involve ceramide in myotubes will be delineated. We will leverage experience utilizing lipidomics and studying insulin kinetics, as well as a justified *Ovis aries* (sheep) model to define the role of ceramide during mammalian lactation. The application of validated pharmacological and recombinant technologies that modulate ceramide synthesis will be employed. The proposed research will describe the homeorhetic role of ceramide as a means to better define the maternal phenomena that drive lactation in mammals.

### Intellectual Merit:

Our work challenges homeorhesis theory by questioning whether maternal insulin resistance involves other mechanisms besides uncoupling of the somatotrophic axis and whether ST promotes glucose partitioning and lactation via ceramide-dependent mechanisms. A physiological axis involving coordinated adaptations in adipose and liver that work in unison to generate ceramide, downregulate muscle insulin signaling, and spare glucose for milk synthesis will be defined. Exposing ceramide as a homeorhetic control will be revealed in lactating sheep which has long been a preferred model system for studies of homeorhesis. The breakthrough would warrant the reconsideration of homeorhesis during other physiological states including gestation. Undeniably, the seminal discovery of ST as a promoter of lactation was of major significance. So much so, recombinant bovine ST (rbST) biotechnology was developed to enhance milk production efficiency and lower environmental impact. We conceive the possibility that the discovery of ceramide as a mediator of ST action and insulin resistance holds similar transformative potential for agricultural industries to develop new approaches to control nutrient utilization as means to promote lactation and growth for food production.

### Broader Impacts:

Due to global population growth and climate change, our ability to secure food and feed the world is threatened. Increasing the efficiency of nutrient use in domestic food animals may be a means to increase global food security and reduce environmental impact. Since public understanding of livestock production efficiency may influence our ability to implement novel strategies (e.g., biotechnology) to achieve this goal, the proposed research will be integrated within an education and outreach plan focused on improving the public's literacy of this science. Our plan includes developing a course where undergraduates will learn about science communication using a "Ruminant On This" podcast platform that will simultaneously educate the public about sustainable animal agriculture and biotechnology. Over 60 students and faculty from Cornell and SUNY Cortland will complete public science communication training led by Youth Program Coordinators at the Sciencenter hands-on museum. At the Sciencenter, Cornell students and SUNY Cortland NSF REU researchers will apply what they learned about sustainable food animal production to teach the public, using hands-on learning interactive experiences, how animal production efficiency and biotechnology are means to feed our world and save our planet. (b) (4)

## TABLE OF CONTENTS

For font size and page formatting specifications, see PAPPG section II.B.2.

	Total No. of Pages	Page No.* (Optional)*
Cover Sheet for Proposal to the National Science Foundation		
Project Summary (not to exceed 1 page)	<u>1</u>	<u>          </u>
Table of Contents	<u>1</u>	<u>          </u>
Project Description (Including Results from Prior NSF Support) (not to exceed 15 pages) ( <b>Exceed only if allowed by a specific program announcement/solicitation or if approved in advance by the appropriate NSF Assistant Director or designee</b> )	<u>15</u>	<u>          </u>
References Cited	<u>7</u>	<u>          </u>
Biographical Sketches (Not to exceed 3 pages each)	<u>4</u>	<u>          </u>
Budget (Plus up to 5 pages of budget justification. For proposals that contain subaward(s), each subaward must include a separate budget justification of no more than 5 pages)	<u>13</u>	<u>          </u>
Current and Pending Support	<u>17</u>	<u>          </u>
Facilities, Equipment and Other Resources	<u>3</u>	<u>          </u>
Special Information/Supplementary Documents (Data Management Plan, Mentoring Plan and Other Supplementary Documents)	<u>17</u>	<u>          </u>
Appendix (List below. ) ( <b>Include only if allowed by a specific program announcement/solicitation or if approved in advance by the appropriate NSF Assistant Director or designee</b> )	<u>          </u>	<u>          </u>
Appendix Items:		

\*Proposers may select any numbering mechanism for the proposal. The entire proposal however, must be paginated. Complete both columns only if the proposal is numbered consecutively.

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References Cited	_____	_____
Biographical Sketches (Not to exceed 3 pages each)	2	_____
Budget (Plus up to 5 pages of budget justification. For proposals that contain subaward(s), each subaward must include a separate budget justification of no more than 5 pages)	7	_____
	12	_____
Current and Pending Support	_____	_____
	2	_____
Facilities, Equipment and Other Resources	_____	_____
	1	_____
Special Information/Supplementary Documents (Data Management Plan, Mentoring Plan and Other Supplementary Documents)	_____	_____
Appendix (List below. ) ( <b>Include only if allowed by a specific program announcement/solicitation or if approved in advance by the appropriate NSF Assistant Director or designee</b> )	_____	_____
Appendix Items:		

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the public to enhance literacy with regard to increasing food animal production efficiency and the use of biotechnology to sustainably address the future gap in global food production<sup>[23, 24]</sup>. Our proposed program

(b) (4)

(b) (4)

## **B. Current background: Homeorhesis and lactation**

### **B.1. Glucose partitioning and somatotropin**

Homeorhesis is defined as the orchestration of metabolic priorities to support a physiological state. The homeorhesis concept is applied to describe maternal adaptations that influence lactation in mammals as summarized in Table 1. Features of homeorhesis include (i) chronic regulation over hours and days, (ii) coordinated action across tissues, and (iii) alterations in tissue response to homeostatic signals. A hallmark example of homeorhetic function to support lactation is the observed decrease in insulin sensitivity (i.e., an elevated insulin concentration to achieve half-maximal response) and responsiveness (i.e., a reduction in maximal response at a given insulin concentration)<sup>[2, 3, 25]</sup>. A reduction in insulin action and glucose utilization is observed in skeletal muscle of early lactation mammals<sup>[3, 26]</sup>. The consequence is the prioritization of glucose for the mammary synthesis of lactose in an insulin-independent manner<sup>[1]</sup>. This is of importance because lactose is the osmotic regulator of milk volume, which may demand up to 70% of total glucose turnover at the onset of lactation<sup>[2, 7]</sup>. These demands for glucose are supported by (i) increased hepatic gluconeogenesis, ketogenesis, and glycogenolysis, (ii) enhanced blood flow to the mammary gland, (iii) reductions in muscle protein synthesis and adipose lipogenesis, (iv) heightened lipolysis and plasma FA supply, and (v) increased utilization of amino acids and FA for maternal oxidative metabolism. Collectively, these responses are attributed to reductions in insulin effectiveness as well as glucose-stimulated pancreatic insulin secretion<sup>[2, 4, 25, 27]</sup>. The net effect is the sparing of glucose for preferential utilization by the mammary gland, a mechanism mammals employ to provide offspring nutrients in the form of milk.

A key endocrine hormone and homeorhetic control of lactation is somatotropin (ST)<sup>[1, 6, 28]</sup>. Circulating ST concentrations are greatest during the copious milk production of early lactation<sup>[27, 29, 30]</sup>. As lactation advances, serum ST and milk production decline<sup>[25, 29, 31]</sup>. Relevant to this proposal, ST enhances hepatic gluconeogenesis as well as adipose tissue lipolysis by inhibiting the anti-lipolytic actions of adenosine<sup>[4, 32, 33]</sup>. The elevation in circulating FA develops with the inactivation of skeletal muscle insulin signaling

**Table 1.** Homeorhetic mechanisms of lactation.

Stage of lactation:	Early	Late
Plasma ST and ceramide levels, lipolysis, hepatic FA uptake and ceramide synthesis, LDL and skeletal muscle ceramide levels, glucose sparing and milk synthesis, neonate demand for milk.	HIGH	LOW
Plasma IGF1 levels, maternal skeletal muscle insulin sensitivity (insulin-stimulated glucose uptake/AKT activation), lipogenesis	LOW	HIGH



downstream of insulin receptor binding<sup>[3, 34]</sup>. The ability of ST to inhibit muscle glucose utilization likely involves the inactivation of insulin receptor substrate-1 (IRS1), phosphatidylinositol 3-kinase (PI3K), and protein kinase B (i.e., AKT) to downregulate the translocation of glucose transporter-4 to the plasma membrane<sup>[35-38]</sup>. These early lactation outcomes develop with the uncoupling of the somatotrophic axis during a catabolic state of negative energy balance<sup>[1, 27, 39]</sup>. Specifically, lactation initiates with a decrease in the release of insulin-like growth factor-1 (i.e., IGF1) from the liver. Because insulin-like growth factor-1 is an insulin-sensitizer<sup>[40, 41]</sup>, low circulating insulin-like growth factor-1 concentrations during early lactation may contribute to the development of insulin resistance. Additionally, the reduction in serum insulin-like growth factor-1 concentrations prevents feedback on the pituitary that normally inhibits ST secretion. The ability of ST and an uncoupled somatotrophic axis to inhibit insulin-stimulated glucose utilization is the explanation for increased milk synthesis. As lactation progresses and positive energy balance is restored, the somatotrophic axis is re-coupled, insulin sensitivity returns, and milk synthesis declines.

## B.2. Ceramide and insulin resistance

Ceramides are bioactive sphingolipids and mediators of insulin resistance<sup>[15, 16, 42]</sup>. Initially, biomedical research demonstrated that lipotoxicity favors the partitioning of saturated FA (e.g., palmitic acid) away from mitochondrial oxidation and towards serine palmitoyltransferase (SPT)-controlled de novo ceramide synthesis<sup>[43, 44]</sup> (Figure 1). The consensus is that hepatic de novo ceramide synthesis and the accumulation of liver-derived ceramide within low-density lipoproteins (LDL) mediates insulin resistance in muscle<sup>[16, 45, 46]</sup>. Specifically, ceramide is transferred from LDL and inserted into the plasma membrane of myotubes where it aggregates within caveolin-enriched microdomains (CEM)<sup>[45, 47-49]</sup>. In turn, ceramide inhibits insulin-stimulated AKT phosphorylation (i.e., activation) and glucose transporter-4 translocation<sup>[15, 49-51]</sup>. These downstream outcomes of insulin antagonism involve the activation of protein kinase C- $\zeta$  (PKC $\zeta$ ), phosphatase and tensin homolog (PTEN), and protein phosphatase 2A (PP2A) by ceramide (Figure 2)<sup>[43, 49, 51]</sup>. The ceramide-dependent CEM-recruitment of PKC $\zeta$  promotes the phosphorylation of AKT at Thr-34 to inhibit function<sup>[52]</sup>. The activation of PTEN transforms phosphatidylinositol triphosphate to phosphatidylinositol biphosphate (PIP2) to downregulate PI3K signal transduction, and PP2A dephosphorylates AKT at Thr-308 and Ser-473. Ceramide is also likely to deactivate IRS1 via Ser-307 phosphorylation<sup>[53]</sup>. **Our work suggests that mammals utilize ceramide-dependent mechanisms to cause insulin resistance and spare glucose for milk synthesis.** This new branch of homeorhesis theory is detailed by McFadden and Rico<sup>[13]</sup> and challenges the concept that the downregulation of insulin signaling by ceramide is only associated with metabolic disease. Instead, ceramide control may represent an intrinsic physiological process mammals employ to support lactation.

The focus on ceramide during early lactation is warranted because this life stage is characterized by heightened body fat mobilization, hepatic FA uptake, and impaired insulin signaling that includes the inactivation of AKT<sup>[11, 12, 37]</sup>. First, we demonstrated that ceramide accumulates in plasma, liver, and skeletal muscle during the transition from gestation to lactation in healthy ruminants<sup>[11, 12]</sup>. Second, we have consistently observed a positive relationship between plasma ceramide accrual, circulating FA, and insulin

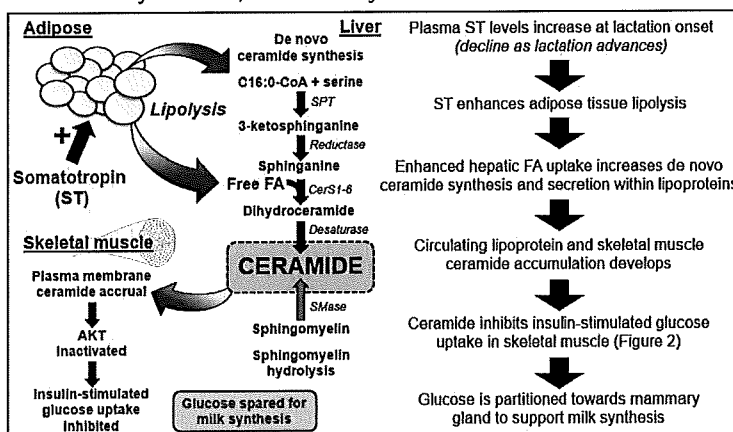


Figure 1: Model of working hypothesis.

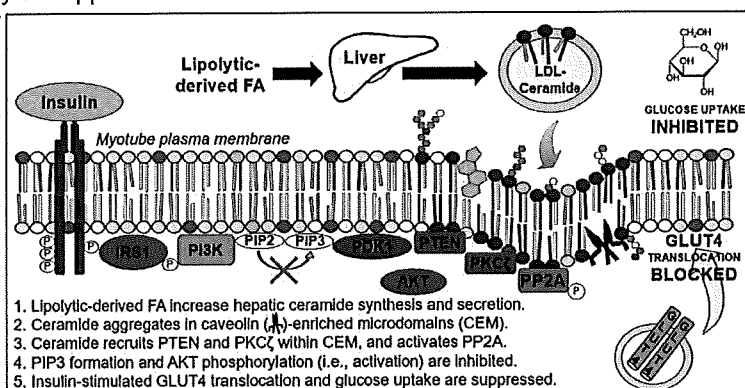


Figure 2: Proposed mechanisms of ceramide action. Potential ability of ceramide to inhibit IRS1 not shown.

resistance<sup>[11, 12, 17, 20]</sup>. If ceramide spares glucose, then ceramide accrual should correlate with enhanced milk yield. To test this question, we fed lactating animals palmitic acid which repeatedly induced ceramide synthesis in positive association with elevated milk yield<sup>[13, 20, 21, 54]</sup>. Consistent with the proposed theory, we observed gradual reductions in circulating ceramide with the progression of lactation and disappearance of homeorhetic mechanisms<sup>[20]</sup>. [REDACTED] (b) (4) [REDACTED] we were also able to confirm that recombinant ST administration increases circulating ceramide concentrations in ruminants in association with increased milk yield and impaired glucose tolerance<sup>[14]</sup>. Therefore, ***the hypothesis is that ST enhances adipose lipolysis, which increases hepatic ceramide synthesis and secretion within lipoproteins. In turn, lipoprotein ceramide inhibits skeletal muscle insulin sensitivity to spare glucose for the mammary synthesis of milk.*** Within this adipose-liver-muscle axis (Figure 1), ceramide represents a biochemical signal that spares glucose for mammary utilization when maternal energy stores are available (i.e., adipose triacylglycerol that can be mobilized during negative energy balance). This theory is supported by the reality that milk synthesis is greatest during early lactation when plasma ST concentrations, circulating FA and ceramides, and maternal insulin resistance are greatest<sup>[6, 11, 12, 27]</sup>. During late lactation, when positive energy balance is restored, plasma ST and ceramide concentrations are low, lipogenesis is favored, insulin sensitivity prevails, and milk synthesis is reduced<sup>[1, 20, 25]</sup>. Our focus on skeletal muscle is merited because this tissue is the main mammalian tissue for glucose utilization and therefore the major site of differences in insulin sensitivity<sup>[3, 55, 56]</sup>, whereas glucose uptake in adipose is minimal (especially during early lactation). Unraveling the role of ceramide within the context of ST action and skeletal muscle insulin resistance will represent a paradigm-shift in our understanding of how mammals adapt to support milk synthesis and neonatal development.

### C. Intellectual merit

Lactation occurs in all post-pregnancy female mammals<sup>[57]</sup>, and the homeorhetic actions that support lactation represent maternal metabolic processes that are essential for the development and survival of offspring. Revisiting the homeorhetic mechanisms of lactation by defining the role of sphingolipids like ceramide has the potential to represent a major breakthrough in our understanding of how mammals adapt to produce milk. The discovery of ST as a homeorhetic promoter of lactation was revolutionary. So much so, that rbST was developed to increase milk production efficiency (i.e., milk produced/energy consumed), in commercial operations. Therefore, it is conceivable that the discovery of ceramide as a novel homeorhetic control holds similar transformative potential. Although our focus is on lactation, the discovery of ceramide as an intrinsic control of glucose partitioning may also have meaning during other physiological states such as gestation. Fetal growth is greatest during late gestation, and maternal skeletal muscle insulin resistance spares glucose for uterine tissue growth and fetal development. These adaptations are likely due to the actions of placental lactogen and ST which promote lipolysis. Therefore, ceramide may mediate the ability of placental lactogen and ST to promote maternal insulin resistance and fetal growth. Because the mechanistic cause of maternal insulin resistance by ST has represented the major gap in knowledge in homeorthesis theory, the discovery of ceramide as the "missing link" would be of major significance. The outcome would have an influential impact on agricultural industries because ceramide would represent a new target to modulate nutrient partitioning for food production. This is of importance when you consider the societal acceptance of recombinant ST has declined, food security is challenged by climate change and population growth<sup>[23, 58-61]</sup>, and ceramide synthesis is responsive to changes in nutrition<sup>[18, 20]</sup>.

#### C.1. Increases in milk production efficiency decreases environmental impact

Milk production per ewe or cow has increased more than 3-fold over the past century. [REDACTED] (b) (4) [REDACTED] Every animal has a certain energy requirement to maintain vital functions and survive, which has stayed constant over time. Livestock of today use a greater proportion of energy consumed to make milk (i.e., efficiency is milk produced/energy consumed). Cattle are able to divert more energy like glucose to milk because of enhanced genetics, nutrition, and management. Indeed, modern high-producing ruminants have a phenotype characterized by a more pronounced uncoupled somatotrophic axis (i.e., high serum ST and lower insulin-like growth factor-1 concentrations) and greater insulin resistance<sup>[63, 64]</sup>. We have shown that cattle that produce more milk have higher circulating ceramide concentrations<sup>[13, 20]</sup>. Modern improvements in milk production efficiency mean that the production of milk requires fewer resources than farming of the past (as reviewed by Capper et al. [62]). For example, modern farming requires 77% less lactating animals and feed, 90% less land, and 65% less water to produce an equivalent amount of milk as compared to 1944. In addition, the production of an equivalent amount of milk



today generates 57% less methane and contributes to a 63% smaller carbon footprint, as compared to 1944. These advancements are often overlooked by the consumer. One argument is that pasture-based farming is more efficient (i.e., sustainable) than conventional farming (where cows are fed corn-based diets in barns). However, grazing livestock reduces milk production efficiency, and requires 25% more animals and 30% more land, and contributes 13% more carbon dioxide equivalents (i.e., global warming potential). One approach that can increase milk production efficiency is the use of recombinant ST. It is estimated that conventional farming would require 12% fewer cows, 8% less feed and land, and produce 8% less methane and carbon dioxide equivalents that contribute to global warming if we used recombinant ST to produce an equivalent amount of milk<sup>[65]</sup>. *Our proposal with REU supplement will characterize how changes in nutrient use, insulin resistance, and milk production efficiency translate into environmental benefit.*

## D. Research plan

### D.1. Introduction and innovation

Based on our developing theory<sup>[13, 14]</sup>, preliminary data, and experience studying lactation, we propose three independent research aims that will determine whether ceramide mediates the development of insulin resistance during lactation. For **Aim 1**, we will determine whether the inhibition of ceramide synthesis enhances insulin sensitivity and blocks the ability of ST to promote milk synthesis during early lactation and negative energy balance. For **Aim 2**, we will determine whether the induction of ceramide synthesis restores homeorhetic action and milk production during late lactation and positive energy balance. For **Aim 3**, we will utilize a focused strategy to determine the mechanisms of insulin antagonism in response to ceramide in primary myotubes. These aims are a culmination of seven years of research effort performed by our team that has challenged the scientific community to revisit homeorthesis mechanisms and the role of sphingolipids in mammals. Our innovative approaches leverage experience performing mass spectrometry-based lipidomics to biochemically map the mammalian sphingolipidome. This will include the use of electrospray ionization and tandem mass spectrometry (ESI-MS/MS) to measure many species of ceramides, glycosylated ceramides, and sphingomyelins (Table 2) in plasma and tissues. Such an approach is helpful because ceramide structure may influence function<sup>[13]</sup>. We developed a fast protein liquid chromatography method that will be utilized in tandem with ESI-MS/MS to measure LDL ceramides<sup>[22]</sup>.

**Table 2: Sphingolipids that we will measure using mass spectrometry.<sup>1</sup>**

<b>ESI-MS/MS - Ceramide:</b> 16:0, 16:1, 18:0, 18:1, 20:0, 20:1, 22:0, 22:1, 24:0, 24:1, 26:0, DH-C16:0, DH-C24:0; <b>GlcCer:</b> 16:0, 16:1, 18:0, 18:1, 20:0, 20:1, 22:0, 22:1, 24:0, 24:1, 26:0, DH-C16:0, DH-C24:0; <b>LacCer:</b> 16:0, 16:1, 18:0, 18:1, 20:0, 22:0, 24:0, 24:1, 26:0, DH-C16:0; <b>Sphingomyelin:</b> 16:0, 16:1, 18:0, 18:1, 20:0, 20:1, 22:0, 22:1, 24:0, 24:1, 26:0, 26:1; <b>DH-C16:0, DH-C22:0, DH-C24:0</b>
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<sup>1</sup>Carbon number reflects second moiety added by ceramide synthase. DH = dihydro; GlcCer = monohexosylceramide; LacCer = lactosylceramide.

(b) (4)

(b) (4)

#### D.1.a. Study system: *Ovis aries* (sheep)

Prior to and since the pivotal 1980 review of homeorthesis mechanisms by (b) (4), (b) (6) even-toed ungulate ruminants (*Artiodactyla*, *Ruminantia*) have long been the preferred model for studying nutrient partitioning during gestation and lactation. The preponderance of research describes homeorhetic control in *Ovis aries* (sheep), *Bos Taurus* (cow), and *Capra hircus* (goat)<sup>[1, 3, 6, 26, 28]</sup>. The reason for the focused effort in ruminants is because modulation of nutrient partitioning in these mammals is routinely studied to promote growth and lactation for efficient food production; albeit, ruminant homeorhetic mechanisms are similar to other mammals including sea lions and fur seals, bears, baleen whales, humans, and rodents<sup>[66-68]</sup>. The reliance on maternal adipose reserves and glucose partitioning in mammals such as ewes could be perceived as an evolutionary advantage to support milk production and offspring survival when far removed from food sources. Herein, we will rely exclusively on the utilization of an ovine model system for the following advantages: (i) preliminary data demonstrates that our observations in lactating ewes are comparable to cows, (ii) homeorhetic physiology and maternal insulin resistance are well-characterized, (iii) milk yields are copious, (iv) ST promotes milk synthesis<sup>[69]</sup>, (v) repeated sampling within animal is possible, (vi) the proposed use of (b) (4) doses would be cost-prohibitive in cattle because of their body size, and (vii) we have confirmed the ability of (b) (4) to inhibit ceramide synthesis in ewes (Section D.2.a.2.).

**D.2. Aim 1: Determine whether ceramide promotes insulin resistance and milk synthesis during early lactation.** *Rationale:* Our previous work, as reviewed by McFadden and Rico<sup>[13]</sup> and preliminary data (Figure 3) have demonstrated the accrual of ceramide in early lactation cows and ewes experiencing insulin

resistance<sup>[11, 12]</sup>. In preparation for this NSF resubmission, Davis and McFadden most recently demonstrated the ability of recombinant ST to increase circulating ceramides in association with increased insulin resistance, milk synthesis, and milk production efficiency in ruminants (please read [14]). This is in addition to other work that has repeatedly revealed a positive relationship between ceramide supply and milk yield in ruminants<sup>[20, 21, 54]</sup>. If ceramide decreases insulin-stimulated glucose utilization by skeletal muscle, then ceramide accumulation during early lactation or in response to ST would spare glucose for milk synthesis by the mammary gland, which occurs independent of insulin. Alternatively, decreases in ceramide synthesis and supply would improve insulin response by skeletal muscle and reduce glucose availability for milk synthesis. Therefore, our hypothesis is that the inhibition of ceramide synthesis will enhance insulin sensitivity to lower milk production in early lactation ewes. (b) (4)

**D.2.a. Preliminary data:**

(b) (4)

(b) (4)

**D.2.a.2.**

(b) (4)

(b) (4)

(b) (4)

Animals were ad libitum fed for 14 d followed by feed removal for 24 h to induce lipolysis. Ewes were slaughtered at the completion of the experiment for tissue

collection.

(b) (4)

(b) (4)

#### D.2.b. Experimental design:

(b) (4)

(b) (4)

(b) (4)

Ewes will be fed and milked every 12 h. Preprandial blood sampling via the caudal vein for plasma and serum collection will occur on the morning of d -1, 0, 1, 3, 5, 7, 9, 10, and 14, relative to start of treatment. Morning and afternoon milk sampling will occur on the same days. Semitendinosus skeletal muscle will be biopsied on d 9 of treatment. Bilateral jugular catheters will be inserted immediately following biopsies for the hyperinsulinemic-euglycemic clamp (clamp) that will occur on d 10, relative to start of treatment (see D.2.b.1 for more details). Feed will be withheld for 3 h before and during the biopsy and clamp. Day 9 and 10 align with the peak effects of slow-release recombinant ST<sup>[4, 14, 80]</sup>. Ceramide concentrations are expected to be suppressed by this time based on our preliminary data. Feed intakes, orts, and milk yields will be recorded daily. Ultrasound scans of back fat thickness and BW will be measured twice weekly. Liver biopsies will not be collected because of the risk for iatrogenic portal vein laceration and we consider the measurement of liver-derived lipoprotein ceramide to be sufficient to test our hypothesis. All biological samples will be snap-frozen on dry ice and stored at -80°C until analysis.

##### D.2.b.1. Hyperinsulinemic-euglycemic clamp

The clamp approach is the gold-standard to measure insulin sensitivity<sup>[81, 82]</sup>. The principal is to variably infuse glucose to achieve euglycemia (i.e., steady state glucose concentrations) during a constant infusion of insulin. Steady state glucose infusion rates are an index of insulin sensitivity (i.e., the higher the glucose infusion rate, the more insulin sensitive the individual). In our investigation, bovine insulin (2 mU/kg of BW per min; ovine homologous)<sup>[83, 84]</sup> will be administered intravenously using an infusion pump to raise blood insulin. Blood glucose will be measured every 5 min using a glucometer before and during the clamp. Concurrent with insulin infusion, glucose (50% dextrose) will be infused at variable rates using a pump for 5 h to achieve euglycemia (within 10% of mean basal level). Glucose infusion rates will be recorded.

We will use a stable-labeled glucose tracer technique before and during the clamp to measure endogenous glucose production and whole body glucose utilization<sup>[82, 85]</sup>. These measurements will be assessed by a primed dose and continuous infusion of 6,6-deuterated glucose (d<sub>2</sub>-glucose; Cambridge Isotope Laboratories, Inc.; 14 µmol/kg of BW and 11.5 µmol/kg of BW/h, respectively)<sup>[86]</sup>. Tracer infusion will begin 3 h prior to the start of the clamp. Blood for plasma collection will be collected during the final 2 h



prior to the start of the clamp to reflect basal conditions and the final 2 h of the clamp during euglycemia at 15 min intervals. Although the PI has experience performing the clamp, the team will rely on experience from (b) (4), (b) (6) who have previously utilized a glucose tracer to evaluate glucose turnover in ruminants.

**D.2.c. Laboratory analyses:** Changes in plasma and tissue ceramide concentrations will be determined by ESI-MS/MS (Table 2). Fast protein liquid chromatography will be utilized to isolate plasma LDL for ceramide quantification using mass spec<sup>[22]</sup>. Our hypothesis requires us to test for changes in skeletal muscle and systemic insulin sensitivity. Therefore, basal and insulin stimulated 2-deoxy-D-[<sup>3</sup>H]-glucose (2DOG; a non-metabolizable form of glucose) uptake in semitendinosus skeletal muscle explants will be determined post biopsy<sup>[89]</sup>. Basal and insulin-stimulated phosphorylation status of IRS1 (Ser-307) and AKT (Ser-473 and Thr-308) in skeletal muscle will be determined by immunoblot. Standard colorimetric and radioimmunoassay practices will be employed to measure changes in circulating glucose, total FA, glycerol, and insulin concentrations on all plasma samples (preprandial and clamp-derived). To characterize glucose turnover as described in D.2.b.1., plasma collected before and during the clamp will be used to measure d<sub>2</sub>-glucose enrichment as the aldonitrile penta-acetate derivative by gas chromatography-mass spectrometry (Metabolic Solution Inc.; Nashua, NH). We will also quantify changes in serum ST and insulin-like growth factor-1 concentrations using established radioimmunoassays in our department<sup>[84, 90]</sup>. Milk total fat, protein, lactose content will be analyzed using infrared procedures to calculate component yields in milk (Dairy One; Ithaca, NY). Feed composition (e.g., crude protein, neutral and acid detergent fiber, and starch content) will be determined using wet chemistry (Cumberland Valley Analytical Services; Waynesboro, PA). The PI has CU Radiation Safety approval and experience working with radioactive isotopes<sup>[15, 91, 92]</sup>.

**D.2.c.1. Calculating glucose turnover:** The use of a glucose tracer before and during the clamp is a necessary approach to calculate rates of glucose appearance (GRa) and disappearance (GRd) from isotope enrichment using Steele's equation for non-steady-state conditions<sup>[93]</sup> and accounting for the extra tracer infused with the glucose infusate<sup>[94]</sup>. Pre clamp, basal endogenous glucose production corresponds to GRa. In steady state during the clamp (i.e., euglycemia during hyperinsulinemia), endogenous glucose production is calculated by subtracting the exogenous steady state glucose infusion rate from GRa. Glucose utilization by whole body mass corresponds to GRd.

(b) (4)



(b) (4)

**D.3. Aim 2: Determine whether the induction of ceramide synthesis inhibits insulin sensitivity to promote milk synthesis.** *Rationale:* Ceramide is an associative and causative biomarker for insulin resistance<sup>[11, 12, 16, 17, 20]</sup>. Moreover, ceramide supply is positively related to milk synthesis<sup>[14, 18, 20, 21, 54]</sup>. (b) (4)  
induction (b) (4)

(b) (4)

(b) (4)

Ewes will be fed and milked every 12 h. Preprandial blood sampling via the caudal vein for plasma and serum collection will occur on the morning of d -1, 0, 1, 4, 7, 10, 14, 19, and 21, relative to start of treatment. Morning and afternoon milk sampling will occur on the same days. Semitendinosus skeletal muscle will be biopsied prior to treatment on d 20, relative to start of treatment. As described in Aim 1, bilateral jugular catheters will be inserted immediately following tissue biopsies in preparation for the hyperinsulinemic-euglycemic clamp with glucose tracer infusion that will occur on d 21 (please see D.2.b.1. for details). Feed will be withheld for 3 h before and during the biopsy and clamp. Feed intakes, milk yields, respiration and heart rates, and rectal temperatures will be recorded daily. BW and ultrasound scans of back fat thickness will be measured twice weekly. (b) (4)

(b) (4)

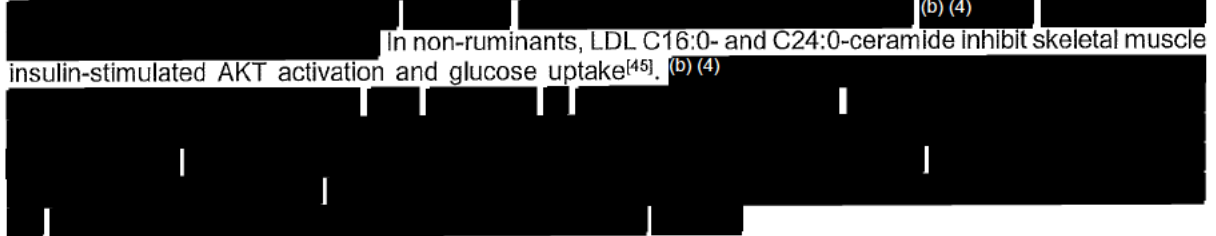
**D.3.b. Laboratory analyses:** Plasma, LDL, and muscle ceramide and sphingomyelin concentrations will be determined using ESI-MS/MS<sup>[12, 22]</sup>. To assess changes in systemic insulin action, plasma samples derived from the clamp will also be analyzed for glucose, insulin, total FA, and glycerol concentrations. Plasma collected before and during the clamp will be used to measure d<sub>2</sub>-glucose enrichment and calculate glucose turnover as described in section D.2.c. To evaluate changes in localized insulin responsiveness, basal and insulin-stimulated 2DOG uptake in skeletal muscle will be determined immediately post-biopsy<sup>[89]</sup>. To evaluate insulin signaling in skeletal muscle, basal and insulin-stimulated phosphorylation of IRS1 and AKT will be determined by immunoblot. Milk and feed composition will be analyzed as described in Aim 1. Changes in preprandial plasma glucose, total FA, glycerol, insulin, insulin-like growth factor-1, and ST concentrations will be quantified using colorimetry and radioimmunoassay to characterize basal metabolic and endocrine status in response to treatments.

(b) (4)



**D.4. Aim 3: Determine whether ceramide inhibits insulin-stimulated glucose uptake in ovine myotubes. Rationale:**

(b) (4) In non-ruminants, LDL C16:0- and C24:0-ceramide inhibit skeletal muscle insulin-stimulated AKT activation and glucose uptake<sup>[45]</sup>. (b) (4)



(b) (4)



**D.4.b. Laboratory analyses:** First, we will confirm whole cell enrichment of ceramide using ESI-MS/MS (Table 2)<sup>[15]</sup>. Because ceramide localizes within CEM of the plasma membrane, we will also isolate detergent resistant membranes on discontinuous sucrose density gradients<sup>[61]</sup>, and then immunoblot the resulting detergent resistant membrane fractions for caveolin-3 (predominant caveolin isoform in skeletal muscle)<sup>[106]</sup>. In turn, we will determine whether C16:0- and C24:0-ceramide co-localize with caveolin-3 by quantifying ceramide concentrations within each detergent resistant membrane fraction. Similar to Aim 1 and 2, basal and insulin-stimulated 2DOG uptake, and IRS1 (Ser-307) and AKT (Ser-473 and Thr-308) phosphorylation status will be evaluated to assess changes in insulin response<sup>[15]</sup>. The translocation of GLUT4 to the plasma membrane using flow cytometry will also be evaluated<sup>[107]</sup>.

(b) (4)



(b) (4)



**D.5.1. Modeling environmental impact:** Our REU Supplement stipulates that REU students will evaluate the potential environmental impact of Aim 1 and 2 for public dissemination. Over 4 years, the REU student cohort will model the environmental impact to produce 1 million kg of milk in response to the treatment scenarios described in Aim 1 and 2. The students will work with McFadden, (b) (6)

(b) (4)

(b) (4)



warranted because less 0.1% of US milk production comes from sheep. Changes in the amount of lactating ewes and cows to produce an equivalent amount of milk will account for changes in replacement young stock. Nutrient requirements will be calculated according to National Research Council<sup>[110, 111]</sup> recommendation for multiparous lactating animals. Total water and land use will be estimated. Waste output (i.e., nitrogen and phosphorus excretion, and manure production) will be determined. Daily methane, carbon dioxide, and nitrous oxide emissions from enteric fermentation and manure will also be calculated. The carbon footprint will represent carbon dioxide emissions plus carbon dioxide equivalents from methane and nitrous oxide. We will adjust calculations for ewes using scientific literature on an as-needed basis.

#### D.6. Animal welfare compliance

Animal care compliance will be adhered.

(b) (4)

(b) (4)

### E. Broader impacts

#### E.1. An integrated research and education plan

Every professor is familiar with the dogma “publish or perish,” but are you familiar with the meaning of “produce or perish”? The phrase brings attention to the pending food crisis<sup>[24]</sup>. The global population will grow by 29% to 9.8 billion in 2050<sup>[112]</sup>. This growth will be centered in India, China, African countries including Nigeria, and the United States. Accelerated growth is attributed to improvements in fertility and life expectancy, and declines in child mortality. Agricultural productivity must grow by an annual rate of 1.75% to double output by 2050<sup>[23]</sup>, relative to 2010 production. Unfortunately, global productivity growth is at an annual average of 1.66%, and a dismal 1.24% in low-income countries that are experiencing rapid population growth<sup>[23]</sup>. The detriment will be the inadequate production of food to feed people. Food security will depend on progressive and sustainable agriculture systems; however, such practices are vulnerable to risks including water scarcity, urbanization, and climate change<sup>[23, 58]</sup>. Urbanization will continue to increase our per capita water consumption and energy utilization, and decrease available land for agricultural use<sup>[59]</sup>. These constraints on food production will be compacted by climate change including erratic precipitation patterns, intense drought, extreme heat, and flooding<sup>[23, 60, 61, 113, 114]</sup>. Improvements in nutrient utilization, animal production efficiency, and biotechnology are potential means to secure nutrient-dense food for a growing population<sup>[115]</sup>. ***Because the public's understanding of the efficiency of nutrient use by livestock has the potential to influence food security and climate change, our integrated plan aims to increase literacy of this science.*** Components of the plan include science communication training for faculty, graduate students, and REU students (sections E.2. and E.3.a), the dissemination of knowledge to the public using interactive exhibits (Section E.3.b.), and the evaluation of impact (Section E.2.a. and E.4.).

#### E.2. Communicate Animal Science: Ruminant On This Podcast!

“Our fallible human nature means that in a democracy diversity of opinion is the first law of survival”, a quote from Quincy Howe in *Science and the Public* published in 1956<sup>[116]</sup>. Sixty-four years later, public opinion still has the potential to influence society's acceptance of science and will shape our food security future<sup>[117, 118]</sup>. Yet, the communication gap between scientist and public persists<sup>[119]</sup>. McFadden has sought to train young scientists to be better communicators and educate the public while doing so. Therefore, in the fall semester of 2020, McFadden created a 1-credit pilot course called *Communicate Animal Science* to prepare for this proposal. The course is designed to teach undergraduates how to understand and enhance public literacy of food animal production within the framework of efficient nutrient use, climate change, and global food security. Instruction relies on the use of a podcast communication platform to train students to communicate scientific advancements in production efficiency while educating the non-scientific





community. The podcast is called *Ruminant On This*. Student's surveyed 900 food consumers using social media and Amazon Mechanical Turk, interviewed food producers and consumers, and scientists, and wrote, narrated, and edited three podcast episodes. The concept episodes will be made available starting in February of 2021 and focus on milk production efficiency including its historical change in the United States, the influence of genetics, nutrition, and management, and the role and impact of rbST.

McFadden proposes to continue and improve the *Communicate Animal Science* course offering. Based on student and faculty feedback and major effort that was required to complete each episode, McFadden proposes to transform the course into a 3-credit offering each fall semester (50 min/credit; 3x weekly). McFadden will lecture concepts in animal production efficiency including biological mechanisms, influential factors, the role of biotechnology, and how efficient nutrient use by livestock lowers enteric gas emissions and natural resource utilization. McFadden will also showcase how consumer opinion and misunderstanding of animal production efficiency and biotechnology may harm our environment. McFadden will leverage his experience studying ST to define work that supports or refutes the use of recombinant ST, and identify the cause of public discontent towards the biotechnology that contributed to its decline in application. He will discuss the role of Monsanto (St. Louis, MO) and Eli Lilly (Indianapolis, IN), and review how the biotechnology received safety approval<sup>[120, 121]</sup>. Students will learn how society's perception and attitude towards rbST was influenced by reading excerpts from "Milk: The Deadly Poison"<sup>[122]</sup> and watching the affiliated tabloid news television episode of Hard Copy<sup>[123-125]</sup>. They will debate the accuracy of these claims using scientific evidence. Dialogue will emphasize how scientific language (e.g., hormone) and imagery (e.g., injectable syringe) may instill public fear and shape opinion. Lastly, McFadden will review how the disuse of rbST may negatively impact our environment by promoting greenhouse gas emissions and fossil fuel use<sup>[65]</sup>. (b) (4)

McFadden and students will use the remainder of class time (twice weekly) to prepare podcasts. Although the course will focus on the science and impact of animal production efficiency, students will choose episode topics based on their interests to maximize engagement. Possibilities include communicating the effects of genus and species, extreme heat (i.e., climate change), grazing versus confinement management, or genetic engineering (e.g., CRISPR) on milk or meat production efficiencies. Comparing the effects of plant vs. animal production on our environment but within the context of nutritive value and available arable land is also a possibility. (b) (4), (b) (6)

will provide a lecture that will teach awareness of social and ethical issues associated with animal food production and biotechnology and tools to disseminate reliable knowledge. For each episode, students will be divided into teams to (i) review social media posts and survey the public within predefined community demographics, (ii) identify and interview guests, (iii) create social media bulletins and online requests for public comment using Twitter, Instagram, Facebook, and LinkedIn, and (iv) utilize data obtained from Aim 1 and 2, and other published work, to share with their audience about how improvements in milk or meat production efficiency relate to a lower carbon footprint, methane and carbon dioxide emissions, and water and land use. At course conclusion, students will be more aware of how public misunderstanding of science has the ability to thwart efficient food production; students will have developed the skills to communicate reliable scientific information about animal production; and podcast listeners will have gained an understanding of how efficient animal production and biotechnology are approaches to provide nutrient-dense food with reduced environmental impact. McFadden's teaching responsibilities at CU include *Nutritional Physiology and Biochemistry* (3-credit course; spring semester) and *Graduate Student Research Updates* (1-credit seminar; spring and fall semesters). He has adequate time to develop this course.

**E.2.a. Classroom assessment:** Effective teaching requires humility and refinement of practice. McFadden has taught over 1,200 students and his student-centered focus has not waived. McFadden will work with Mathew Ouellett (Executive Director for the CU Center for Teaching Innovation) to complete a standard development and evaluation cycle of assessment of student learning. For formative assessment, students will write mini-summaries of lectures, share social media examples of misinterpreted science for in-class discussion, generate interview questions for group discussion, and peer-review podcasts. For summative assessment, podcast episodes will be created. Students will be challenged to communicate the role of efficient nutrient use by livestock on our environment and food security via oral and social media presentation. Information literacy and oral communication will be assessed using VALUE rubrics obtained from the Association of American Colleges and Universities<sup>[126]</sup>. Students will evaluate McFadden's instruction by completing evaluations. Recorded video observation of lectures with critique from Center for Teaching Innovation will be employed. Feedback will be utilized to refine the course to improve learning.

**E.3. Public engagement with the Sciencenter museum and The Great New York State Fair**

**E.3.a. Portal to the Public Communications Training:** In 2007, an NSF-funded *Portal to the Public (PoP)* project (Award #1610039) was conceived to bring scientists and public audiences together within informal science education (ISE) institutions including museums and science centers<sup>[127, 128]</sup>. The PoP model provides scientists with communication strategies for diverse public audiences, and provides researchers with a broader understanding of how people learn and the nature of informal learning environments. One example of an ISE that provides PoP training for scientists is the Sciencenter in Ithaca, NY, a non-profit interactive science museum that hosts over 100,000 guests annually. McFadden and Davis will work with Senior Personnel Michelle Kortenaar (Sciencenter Executive Director). In accordance with the PoP model, Sciencenter Youth Program Coordinators will provide the McFadden and Davis labs, ~15 additional faculty members, 8 NSF REU participants from SUNY Cortland, and ~25 graduate and undergraduate students within the CU department with training focused on the principles of effective science engagement in informal science settings such as the Sciencenter. We will learn how to utilize a learner-centered, inquiry-based approach that focuses on interactive, "minds-on" experiences to strengthen our abilities to serve as informal science educators and promote STEM literacy. Moreover, we will be trained in the application of manipulatives (i.e., hands-on exercises that promote learning). The PoP training we receive will be practiced to inform the public about the importance of improving the efficiency of nutrient utilization in ruminants to maintain food security and (b) (4)

(b) (4)

(b) (4) Our learning objective is to educate children and adults about how improvements in the efficiency of nutrient utilization in domestic food animals is necessary to maintain global food security and reduce environmental impact. We will also share information about biotechnologies, like recombinant ST, that enhance animal production efficiency and sustainability. Data obtained from aims 1 and 2 of this proposal will be integrated into the program by REU students. To achieve our learning outcome, we will avoid technical jargon and rely on Sciencenter PoP training practices. (b) (4)

(b) (4) REU students will lead the events with guidance from graduate students, Davis, and McFadden. We expect to engage ~500 children and adults at the Sciencenter. (b) (4)

(b) (4)

(b) (4)

Children and adults will learn how improvements in the efficiency of nutrient use in food animals influences our ability to secure food and reduce the environment impact. To facilitate learning, participants will view outcomes from milk produced from dairy ewes and cows managed (1) during the pre-agricultural revolution (i.e., 1940s), (2) today following advancements in genetics, nutrition, and management without the use of recombinant ST, and (3) today with the use of recombinant ST. For example, differences in milk production under these three scenarios will be visualized using graduated cylinders filled with different volumes of milk. The amount of nutrients consumed per unit of milk produced will be visualized by weighing out a specified amount of feed into sandwich bags. This activity will allow participants to understand how modern ewes and cows achieve higher milk production per unit of feed (i.e., nutrient) intake as compared to ewes and cows in the 1940s. Similarly, participants will understand how the use of recombinant ST can further enhance milk production efficiency. To reinforce these concepts, a live ewe and rumen-fistulated cow will be present, which attracts people to the Sciencenter. Participants will look and feel inside the rumen to learn how microorganisms transform feed to nutrients that will be converted to milk.

Due to population growth, climate change, and limitations in food productivity, food security is threatened<sup>[129]</sup>. Children and adults will learn about these issues and how improvements in milk production efficiency translate into greater food availability with less environmental impact. Population growth will be visualized using LEGO figures. To convey how climate change may impact our ability to secure food, we will display a large map with small milk-filled graduated cylinders on each state, representing the predicted milk loss due to extreme heat<sup>[130]</sup>. Dairy products made with milk from the CU Dairy (i.e., cartons of milk,



cheese, and yogurt) will be utilized to demonstrate impacts of population growth and climate change on food availability. Participants will be able to take these items home. We will also showcase how ewes and cows of today or those that receive recombinant ST use less land, water, and fossil fuels to produce an equivalent amount of milk by using cylinders of soil, water, and coal. Improved efficiency also means that the carbon footprint and enteric methane and carbon dioxide emissions are lower today, as compared to a century ago, or with the use of recombinant ST. To visualize differences in methane and carbon dioxide release, balloons labeled with these gases and fun facts will hang above the exhibit and provided to visitors. Data that REU students generate (i.e., changes in milk production efficiency, animal requirements, feed, land, and water requirements, methane and carbon dioxide production, and carbon footprint that would be required to produce an equivalent amount of milk [section D.5.1.]) will be explained to participants. This information will be compiled concisely into laminated fact sheets and take-home brochures for participants.

Behind the exhibit will be a 20' wide × 8' tall display board. The major concept portrayed will be that increasing the efficiency of nutrient utilization in ewes and cows (through improvements in genetics, diet, management, and biotechnology) reduces the total number of animals and feedstuffs, land and water, greenhouse gas emissions, and fossil fuels needed to produce an equivalent amount of milk, leading to improved food security. This station will also feature an "Ask a Scientist" component where participants can ask Davis and McFadden questions about animal food production. A "Fact vs. Fiction" illustration will be included to clarify common misconceptions about the agricultural industry. We will also utilize this opportunity to advertise our *Ruminant On This* podcast and collect questions for future episodes.

#### E.4. Evaluating the impact of public outreach efforts

Sciencenter evaluator Michelle Kortenaar will measure progress through a combination of pre- and post-assessments of Sciencenter participants. The evaluator, PI, and Co-PI will utilize the Team-Based Inquiry model of evaluation that was developed through NSF grant DRL-1610039 led by Michelle Kortenaar. In active partnership, Michelle will create evaluation questions, collect data from participants, and analyze these data to make decisions (i.e., reflect) to improve our educational efforts and enhance impact. The following methods will be employed: (i) matched pre-post assessments of participants on their knowledge about the relationship between nutrient use by animals, biotechnology, and environmental impact; and their opinions about and comfort with science communication; (ii) reflections by Sciencenter staff regarding the potential and actualized project outcomes; and (iii) compilations of the Team-Based Inquiry studies conducted as part of the project to assess changes in impact, diversity, and magnitude of participation.

#### F. Timeline

The project timeline is shown in Table 3. McFadden will manage research aims with summer support from REU students and Davis. McFadden will teach Communicate Animal Science with the Ruminant On This podcast every fall semester as part of his teaching responsibilities. Portal to the Public Communications Training will be provided to CU and SUNY Cortland faculty and students one day each year in June. This training will be in alignment with the start of the 8-wk REU program led by Davis and supported by McFadden in years 1 through 4. REU students led by Davis and supported by McFadden will lead the Ruminant with Ruminants event at the Sciencenter in years 1 through 3. Although the exhibit will be showcased for visitors for 1 week; on-site participation by the project team with animals will be reserved for the Saturday Showtime Series. In

Table 3. Timeline of proposed work shared by McFadden and Davis.

Year:	2021-2022	2022-2023	2023-2024	2024-2025
Research aim 1				
Research aim 2				
Research aim 3				
Communicate animal science course with Ruminant On This podcast				
(b) (4)				
Research experience for undergraduates				
Assess learning and evaluate progress				

#### G. Major outcomes

Funding this proposal provides the means to define the mammalian homeorhetic mechanisms that support neonatal development using *Ovis aries*. The innovative approaches leverage experience performing lipidomics and studying insulin kinetics that are showcased by a large body of work performed by McFadden and Davis. Educating the public about the importance of improving livestock production efficiency may promote acceptance of novel strategies (e.g. biotechnologies) to reach this goal, leading to improved food security and reduced environmental impact. The relationships fostered between CU and SUNY Cortland faculty and students and the Sciencenter will generate impactful and long-lasting education.

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**SUMMARY  
PROPOSAL BUDGET****YEAR 1**

ORGANIZATION <b>Cornell University</b>		PROPOSAL NO. <b>2114725</b>		DURATION (months)	
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>		AWARD NO.		Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months		Funds Requested By proposer	Funds granted by NSF (if different)
		CAL	ACAD	SUMR	
1. <b>Joseph Mcfadden - Principal Inv</b>		(b) (4), (b) (6)			
2.					
3.					
4.					
5.					
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)					
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)					
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS					
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)					
3. ( <b>1</b> ) GRADUATE STUDENTS					
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS					
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)					
6. ( <b>0</b> ) OTHER					
TOTAL SALARIES AND WAGES (A + B)					
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)					
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)					
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)					
TOTAL EQUIPMENT				0	
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)				0	
2. INTERNATIONAL				0	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS \$ _____ <b>0</b>					
2. TRAVEL _____ <b>0</b>					
3. SUBSISTENCE _____ <b>0</b>					
4. OTHER _____ <b>0</b>					
TOTAL NUMBER OF PARTICIPANTS ( <b>0</b> ) TOTAL PARTICIPANT COSTS				0	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				(b) (4), (b) (6)	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION					
3. CONSULTANT SERVICES					
4. COMPUTER SERVICES					
5. SUBAWARDS					
6. OTHER					
TOTAL OTHER DIRECT COSTS					
H. TOTAL DIRECT COSTS (A THROUGH G)					
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) <b>Modified Total Direct Costs</b> (b) (4)				(b) (4)	
TOTAL INDIRECT COSTS (F&A)					
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				220,086	
K. FEE				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				220,086	
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>		AGREED LEVEL IF DIFFERENT \$			
PI/PD NAME <b>Joseph Mcfadden</b>		FOR NSF USE ONLY			
ORG. REP. NAME* <b>Elizabeth Estabrook</b>		INDIRECT COST RATE VERIFICATION			
		Date Checked	Date Of Rate Sheet	Initials - ORG	

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

# SUMMARY PROPOSAL BUDGET

YEAR 2

ORGANIZATION <b>Cornell University</b>				FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>				PROPOSAL NO. <b>2114725</b>	DURATION (months)	
				AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)				NSF Funded Person-months		Funds Requested By proposer
				CAL	ACAD	SUMR
1. <b>Joseph Mcfadden - Principal Inv</b>				(b) (4), (b) (6)		
2.						
3.						
4.						
5.						
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)						
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)						
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)						
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS						
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)						
3. ( <b>2</b> ) GRADUATE STUDENTS						
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS						
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)						
6. ( <b>0</b> ) OTHER						
TOTAL SALARIES AND WAGES (A + B)						
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)						
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)						
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000)						
TOTAL EQUIPMENT						0
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)						0
2. INTERNATIONAL						0
F. PARTICIPANT SUPPORT COSTS						
1. STIPENDS \$ <b>0</b>						
2. TRAVEL <b>0</b>						
3. SUBSISTENCE <b>0</b>						
4. OTHER <b>0</b>						
TOTAL NUMBER OF PARTICIPANTS ( <b>0</b> ) TOTAL PARTICIPANT COSTS						0
G. OTHER DIRECT COSTS						
1. MATERIALS AND SUPPLIES				(b) (4), (b) (6)		
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION						
3. CONSULTANT SERVICES						
4. COMPUTER SERVICES						
5. SUBAWARDS						
6. OTHER						
TOTAL OTHER DIRECT COSTS						
H. TOTAL DIRECT COSTS (A THROUGH G)						
I. INDIRECT COSTS (F&A) (SPECIFY RATE AND BASE)						
Modified Total Direct Costs (b) (4)				(b) (4)		
TOTAL INDIRECT COSTS (F&A)						
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)						311,004
K. FEE						0
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)						311,004
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>				AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Joseph Mcfadden</b>				FOR NSF USE ONLY		
ORG. REP. NAME* <b>Elizabeth Estabrook</b>				INDIRECT COST RATE VERIFICATION		
				Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

**SUMMARY  
PROPOSAL BUDGET****YEAR 3**

ORGANIZATION <b>Cornell University</b>		FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>		PROPOSAL NO. <b>2114725</b>	DURATION (months)	
		AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months		
		CAL	ACAD	SUMR
1. <b>Joseph Mcfadden - Principal Inv</b>		(b) (4), (b) (6)		
2.				
3.				
4.				
5.				
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)				
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)				
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)				
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS				
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)				
3. ( <b>2</b> ) GRADUATE STUDENTS				
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS				
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				
6. ( <b>0</b> ) OTHER				
TOTAL SALARIES AND WAGES (A + B)				
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)				
TOTAL EQUIPMENT		0		
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)		0		
2. INTERNATIONAL		0		
F. PARTICIPANT SUPPORT COSTS				
1. STIPENDS \$ _____		0		
2. TRAVEL _____		0		
3. SUBSISTENCE _____		0		
4. OTHER _____		0		
TOTAL NUMBER OF PARTICIPANTS ( <b>0</b> )		TOTAL PARTICIPANT COSTS		0
G. OTHER DIRECT COSTS		(b) (4), (b) (6)		
1. MATERIALS AND SUPPLIES				
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				
3. CONSULTANT SERVICES				
4. COMPUTER SERVICES				
5. SUBAWARDS				
6. OTHER				
TOTAL OTHER DIRECT COSTS				
H. TOTAL DIRECT COSTS (A THROUGH G)				
I. INDIRECT COSTS (F&A) (SPECIFY RATE AND BASE) <b>Modified Total Direct Costs</b> (b) (4)		(b) (4)		
TOTAL INDIRECT COSTS (F&A)				
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)		303,820		
K. FEE		0		
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)		303,820		
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>		AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Joseph Mcfadden</b>		FOR NSF USE ONLY		
ORG. REP. NAME* <b>Elizabeth Estabrook</b>		INDIRECT COST RATE VERIFICATION		
		Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET



**SUMMARY  
PROPOSAL BUDGET****YEAR 4**

ORGANIZATION <b>Cornell University</b>		PROPOSAL NO. <b>2114725</b>		DURATION (months)	
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>		AWARD NO.		Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months		Funds Requested By proposer	Funds granted by NSF (if different)
		CAL	ACAD	SUMR	
1. <b>Joseph Mcfadden - Principal Inv</b>		(b) (4), (b) (6)			
2.					
3.					
4.					
5.					
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)					
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)					
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS					
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)					
3. ( <b>1</b> ) GRADUATE STUDENTS					
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS					
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)					
6. ( <b>0</b> ) OTHER					
TOTAL SALARIES AND WAGES (A + B)					
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)					
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)					
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)					
TOTAL EQUIPMENT				0	
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)		(b) (4)		0	
2. INTERNATIONAL				0	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS \$ _____		0			
2. TRAVEL _____		0			
3. SUBSISTENCE _____		0			
4. OTHER _____		0			
TOTAL NUMBER OF PARTICIPANTS ( <b>0</b> ) TOTAL PARTICIPANT COSTS				0	
G. OTHER DIRECT COSTS		(b) (4), (b) (6)			
1. MATERIALS AND SUPPLIES					
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION					
3. CONSULTANT SERVICES					
4. COMPUTER SERVICES					
5. SUBAWARDS					
6. OTHER					
TOTAL OTHER DIRECT COSTS					
H. TOTAL DIRECT COSTS (A THROUGH G)					
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) <b>Modified Total Direct Costs</b> (b) (4)		(b) (4)			
TOTAL INDIRECT COSTS (F&A)					
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				186,699	
K. FEE				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				186,699	
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>		AGREED LEVEL IF DIFFERENT \$			
PI/PD NAME <b>Joseph Mcfadden</b>		FOR NSF USE ONLY			
ORG. REP. NAME* <b>Elizabeth Estabrook</b>		INDIRECT COST RATE VERIFICATION			
		Date Checked	Date Of Rate Sheet	Initials - ORG	

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

**SUMMARY  
PROPOSAL BUDGET**

Cumulative

ORGANIZATION <b>Cornell University</b>		FOR NSF USE ONLY	
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>		PROPOSAL NO. <b>2114725</b>	DURATION (months) Proposed      Granted
		AWARD NO.	
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL    ACAD    SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. <b>Joseph Mcfadden - Principal Inv</b>	(b) (4), (b) (6)		
2.			
3.			
4.			
5.			
6. (    ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)			
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)			
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)			
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS			
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)			
3. ( <b>6</b> ) GRADUATE STUDENTS			
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS			
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)			
6. ( <b>0</b> ) OTHER			
TOTAL SALARIES AND WAGES (A + B)			
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)			
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)			
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)			
TOTAL EQUIPMENT		0	
E. TRAVEL      1. DOMESTIC (INCL. U.S. POSSESSIONS)		(b) (4)	
2. INTERNATIONAL		0	
F. PARTICIPANT SUPPORT COSTS			
1. STIPENDS      \$ _____	0		
2. TRAVEL      _____	0		
3. SUBSISTENCE      _____	0		
4. OTHER      _____	0		
TOTAL NUMBER OF PARTICIPANTS      ( <b>0</b> )	TOTAL PARTICIPANT COSTS	0	
G. OTHER DIRECT COSTS			
1. MATERIALS AND SUPPLIES		(b) (4), (b) (6)	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION			
3. CONSULTANT SERVICES			
4. COMPUTER SERVICES			
5. SUBAWARDS			
6. OTHER			
TOTAL OTHER DIRECT COSTS			
H. TOTAL DIRECT COSTS (A THROUGH G)			
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)			
TOTAL INDIRECT COSTS (F&A)		(b) (4)	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)		1,021,609	
K. FEE		0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)		1,021,609	
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>	AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Joseph Mcfadden</b>	FOR NSF USE ONLY		
ORG. REP. NAME* <b>Elizabeth Estabrook</b>	INDIRECT COST RATE VERIFICATION		
	Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

## BUDGET JUSTIFICATION

Cornell University

Cornell utilizes the calendar year (i.e., January through December) for the purpose of compliance with the NSF's limitation on senior personnel salary requests.

### Senior Personnel:

**Joseph McFadden (PI)**, Associate Professor in the Department of Animal Science, will be responsible for the overall administration and direction of the project. Major roles include mentoring graduate students, overseeing experimental planning, ensuring IACUC and Radiation Safety compliance, adhering to the Data Management Plan, assisting with sample collection and analyses, overseeing statistical analyses, and proofing manuscripts for peer-review evaluation. He will serve as the primary director for all research aims and course instruction, and (b) (4). Funds will cover his effort for (b) (4), (b) (6) each year of the project.

### Other Personnel:

**TBD, Graduate Research Assistants**, will join the McFadden lab as a Ph.D. and M.S. student. The students will work with a lab as defined in the Facilities, Equipment and Other Resources document. These students will have the principal role of executing experimental designs as described in the Project Description. They will be responsible for collecting and storing all data and samples as described in the Data Management Plan, making measurements, analyzing data, and preparing manuscript drafts for peer-review publication. The Ph.D. student will be responsible for Aim 1 and 3. The M.S. student will be responsible for Aim 2. The student will also assist with outreach efforts including Ruminant with Ruminants at the Sciencenter and participate in all communications training and REU student activities. Funds will be used to support 1 graduate student for 12 months of Years 1 and 4; and 2 graduate students for 12 months in Years 2-3 of the project.

The Cornell University Graduate School sets the graduate support amounts annually. The stipend includes an annual escalation factor of (b) (4) over the current rates.

Find current rates at <https://gradschool.cornell.edu/financial-support/stipend-rates/>

### Escalations:

Faculty and staff salaries reflect an anticipated (b) (4) escalation effective July 1 of each year, unless stated otherwise above.

### Fringe Benefits:

The negotiated rate in place at the time salary costs are incurred will be charged to the project. Fringe benefits are calculated at the university established rates of 63.9% (07/01/19 – 06/30/20), 61.0% (07/01/20 – 06/30/21) 62.20% (07/01/21-06/30/22), 63.50% (07/01/22-06/30/23), and 65% thereafter. No fringe benefits on graduate student stipends or undergraduate student wages are calculated.

Find current rates at <https://www.dfa.cornell.edu/capitalassets/cost/employee>

### Travel:

#### Domestic Travel: (b) (4) in Year 4)

- Funding will cover travel costs for a graduate student to travel to a Professional Meeting in Year 4 such as the annual meeting for the Society for Integrative & Comparative Biology. Anticipated costs include: airline tickets (b) (4), registration fees (b) (4), accommodations (b) (4)/night for 3 nights), and per diem (b) (4)/day for 4 days).
- Funding will cover travel costs for the PI, Co-PI, graduate student(s), and REU students (b) (4). Anticipated costs include: accommodations (b) (4) night for 12 nights), and per diem (b) (4)/day for 13 days). Mileage is based on current IRS rates, currently at (b) (4) /mile.

*Other Direct Costs:*

(b) (4)

(b) (4)

(b) (4)

**Publications:** Funds (b) (4) in Year 2 and (b) (4) in Years 3-4, respectively) will cover the costs of peer review publication of research results in appropriate refereed journals such as the *American Journal of Physiology Regulatory, Integrative and Comparative Physiology* or *Integrative & Comparative Biology*. Costs are estimated for 6 or more publications at (b) (4) page.

**Subawards/Consortium/Contractual Costs:** Cornell will establish subcontracts for this research project with the following institution(s):

(b) (4)

The Sciencenter

Led by Elizabeth McDonald

The Sciencenter has a work plan established to indicate their commitment of the deliverables and expected outcomes and is included in the Project Description. See separate budget and budget justification for details.

**Other:** (b) (4) in Years 1-4 respectively)

- **Printing Services:** (b) (4) in Year 4 to print (b) (4), flyers (b) (4) a (b) (4) per color flyer = (b) (4) editorial book with coil binding (b) (4), and glossy posters (b) (4). All other exhibit materials (e.g., Cornell banners, tables with covers) will be borrowed from Cornell Cooperative Extension at no cost or budgeted by Co-PI Davis. The CU College of Agriculture and Life Sciences will also provide giveaway merchandise at no cost.
- **Graduate Tuition & Fees:** Find current rates at <https://gradschool.cornell.edu/financial-support/>. The Cornell University Graduate School sets the graduate support amounts annually. No escalation is included for tuition. The health insurance includes an annual escalation factor of (b) (4) over the current rates.



GRA Expenses	Year 1	Year 2	Year 3	Year 4
Tuition	(b) (4)			
Health Insurance				

*Indirect Costs:*

F&A (indirect) costs are proposed at Cornell's Federally-Negotiated Indirect Cost Rate Agreement (NICRA) rate on Modified Total Direct Costs (MTDC). MTDC includes exclusions, if applicable, of GRA tuition and health insurance, capital equipment in excess of \$5,000, rental costs of off-site facilities, participant support costs, and subcontracts in excess of \$25,000. Predetermined NICRA rates are (b) (4) through June 30, 2021, and provisional NICRA rate of (b) (4) thereafter.

Find current rate agreement with the Department of Health and Human Service at  
<https://www.dfa.cornell.edu/capitalassets/cost/facilities>

Years	Year 1	Year 2	Year 3	Year 4	Totals
<b>Total Direct Costs</b>	(b) (4)				
(Minus GRA Tuition)					
(Minus GRA Health Insurance)					
Contract Modified Direct Costs (On Campus)					
<b>Total Indirect Costs</b>					
<b>TOTALS</b>	(b) (4)				\$1,021,609

# SUMMARY PROPOSAL BUDGET

YEAR 1

ORGANIZATION <b>Sciencenter</b>				FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>				PROPOSAL NO. <b>2114725</b>	DURATION (months)	
				AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)				NSF Funded Person-months		Funds Requested By proposer
				CAL	ACAD	SUMR
1.						
2.						
3.						
4.						
5.						
6.	( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)			0.0		0
7.	( ) TOTAL SENIOR PERSONNEL (1 - 6)			0.0		0
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)						
1.	( 0 ) POST DOCTORAL SCHOLARS			0.0		0
2.	( 0 ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)			0.0		0
3.	( 0 ) GRADUATE STUDENTS					0
4.	( 0 ) UNDERGRADUATE STUDENTS					0
5.	( 0 ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)					0
6.	( 0 ) OTHER					0
TOTAL SALARIES AND WAGES (A + B)						0
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)						0
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)						0
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)						
TOTAL EQUIPMENT						0
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)						0
2. INTERNATIONAL						0
F. PARTICIPANT SUPPORT COSTS						
1. STIPENDS \$ _____				0		
2. TRAVEL _____				0		
3. SUBSISTENCE _____				0		
4. OTHER _____				0		
TOTAL NUMBER OF PARTICIPANTS ( 0 ) TOTAL PARTICIPANT COSTS						0
G. OTHER DIRECT COSTS						
1. MATERIALS AND SUPPLIES						0
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION						0
3. CONSULTANT SERVICES						0
4. COMPUTER SERVICES						0
5. SUBAWARDS						0
6. OTHER						(b) (4)
TOTAL OTHER DIRECT COSTS						
H. TOTAL DIRECT COSTS (A THROUGH G)						
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)						
Modified Total Direct Costs (b) (4)						
TOTAL INDIRECT COSTS (F&A)						(b) (4)
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)						
K. FEE						
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)						
M. COST SHARING PROPOSED LEVEL \$ 0				AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Joseph Mcfadden</b>				FOR NSF USE ONLY		
ORG. REP. NAME* <b>Elizabeth Estabrook</b>				INDIRECT COST RATE VERIFICATION		
				Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

# SUMMARY PROPOSAL BUDGET

YEAR 2

ORGANIZATION <b>Sciencenter</b>				FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>				PROPOSAL NO. <b>2114725</b>	DURATION (months)	
				AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)				NSF Funded Person-months		Funds Requested By proposer
				CAL	ACAD	SUMR
1.						
2.						
3.						
4.						
5.						
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.0					0
7. ( ) TOTAL SENIOR PERSONNEL (1 - 6)	0.0					0
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)						
1. ( 0 ) POST DOCTORAL SCHOLARS	0.0					0
2. ( 0 ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.0					0
3. ( 0 ) GRADUATE STUDENTS						0
4. ( 0 ) UNDERGRADUATE STUDENTS						0
5. ( 0 ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)						0
6. ( 0 ) OTHER						0
TOTAL SALARIES AND WAGES (A + B)						0
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)						0
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)						0
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)						
TOTAL EQUIPMENT						0
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)						0
2. INTERNATIONAL						0
F. PARTICIPANT SUPPORT COSTS						
1. STIPENDS \$	0					
2. TRAVEL	0					
3. SUBSISTENCE	0					
4. OTHER	0					
TOTAL NUMBER OF PARTICIPANTS ( 0 ) TOTAL PARTICIPANT COSTS						0
G. OTHER DIRECT COSTS						
1. MATERIALS AND SUPPLIES						(b) (4)
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION						
3. CONSULTANT SERVICES						
4. COMPUTER SERVICES						
5. SUBAWARDS						
6. OTHER						
TOTAL OTHER DIRECT COSTS						
H. TOTAL DIRECT COSTS (A THROUGH G)						
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)						
Modified Total Direct Costs (b) (4)						
TOTAL INDIRECT COSTS (F&A)						(b) (4)
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)						
K. FEE						
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)						
M. COST SHARING PROPOSED LEVEL \$ 0				AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Joseph Mcfadden</b>				FOR NSF USE ONLY		
ORG. REP. NAME* <b>Elizabeth Estabrook</b>				INDIRECT COST RATE VERIFICATION		
				Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

**SUMMARY  
PROPOSAL BUDGET****YEAR 3**

ORGANIZATION <b>Sciencenter</b>				FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>				PROPOSAL NO. <b>2114725</b>	DURATION (months)	
				AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: P/PI, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)				NSF Funded Person-months		Funds Requested By proposer
	CAL	ACAD	SUMR			
1.						
2.						
3.						
4.						
5.						
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.0					0
7. ( ) TOTAL SENIOR PERSONNEL (1 - 6)	0.0					0
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)						
1. ( 0 ) POST DOCTORAL SCHOLARS	0.0					0
2. ( 0 ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.0					0
3. ( 0 ) GRADUATE STUDENTS						0
4. ( 0 ) UNDERGRADUATE STUDENTS						0
5. ( 0 ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)						0
6. ( 0 ) OTHER						0
TOTAL SALARIES AND WAGES (A + B)						0
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)						0
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)						0
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)						
TOTAL EQUIPMENT						0
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)						0
2. INTERNATIONAL						0
F. PARTICIPANT SUPPORT COSTS						
1. STIPENDS \$			0			
2. TRAVEL			0			
3. SUBSISTENCE			0			
4. OTHER			0			
TOTAL NUMBER OF PARTICIPANTS ( 0 ) TOTAL PARTICIPANT COSTS						0
G. OTHER DIRECT COSTS						
1. MATERIALS AND SUPPLIES						(b) (4)
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION						
3. CONSULTANT SERVICES						
4. COMPUTER SERVICES						
5. SUBAWARDS						
6. OTHER						
TOTAL OTHER DIRECT COSTS						
H. TOTAL DIRECT COSTS (A THROUGH G)						
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)						
Modified Total Direct Costs (b) (4)						
TOTAL INDIRECT COSTS (F&A)						(b) (4)
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)						
K. FEE						
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)						
M. COST SHARING PROPOSED LEVEL \$ 0				AGREED LEVEL IF DIFFERENT \$		
P/PI NAME <b>Joseph Mcfadden</b>				FOR NSF USE ONLY		
ORG. REP. NAME* <b>Elizabeth Estabrook</b>				INDIRECT COST RATE VERIFICATION		
		Date Checked	Date Of Rate Sheet	Initials - ORG		

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET



# SUMMARY PROPOSAL BUDGET

Cumulative

ORGANIZATION <b>Sciencenter</b>				FOR NSF USE ONLY			
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Joseph Mcfadden</b>				PROPOSAL NO. <b>2114725</b>		DURATION (months)	
				AWARD NO.		Proposed	Granted
A. SENIOR PERSONNEL: PI/PI, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)				NSF Funded Person-months		Funds Requested By proposer	Funds granted by NSF (if different)
				CAL	ACAD	SUMR	
1.							
2.							
3.							
4.							
5.							
6.	( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)						
7.	( ) TOTAL SENIOR PERSONNEL (1 - 6)			0.0			0
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)							
1.	( 0 ) POST DOCTORAL SCHOLARS			0.0			0
2.	( 0 ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)			0.0			0
3.	( 0 ) GRADUATE STUDENTS						0
4.	( 0 ) UNDERGRADUATE STUDENTS						0
5.	( 0 ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)						0
6.	( 0 ) OTHER						0
TOTAL SALARIES AND WAGES (A + B)							0
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)							0
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)							0
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)							
TOTAL EQUIPMENT							0
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)							0
2. INTERNATIONAL							0
F. PARTICIPANT SUPPORT COSTS							
1. STIPENDS \$ 0							
2. TRAVEL 0							
3. SUBSISTENCE 0							
4. OTHER 0							
TOTAL NUMBER OF PARTICIPANTS ( 0 ) TOTAL PARTICIPANT COSTS							0
G. OTHER DIRECT COSTS							
1. MATERIALS AND SUPPLIES							(b) (4)
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION							
3. CONSULTANT SERVICES							
4. COMPUTER SERVICES							
5. SUBAWARDS							
6. OTHER							
TOTAL OTHER DIRECT COSTS							
H. TOTAL DIRECT COSTS (A THROUGH G)							
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)							
TOTAL INDIRECT COSTS (F&A)							(b) (4)
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)							
K. FEE							
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)							
M. COST SHARING PROPOSED LEVEL \$ 0				AGREED LEVEL IF DIFFERENT \$			
PI/PD NAME <b>Joseph Mcfadden</b>				FOR NSF USE ONLY			
ORG. REP. NAME* <b>Elizabeth Estabrook</b>				INDIRECT COST RATE VERIFICATION			
				Date Checked	Date Of Rate Sheet	Initials - ORG	

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

**BUDGET JUSTIFICATION**  
**NSF**  
**Sciencenter**

(b) (4) over three years will support the Sciencenter in work with the PIs and graduate students to develop a comprehensive package of hands-on, educational, and outreach activities. Funding will be broken down as follows:

**Direct Costs:** (b) (4)

Portal to the Public Training (b) (4)

In Year 1, PIs, graduate students, and any REU students will attend training on communicating science to public audiences through the development and facilitation of hands-on activities. The end goal of this training will be to help the PI and grad students work with Sciencenter staff to develop multiple hands-on activities that will be used to educate the public during a variety of outreach and engagement events.

Public engagement events (b) (4)

Using what they've learned at the training, lab members will facilitate hands-on activities for use on the Sciencenter's floor, in interactive presentations with public audiences at the Sciencenter, and in outreach to rural families during community outreach events. The Sciencenter will provide PR and marketing for these events, assistance with set-up and a venue.

Evaluation (b) (4)

Sciencenter staff will lead ongoing evaluation and assessment of the impact of both the training and the educational and outreach activities. The evaluation efforts will include collecting and analyzing visitor data. This will be both an iterative process for project improvement over time and a final assessment to ensure that learning objectives have been met. Results will be shared with the PIs.

**Indirect Costs:** (b) (4)

The Sciencenter has a negotiated indirect cost rate with the Department of the Interior for an indirect cost recovery rate of (b) (4) for 2020. (b) (4) of (b) (4) = (b) (4)

**TOTAL:** (b) (4)

# SUMMARY PROPOSAL BUDGET

YEAR 1

ORGANIZATION <b>SUNY College at Cortland</b>		FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Amanda Davis</b>		PROPOSAL NO. <b>2114726</b>	DURATION (months)	
		AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months		
		CAL	ACAD	SUMR
1. <b>Amanda Davis - Principal Inv</b>		(b) (4), (b) (6)		
2.				
3.				
4.				
5.				
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)				
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)				
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)				
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS				
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)				
3. ( <b>0</b> ) GRADUATE STUDENTS				
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS				
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				
6. ( <b>0</b> ) OTHER				
TOTAL SALARIES AND WAGES (A + B)				
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)				
TOTAL EQUIPMENT		0		
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)		0		
2. INTERNATIONAL		0		
F. PARTICIPANT SUPPORT COSTS (b) (4)				
1. STIPENDS \$				
2. TRAVEL				
3. SUBSISTENCE				
4. OTHER 0				
TOTAL NUMBER OF PARTICIPANTS ( <b>2</b> )		TOTAL PARTICIPANT COSTS (b) (4)		
G. OTHER DIRECT COSTS				
1. MATERIALS AND SUPPLIES		(b) (4), (b) (6)		
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				
3. CONSULTANT SERVICES				
4. COMPUTER SERVICES				
5. SUBAWARDS				
6. OTHER				
TOTAL OTHER DIRECT COSTS				
H. TOTAL DIRECT COSTS (A THROUGH G)				
I. INDIRECT COSTS (F&A) (SPECIFY RATE AND BASE) <b>MDTC (Rate: 59.7, Base: 30653.0)</b>				
TOTAL INDIRECT COSTS (F&A)		(b) (4), (b) (6)		
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				
K. FEE				
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>		AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Amanda Davis</b>		FOR NSF USE ONLY		
ORG. REP. NAME* <b>Thomas Frank</b>		INDIRECT COST RATE VERIFICATION		
		Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

# SUMMARY PROPOSAL BUDGET

YEAR 2

ORGANIZATION <b>SUNY College at Cortland</b>		FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Amanda Davis</b>		PROPOSAL NO. <b>2114726</b>	DURATION (months)	
		AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months		
		CAL	ACAD	SUMR
1. <b>Amanda Davis - Principal Inv</b>		(b) (4), (b) (6)		
2.				
3.				
4.				
5.				
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)				
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)				
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)				
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS				
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)				
3. ( <b>0</b> ) GRADUATE STUDENTS				
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS				
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				
6. ( <b>0</b> ) OTHER				
TOTAL SALARIES AND WAGES (A + B)				
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)				
TOTAL EQUIPMENT		0		
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)		0		
2. INTERNATIONAL		0		
F. PARTICIPANT SUPPORT COSTS (b) (4)				
1. STIPENDS \$				
2. TRAVEL				
3. SUBSISTENCE		0		
4. OTHER				
TOTAL NUMBER OF PARTICIPANTS ( <b>2</b> )		TOTAL PARTICIPANT COSTS (b) (4)		
G. OTHER DIRECT COSTS		(b) (4), (b) (6)		
1. MATERIALS AND SUPPLIES				
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				
3. CONSULTANT SERVICES				
4. COMPUTER SERVICES				
5. SUBAWARDS				
6. OTHER				
TOTAL OTHER DIRECT COSTS				
H. TOTAL DIRECT COSTS (A THROUGH G)				
I. INDIRECT COSTS (F&A)/SPECIEY RATE AND BASE) <b>MDTC</b> (b) (4)		(b) (4), (b) (6)		
TOTAL INDIRECT COSTS (F&A)				
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				
K. FEE				
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>		AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Amanda Davis</b>		FOR NSF USE ONLY		
ORG. REP. NAME* <b>Thomas Frank</b>		INDIRECT COST RATE VERIFICATION		
		Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET



# SUMMARY PROPOSAL BUDGET

YEAR 3

ORGANIZATION <b>SUNY College at Cortland</b>		FOR NSF USE ONLY	
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Amanda Davis</b>		PROPOSAL NO. <b>2114726</b>	DURATION (months) Proposed _____ Granted _____
		AWARD NO.	
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL ACAD SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. <b>Amanda Davis - Principal Inv</b>	(b) (4), (b) (6)		
2.			
3.			
4.			
5.			
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)			
7. ( <b>1</b> ) TOTAL SENIOR PERSONNEL (1 - 6)			
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)			
1. ( <b>0</b> ) POST DOCTORAL SCHOLARS			
2. ( <b>0</b> ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)			
3. ( <b>0</b> ) GRADUATE STUDENTS			
4. ( <b>0</b> ) UNDERGRADUATE STUDENTS			
5. ( <b>0</b> ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)			
6. ( <b>0</b> ) OTHER			
TOTAL SALARIES AND WAGES (A + B)			
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)			
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)			
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)			
TOTAL EQUIPMENT			<b>0</b>
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)			<b>0</b>
2. INTERNATIONAL			<b>0</b>
F. PARTICIPANT SUPPORT COSTS (b) (4)			
1. STIPENDS \$ _____			
2. TRAVEL _____			
3. SUBSISTENCE _____			
4. OTHER _____			
TOTAL NUMBER OF PARTICIPANTS ( <b>2</b> )	TOTAL PARTICIPANT COSTS	(b) (4)	
G. OTHER DIRECT COSTS			
1. MATERIALS AND SUPPLIES		(b) (4)	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION			
3. CONSULTANT SERVICES			
4. COMPUTER SERVICES			
5. SUBAWARDS			
6. OTHER			
TOTAL OTHER DIRECT COSTS			
H. TOTAL DIRECT COSTS (A THROUGH G)			
I. INDIRECT COSTS (F&A) (SPECIFY RATE AND BASE) <b>MDTC (b) (4)</b>			
TOTAL INDIRECT COSTS (F&A)		(b) (4)	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)			
K. FEE			
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)			
M. COST SHARING PROPOSED LEVEL \$ <b>0</b>	AGREED LEVEL IF DIFFERENT \$		
PI/PD NAME <b>Amanda Davis</b>	FOR NSF USE ONLY		
ORG. REP. NAME* <b>Thomas Frank</b>	INDIRECT COST RATE VERIFICATION		
	Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

# SUMMARY PROPOSAL BUDGET

YEAR 4

ORGANIZATION <b>SUNY College at Cortland</b>		FOR NSF USE ONLY		
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Amanda Davis</b>		PROPOSAL NO. <b>2114726</b>	DURATION (months)	
		AWARD NO.	Proposed	Granted
A. SENIOR PERSONNEL: PI/PI, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months	Funds Requested By proposer	Funds granted by NSF (if different)
1. <b>Amanda Davis - Principal Inv</b>		(b) (4), (b) (6)		
2.				
3.				
4.				
5.				
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)				
7. ( 1 ) TOTAL SENIOR PERSONNEL (1 - 6)				
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)				
1. ( 0 ) POST DOCTORAL SCHOLARS				
2. ( 0 ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)				
3. ( 0 ) GRADUATE STUDENTS				
4. ( 0 ) UNDERGRADUATE STUDENTS				
5. ( 0 ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				
6. ( 0 ) OTHER				
TOTAL SALARIES AND WAGES (A + B)				
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)				
TOTAL EQUIPMENT			0	
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)			0	
2. INTERNATIONAL			0	
F. PARTICIPANT SUPPORT COSTS (b) (4)				
1. STIPENDS \$				
2. TRAVEL				
3. SUBSISTENCE				
4. OTHER				
TOTAL NUMBER OF PARTICIPANTS ( 2 ) TOTAL PARTICIPANT COSTS			(b) (4)	
G. OTHER DIRECT COSTS				
1. MATERIALS AND SUPPLIES			(b) (4), (b) (6)	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				
3. CONSULTANT SERVICES				
4. COMPUTER SERVICES				
5. SUBAWARDS				
6. OTHER				
TOTAL OTHER DIRECT COSTS				
H. TOTAL DIRECT COSTS (A THROUGH G)				
I. INDIRECT COSTS (F&A)/SPECIFY RATE AND BASE MDTC (b) (4)				
TOTAL INDIRECT COSTS (F&A)			(b) (4), (b) (6)	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				
K. FEE				
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				
M. COST SHARING PROPOSED LEVEL \$ 0		AGREED LEVEL IF DIFFERENT \$		
PI/PI NAME <b>Amanda Davis</b>		FOR NSF USE ONLY		
ORG. REP. NAME* <b>Thomas Frank</b>		INDIRECT COST RATE VERIFICATION		
		Date Checked	Date Of Rate Sheet	Initials - ORG

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

# SUMMARY PROPOSAL BUDGET

Cumulative

ORGANIZATION <b>SUNY College at Cortland</b>		FOR NSF USE ONLY	
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR <b>Amanda Davis</b>		PROPOSAL NO. <b>2114726</b>	DURATION (months) Proposed      Granted
		AWARD NO.	
A. SENIOR PERSONNEL: PI/PI, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)		NSF Funded Person-months	Funds Requested By proposer
		CAL	ACAD
		SUMR	Funds granted by NSF (if different)
1. <b>Amanda Davis - Principal Inv</b>		(b) (4), (b) (6)	
2.			
3.			
4.			
5.			
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)			
7. ( 1 ) TOTAL SENIOR PERSONNEL (1 - 6)			
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)			
1. ( 0 ) POST DOCTORAL SCHOLARS			
2. ( 0 ) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)			
3. ( 0 ) GRADUATE STUDENTS			
4. ( 0 ) UNDERGRADUATE STUDENTS			
5. ( 0 ) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)			
6. ( 0 ) OTHER			
TOTAL SALARIES AND WAGES (A + B)			
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)			
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)			
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.)			
TOTAL EQUIPMENT		0	
E. TRAVEL 1. DOMESTIC (INCL. U.S. POSSESSIONS)		0	
2. INTERNATIONAL		0	
F. PARTICIPANT SUPPORT COSTS (b) (4)			
1. STIPENDS \$			
2. TRAVEL			
3. SUBSISTENCE			
4. OTHER		0	
TOTAL NUMBER OF PARTICIPANTS ( 8 )		TOTAL PARTICIPANT COSTS (b) (4)	
G. OTHER DIRECT COSTS			
1. MATERIALS AND SUPPLIES		(b) (4), (b) (6)	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION			
3. CONSULTANT SERVICES			
4. COMPUTER SERVICES			
5. SUBAWARDS			
6. OTHER			
TOTAL OTHER DIRECT COSTS			
H. TOTAL DIRECT COSTS (A THROUGH G)			
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)			
TOTAL INDIRECT COSTS (F&A)		(b) (4), (b) (6)	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)			
K. FEE			
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)			
M. COST SHARING PROPOSED LEVEL \$ 0		AGREED LEVEL IF DIFFERENT \$	
PI/PI NAME <b>Amanda Davis</b>		FOR NSF USE ONLY	
ORG. REP. NAME* <b>Thomas Frank</b>		INDIRECT COST RATE VERIFICATION	
		Date Checked	Date Of Rate Sheet
		Initials - ORG	

\*ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

*Collaborative Research: Revisiting the homeorhetic mechanisms of lactation: The role of ceramide***BUDGET JUSTIFICATION**

SUNY Cortland

**Senior Personnel:**

**Amanda Davis (Co-PI)**, Assistant Professor in the Biological Sciences Department, will serve as the primary director for REU initiatives, as well as science communication training and outreach at the Sciencenter. Major roles include selection of REU students from SUNY Cortland and providing guidance as they execute an individual research project that will involve collecting samples, performing laboratory assays, and organizing, analyzing, and presenting their results. The specific laboratory assays Davis and her students will be responsible for include colorimetric assays to determine plasma glucose, glycerol, and fatty acid concentrations; radioimmunoassays to determine serum insulin concentrations; and immunoblotting for proteins in the insulin signaling pathway. Davis will also mentor REU students by meeting with them three times per week to discuss expectations and give feedback, as well as oversee the planning and execution of REU journal clubs, workshops, farm visits, presentations, and outreach activities. Davis will coordinate the science communication training and *Ruminant with Ruminants* event at the Sciencenter, which will include creating exhibits and preparing student participants for their interactions with the public. Funds will cover her effort for (b) (4), (b) (6) each year of the project. Salary is escalated at (b) (4) per year. Year 1: (b) (4), (b) (6) Year 2: (b) (4), (b) (6) Year 3: (b) (4), (b) (6) Year 4: (b) (4), (b) (6) = (b) (4), (b) (6)

**Fringe Benefits:** Benefits are calculated on the Research Foundation for SUNY for summer salary.

Year 1 benefits are (b) (4) Year 2 benefits are (b) (4) Year 3 benefits are (b) (4)  
Year 4 benefits are (b) (4)

**Participant costs:**

**REU Supplement.** A total of (b) (4) is requested as an REU supplement to provide a stipend of (b) (4) (b) (4) a week for 8 weeks) each for two SUNY-Cortland students and (b) (4) for housing for each student for a total of (b) (4) per student per year.

**Travel:** Funds are requested to cover travel costs for REU students to travel from SUNY

Cortland to Cornell roundtrip 3 times per week. Mileage cost is based on Federal mileage rates at (b) (4) mile, with 50 miles per trip for a total of (b) (4) per year for total of (b) (4)

**Other Direct Costs:**

**Materials and Supplies:** Funds (b) (4) in Years 1-4, respectively) are required to achieve the outlined research aims. These funds will be used for lab plastics and glassware (b) (4) for Aim 1; (b) (4) for Aim 2; (b) (4) for Aim 3); pipette and balance calibrations (b) (4) for each Aim); colorimetric assays for determining preprandial and clamp glucose (b) (4) sample; 89 samples/ewe for Aims 1 and 2; 1 sample/ewe for Aim 3), total fatty acid (b) (4) sample; 29 samples/ewe for Aims 1 and 2; 1 sample/ewe for Aim 3), and glycerol concentrations (b) (4) sample; 29 samples/ewe for Aims 1 and 2; 1 sample/ewe for Aim 3); radioimmunoassays for determining preprandial and clamp serum insulin concentrations (b) (4)/sample; 29 samples/ewe for Aims 1 and 2; 1 sample/ewe for Aim 3); immunoblotting for IRS1 and AKT (b) (4) sample; 2 samples/ewe for Aim 1 and 2; 24 samples/ewe for Aim 3), immunoblotting for PP2A, and PKC (b) (4)/sample; 2 samples/ewe for Aims 1 and 2; (b) (4) for Aim 3).



All plasma and serum samples for the abovementioned assays will be performed in duplicate. Measurement of plasma glucose will be used to confirm on-site glucometer readings. For the *Ruminate with Ruminants* initiative at the Sciencenter museum and (b) (4), an additional (b) (4) will be used in year 1 to purchase supplies to create the exhibit, including balloons, LEGOs, coal, a 20' wide x 8' tall display board, brochures, laminated fact sheets, CU dairy products (i.e., milk, cheese, and yogurt), graduated cylinders, maps, sandwich bags, and scales. Gloves, protective goggles, and disposable lab coats will also be required for children and adults to feel inside the rumen of the fistulated cow. *Ruminate with Ruminants* supplies will be re-used each year for the duration of the award. The total estimated cost for materials and supplies is (b) (4).

**Project Costs:**

**Total Direct Costs:** Yr. 1: (b) (4) 97; Yr. 2: (b) (4); Yr. 3: (b) (4); Yr. 4: (b) (4)

**Modified Total Direct Costs:** Excludes Participant Support Costs. Yr. 1: (b) (4); Yr. 2: (b) (4); Yr. 3: (b) (4); Yr. 4: (b) (4)

**Indirect Costs:** Indirect Costs is applied at SUNY Cortland's negotiated rate with the US. Department of Health and Human Services at (b) (4). Yr. 1: (b) (4); Yr. 2: (b) (4); Yr. 3: (b) (4); Yr. 4: (b) (4)

**Total Project Cost:** Yr. 1=\$ (b) (4); Yr. 2=\$ (b) (4); Yr. 3: (b) (4); Yr. 4: (b) (4)

## **FACILITIES, EQUIPMENT AND OTHER RESOURCES: Cornell University**

### **A. Internal resources at Cornell University**

Cornell University (CU), located in Ithaca, NY, has the necessary facilities, resources and equipment required for the successful execution of this project. The project will be administered within CU College of Agriculture and Life Sciences (CALS). With more than 3,000 students, CALS is the second largest undergraduate college at CU and the third largest college of its kind in the United States. CALS educational programs are geared towards contemporary, real-world issues. Faculty, staff, and students at CALS are at the cutting edge of research in the life sciences, environmental sciences, food and energy systems, and community and economic vitality. In national surveys, CALS consistently ranks as the best college of agriculture and related sciences in the country. The land-grant mission of the College, which encompasses research, education, and extension programs, allows for the creation and dissemination of knowledge that improves lives for not only citizens of New York, but also the nation, and people around the globe.

The project team will have access to administrative support, facilities, offices, and computers as described. Fiscal management for McFadden will be through the Department of Animal Science, supported by CALS Office of Sponsored Research. They also will provide the legal and contractual support to ensure that the project requirements are completed in a timely manner.


(b) (4)



(b) (4)



(b) (4), (b) (6)




**A.2. Department resources:** Within the department are labs with state of the art resources including real-time PCR thermocyclers, multi-spectrum spectrophotometers, vacuum concentrators, cryotome, ultracentrifuges, scintillation counters, infrared imager, a gel documentation bioimager, additional refrigerators and freezers, and ultrasounds. A central autoclave is also available. For the proposed teaching effort, 12 classrooms are available with projection systems and internet access.

**A.3. Relevant animal resources:** CU is accredited by AAALAC and meets all federal and state regulations for animal experimentation. McFadden will work with (b) (4), (b) (6), to maintain animal care compliance. The research team will utilize the following units:

(b) (4)



**A.7. Cornell Cooperative Extension (CCE; [cce.cornell.edu](http://cce.cornell.edu)):** The CCE educational system includes highly committed CU faculty and extension associates to help apply Cornell's world class research to meaningful programming. Nationally, the CCE reaches 1.9 million people directly each year, and 15 million indirectly through print and social media. To achieve this wide span of influence, the CCE operates across 57 distance learning centers across New York State. Each county CCE office provides their community with access to educational programming focused on agriculture, community, energy, and our environment. Moreover, the CCE actively provides youth with opportunities to engage in STEM. Within the context of this proposal, McFadden will work with (b) (4), (b) (6)



**A.8. Cornell Statistical Consulting Unit ([cscu.cornell.edu](http://cscu.cornell.edu)):** Although McFadden and Davis are experienced in performing the proposed statistical analyses, CU provides consulting services if needed.

**A.9. Computers:** Eight computers (Dell PC) are found in McFadden's lab and affiliated offices. Two central printers are also available.

(b) (4), (b) (6)

**A.10. Office:** [REDACTED] and all trainees are provided office space with computer and internet access.

**A.11. Other key personnel**

(b) (4), (b) (6)

**B. External Resources**

(b) (4)



## **FACILITIES, EQUIPMENT AND OTHER RESOURCES**

### **A. Internal Resources at SUNY Cortland**

SUNY Cortland, located in Cortland, NY, is a four-year, primarily undergraduate institution (PUI) with just over 6,800 students. It is comprised of 27 departments and 67 undergraduate majors. This university has the necessary facilities, resources, and equipment for successful execution of this project. If this proposal receives NSF funding, Dr. Davis will devote effort to this project during each academic year as part of her professional obligation to the institution. In addition, the institution will provide administrative support to the NSF-funded project through its Research and Sponsored Programs Office, Business Office, and the Research Foundation for SUNY on behalf of and in conjunction with SUNY Cortland. The university also has computer support services and a machine shop on campus.

(b) (4)



**A.1.a. Office:** Dr. Davis has been allocated a dedicated office located in the same hallway as her laboratory.

**A.1.b. Computers:** Dr. Davis will have a computer in her office and her laboratory. All computers will have access to internet and printers. Several other equipment-associated computers, printers, scanners, and related facilities are available in the biology department.

### **A.1.c. Laboratory:**

(b) (4)



### **A.1.d. Other Departmental Resources:**

Important for meeting the aims of this proposal, the Davis lab will have access to a BioTek 96-well colorimetric plate reader hooked to a computer, an electrophoretic gel transfer apparatus for immunoblotting, and a syngene pxi9 chemiluminescence imager, and has the ability to perform radioactive material work. Several -80°C and -20°C freezer spaces are also shared among faculty in the department. In the unforeseen event that additional analyses need to be

done to meet the objectives of this proposal, the department has several other pieces of shared equipment and equipment in individual PI's laboratories that could be utilized, including: several microscopes (i.e., an Olympus IX83 inverted fluorescence microscope, an Olympus BX51 upright fluorescent microscope, and an Olympus SZX10 fluorescence stereomicroscope), a shared-use biosafety cabinet, two Sorval ST8 desktop centrifuges, a Sorvall Lynx 4000 clinical centrifuge, three Eppendorf 5424 microfuges, two Thermo MaxQ 4950 shaking incubators, a refrigerated Sorvall microfuge, and autoclaves. Molecular biology equipment includes two Nanodrop spectrophotometers, multiple PCR machines, an electroporator, a chem Docit<sup>2</sup> gel imager, a Biorad Gel Doc EZ, and equipment for running DNA agarose and SDS-PAGE gels. The Chemistry Department is also housed (b) (4)

Chemistry Department instrumentation includes: a Thermo Fisher LC-MS (Ultimate UPLC / LTQ XL with ESI and ACPI sources), a Thermo Fisher Ultimate HPLC/UV-Vis with fraction collector, a Bruker AVANCE 300 MHz NMR, a GE Health Sciences Akta Prime Plus FPLC, and an Agilent Cary Eclipse. The department budget supports routine maintenance of all instrumentation, the purchase of cryogens for the NMR spectrometer, and the purchase of common solvents for research labs. The university employs a full-time chemical hygiene specialist and pays for chemical waste disposal.

#### **A.2. External Resources:**

Cornell University is a 40-minute drive from SUNY Cortland and is located close to Dr Davis's commute to SUNY-Cortland. This enables us to easily take advantage of equipment necessary for performing radioimmunoassay if deemed necessary. Davis already has approval to work with radioactive materials in the Animal Science Department at Cornell under the permit of Dr. McFadden and has used the facility for this purpose many times. The resources available to perform radioimmunoassay at Cornell include a 4°C cold room, refrigerated floor centrifuge that fits over 200 tubes, a VWR multitube vortexer, an LKB-Wallac CliniGamma gamma counter, and a Geiger meter. Cornell University pays for the removal of radioactive materials from the lab.

**NSF BIOGRAPHICAL SKETCH**

NAME: McFadden, Joseph

POSITION TITLE &amp; INSTITUTION: Associate Professor, Cornell University

**(a) PROFESSIONAL PREPARATION**

INSTITUTION	LOCATION	MAJOR / AREA OF STUDY	DEGREE (if applicable)	YEAR YYYY
Cornell University	Ithaca, NY	Animal Science	BS	(b) (6)
University of Illinois	Champaign, IL	Animal Science	MS	
Virginia Tech	Blacksburg, VA	Dairy Science	PHD	
Johns Hopkins University School of Medicine	Baltimore, MD	Neuroscience	Postdoctoral Fellow	2009 - 2012

**(b) APPOINTMENTS**

2020 - present Associate Professor, Cornell University, Department of Animal Science, Ithaca, NY  
 2017 - 2020 Assistant Professor, Cornell University, Department of Animal Science, Ithaca, NY  
 2012 - 2017 Assistant Professor, West Virginia University, Division of Animal and Nutritional Sciences, Morgantown, WV  
 2010 - 2012 Adjunct Professor, Anne Arundel Community College, Department of Biology, Arnold, MD

**(c) PRODUCTS****Products Most Closely Related to the Proposed Project**

- McFadden JW, Rico JE. Invited review: Sphingolipid biology in the dairy cow: The emerging role of ceramide. J Dairy Sci. 2019 Sep;102(9):7619-7639. PubMed PMID: [31301829](#).
- Davis AN, Myers WA, Chang C, Tate BN, Rico JE, Moniruzzaman M, Haughey NJ, McFadden JW. Somatotropin increases plasma ceramide in relation to enhanced milk yield in cows. Domest Anim Endocrinol. 2021 Jan;74:106480. PubMed PMID: [32615506](#).
- Rico JE, Myers WA, Laub DJ, Davis AN, Zeng Q, McFadden JW. Hot topic: Ceramide inhibits insulin sensitivity in primary bovine adipocytes. J Dairy Sci. 2018 Apr;101(4):3428-3432. PubMed PMID: [29395144](#).
- Davis AN, Clegg JL, Perry CA, McFadden JW. Nutrient Restriction Increases Circulating and Hepatic Ceramide in Dairy Cows Displaying Impaired Insulin Tolerance. Lipids. 2017 Sep;52(9):771-780. PubMed PMID: [28836149](#).
- Rico JE, Bandaru VV, Dorskind JM, Haughey NJ, McFadden JW. Plasma ceramides are elevated in overweight Holstein dairy cows experiencing greater lipolysis and insulin resistance during the transition from late pregnancy to early lactation. J Dairy Sci. 2015 Nov;98(11):7757-70. PubMed PMID: [26342987](#); PubMed Central PMCID: [PMC6075710](#).

**Other Significant Products, Whether or Not Related to the Proposed Project**

- Rico JE, Specker B, Perry CA, McFadden JW. Plasma Ceramides and Triglycerides Are Elevated during Pregnancy in Association with Markers of Insulin Resistance in Hutterite Women. Lipids.

BS-1 of 2

- 2020 Jul;55(4):375-386. PubMed PMID: [32430917](#).
2. McFadden JW. Review: Lipid biology in the periparturient dairy cow: contemporary perspectives. *Animal*. 2020 Mar;14(S1):s165-s175. PubMed PMID: [32024571](#).
  3. Rico JE, Giesy SL, Haughey NJ, Boisclair YR, McFadden JW. Intravenous Triacylglycerol Infusion Promotes Ceramide Accumulation and Hepatic Steatosis in Dairy Cows. *J Nutr*. 2018 Oct 1;148(10):1529-1535. PubMed PMID: [30281114](#).
  4. Rico JE, Saed Samii S, Mathews AT, Lovett J, Haughey NJ, McFadden JW. Temporal changes in sphingolipids and systemic insulin sensitivity during the transition from gestation to lactation. *PLoS One*. 2017;12(5):e0176787. PubMed PMID: [28486481](#); PubMed Central PMCID: [PMC5423608](#).
  5. Rico JE, Mathews AT, Lovett J, Haughey NJ, McFadden JW. Palmitic acid feeding increases ceramide supply in association with increased milk yield, circulating nonesterified fatty acids, and adipose tissue responsiveness to a glucose challenge. *J Dairy Sci*. 2016 Nov;99(11):8817-8830. PubMed PMID: [27638262](#).

**(d) SYNERGISTIC ACTIVITIES**

1. Communicate Animal Science: Ruminant On This | At Cornell University, I developed an animal science communications course for undergraduates that integrates the use of a podcast, called Ruminant On This, to educate the public about the science of food animal production and the impact it has on our environment and food security. Students interview food consumers, scientists, and producers to address scientific misconceptions and highlight how scientific innovations like biotechnology have advanced sustainable food production.
2. Ruminant with Ruminants at the Sciencenter! | At the Sciencenter (Ithaca, NY), this hands-on workshop for 30 children and 20 adults allowed attendees to explore a fistulated cow rumen. Students were guided through a series of science stations that taught them (a) the importance of the rumen microflora for digestion, (b) how nutrient composition of feeds influences fetal growth and milk production, and (c) common misconceptions and myths about recombinant somatotropin and plant-based GMOs were discussed with attending adults. Participants gained an understanding of ruminant physiology and how the use of recombinant somatotropin may be a means to support sustainable food production.
3. Mentor: I mentored four postdocs, eight PhD students (including 3 fellows; 4 completed degrees), four MS students (4 completed degrees), forty-nine undergraduate researchers (11 as published co-authors) and three visiting research interns. The majority of my trainees are minorities and female.
4. The Cow Workshop | As part of the Science Saturday series, I partnered with Learning Options, Inc. (Fairmont, WV) to teach middle school children ruminant biology using hands-on learning. Children compared their own diet with what ruminants eat. Students were challenged to understand the importance of fat, protein, and carbohydrate intake to support their own growth but also lactation in mammals. The students used math to calculate nutrient intake and efficiency to make milk.
5. Integrated use of 3D printing in Biochemistry | As the instructor of Biochemistry at West Virginia University, I incorporated the use of 3D printing technology as a learning tool to better understand secondary, tertiary, and quaternary protein structure. Undergraduates worked in unison to prepare a 4'x20' diorama of oxidative phosphorylation that included 3D-printed enzymes of the electron transport chain and ATP synthase. Students gained a better understanding of structural motifs, non-covalent interactions, and their relationship with structure and function.



**NSF BIOGRAPHICAL SKETCH**

NAME: Davis, Amanda

ORCID: 0000-0002-6370-3075

POSITION TITLE &amp; INSTITUTION: Assistant Professor of Biological Sciences, SUNY Cortland

**(a) PROFESSIONAL PREPARATION**

INSTITUTION	LOCATION	MAJOR / AREA OF STUDY	DEGREE (if applicable)	YEAR YYYY
West Virginia Wesleyan College	Buckhannon, WV	Biology	BS	(b) (6)
West Virginia University	Morgantown, WV	Animal Physiology	MS	
Cornell University	Ithaca, NY	Animal Science	PHD	

**(b) APPOINTMENTS**

2020 - present Assistant Professor of Biological Sciences, SUNY Cortland, Cortland, NY

2019 - 2020 Adjunct Professor, SUNY Cortland, Cortland, NY

**(c) PRODUCTS****Products Most Closely Related to the Proposed Project**

1. Davis AN, Myers WA, Chang C, Tate BN, Rico JE, Moniruzzaman M, Haughey NJ, McFadden JW. Somatotropin increases plasma ceramide in relation to enhanced milk yield in cows. *Domest Anim Endocrinol*. 2021 Jan;74:106480. PubMed PMID: [32615506](#).
2. Davis AN, Rico JE, Myers WA, Coleman MJ, Clapham ME, Haughey NJ, McFadden JW. Circulating low-density lipoprotein ceramide concentrations increase in Holstein dairy cows transitioning from gestation to lactation. *J Dairy Sci*. 2019 Jun;102(6):5634-5646. PubMed PMID: [30904311](#).
3. Davis AN, Clegg JL, Perry CA, McFadden JW. Nutrient Restriction Increases Circulating and Hepatic Ceramide in Dairy Cows Displaying Impaired Insulin Tolerance. *Lipids*. 2017 Sep;52(9):771-780. PubMed PMID: [28836149](#).
4. Rico JE, Myers WA, Laub DJ, Davis AN, Zeng Q, McFadden JW. Hot topic: Ceramide inhibits insulin sensitivity in primary bovine adipocytes. *J Dairy Sci*. 2018 Apr;101(4):3428-3432. PubMed PMID: [29395144](#).
5. Phipps ZC, Seck F, Davis AN, Rico JE, McFadden JW. Technical note: Characterization of ceramide in bovine lipoproteins. *J Dairy Sci*. 2017 Oct;100(10):8602-8608. PubMed PMID: [28755941](#).

**Other Significant Products, Whether or Not Related to the Proposed Project**

1. Myers WA, Rico JE, Davis AN, Fontoura ABP, Dineen MJ, Tate BN, McFadden JW. Effects of abomasal infusions of fatty acids and one-carbon donors on hepatic ceramide and phosphatidylcholine in lactating Holstein dairy cows. *J Dairy Sci*. 2019 Aug;102(8):7087-7101. PubMed PMID: [31178188](#).
2. Samii SS, Rico JE, Mathews AT, Davis AN, Orndorff CL, Aromeh LO, McFadden JW. Effects of body condition score on direct and indirect measurements of insulin sensitivity in periparturient

BS-1 of 2

- dairy cows. *Animal*. 2019 Nov;13(11):2547-2555. PubMed PMID: [31104643](#).
3. Zang Y, Samii SS, Myers WA, Bailey HR, Davis AN, Grilli E, McFadden JW. Methyl donor supplementation suppresses the progression of liver lipid accumulation while modifying the plasma triacylglycerol lipidome in periparturient Holstein dairy cows. *J Dairy Sci*. 2019 Feb;102(2):1224-1236. PubMed PMID: [30471914](#).
  4. Fontoura ABP, Rico JE, Davis AN, Myers WA, Tate BN, Gervais R, McFadden JW. Effects of dietary deoiled soy lecithin supplementation on milk production and fatty acid digestibility in Holstein dairy cows. *J Dairy Sci*. 2020 Nov 24; PubMed PMID: [33246607](#).
  5. McGuckin MM, Giesy SL, Davis AN, Abyeta MA, Horst EA, Saed Samii S, Zang Y, Butler WR, Baumgard LH, McFadden JW, Boisclair YR. The acute phase protein orosomucoid 1 is upregulated in early lactation but does not trigger appetite-suppressing STAT3 signaling via the leptin receptor. *J Dairy Sci*. 2020 May;103(5):4765-4776. PubMed PMID: [32229118](#).

#### **(d) SYNERGISTIC ACTIVITIES**

1. Educator: Ruminant with Ruminants at the Sciencenter (2018): I worked with the Sciencenter (Ithaca, NY) to provide a hands-on workshop to 30 children and 20 adults. Attendees explored the rumen of a fistulated cow and were guided through stations highlighting the importance of rumen microflora for digestion, and how nutrient composition of feeds influences fetal growth and milk production. Common misconceptions about recombinant somatotropin and genetically modified organisms were discussed with parents. Participants gained a better understanding of ruminant physiology and how recombinant somatotropin use may support sustainable food production.
2. Educator: Expand Your Horizons (EYH) Workshop (2019-2020): I served as a female scientist role model for EYH — a one-day conference designed to spark interest in STEM and foster awareness of opportunities in STEM-related careers in 7th-9th grade girls through hands-on workshops. In my ruminant physiology and nutrition workshop, students learned the differences and similarities between a human and a cow digestive tract and why a cow is better equipped to digest forages compared to humans. I also spoke to the students about my research and helped them better understand what careers are available in animal science.
3. Educator: The Cow Workshop (2017): As part of the Science Saturday series, I partnered with Learning Options, Inc. (Fairmont, WV) to teach middle school children ruminant biology using hands-on learning. Children compared their own diet with what ruminants eat. Students were challenged to understand the importance of fat, protein, and carbohydrate intake to support their own growth but also lactation in mammals. The use of math to formulate diets to meet mammalian energy requirements was emphasized.
4. Professional Development: Cornell Animal Science Research Symposium (2018): I organized this symposium to give graduate students and undergraduates an opportunity to compete in oral talks or poster presentations within our department. This symposium was impactful because students disseminated knowledge about their research to their colleagues and received feedback from faculty judges.
5. Mentor (2015-2020): As a graduate student, I have mentored 28 undergraduate students and 5 graduate students on lab and in vivo techniques. Of those students, I guided 1 on the completion of his undergraduate thesis, and 6 of them became co-authors on publications. At SUNY Cortland, I have 1 undergraduate who will participate in research in my lab this year.

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**Other Personnel Biographical Information**

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**Data Not Available**

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**Other Personnel Biographical Information**

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**Data Not Available**



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**NSF CURRENT AND PENDING SUPPORT**

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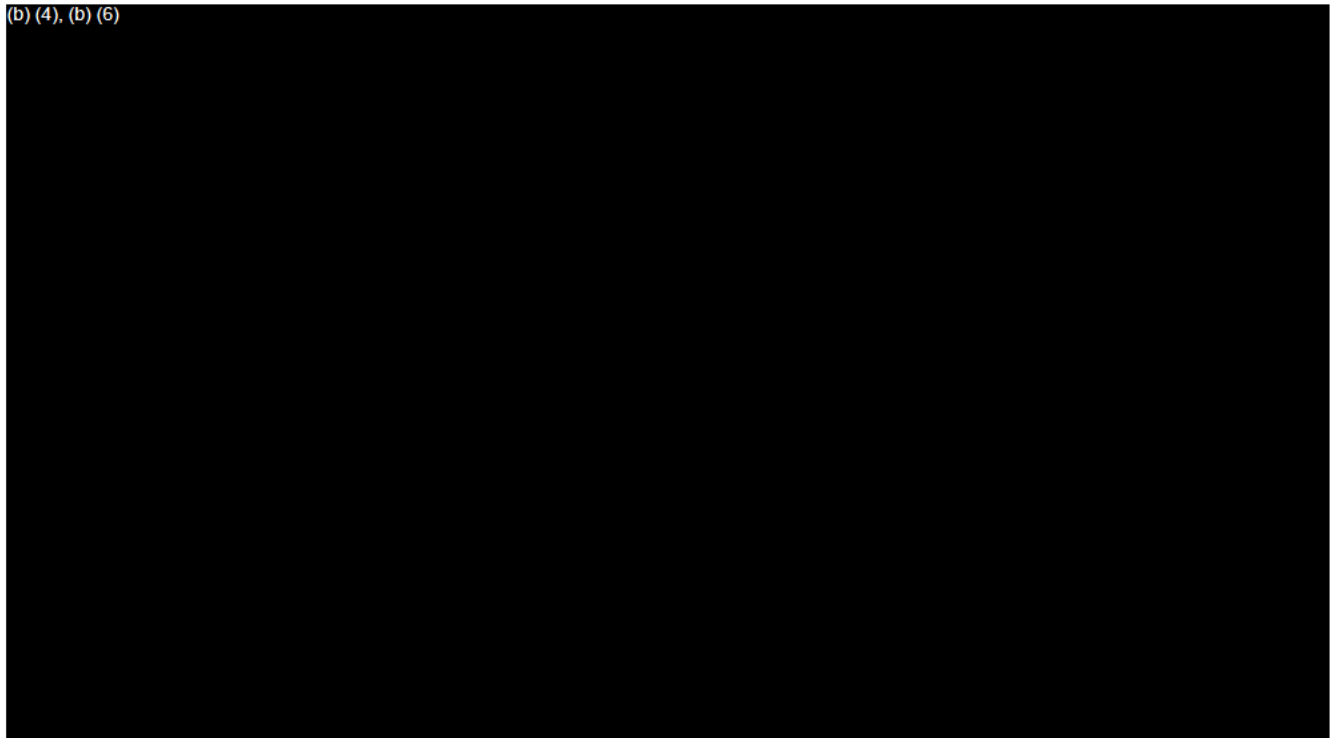
PI/co-PI/Senior Personnel: McFadden, Joseph

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**PROJECT/PROPOSAL CURRENT SUPPORT**

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(b) (4), (b) (6)



2. Project/Proposal Title: The therapeutic potential of lysophospholipids as immunomodulatory compounds

Proposal/Award Number (if available): 2019-04986

Source of Support: USDA NIFA AFRI Exploratory

Primary Place of Performance: Cornell University

Project/Proposal Support Start Date (if available): 2020/01

Project/Proposal Support End Date (if available): 2021/12

Total Award Amount (including Indirect Costs): \$199,985

Person-Month(s) (or Partial Person-Months) Per Year Committed to the Project:

Year	Person-months per year committed
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Year	Person-months per year committed
2020	(b) (4), (b) (6)
2021	

3. Project/Proposal Title: Methyl donor supplementation to mitigate fatty liver disease in dairy cattle

Proposal/Award Number (if available): NYC-127300

Source of Support: USDA Federal Capacity Funding (Hatch)

Primary Place of Performance: Cornell University

Project/Proposal Support Start Date (if available): 2019/10

Project/Proposal Support End Date (if available): 2022/09

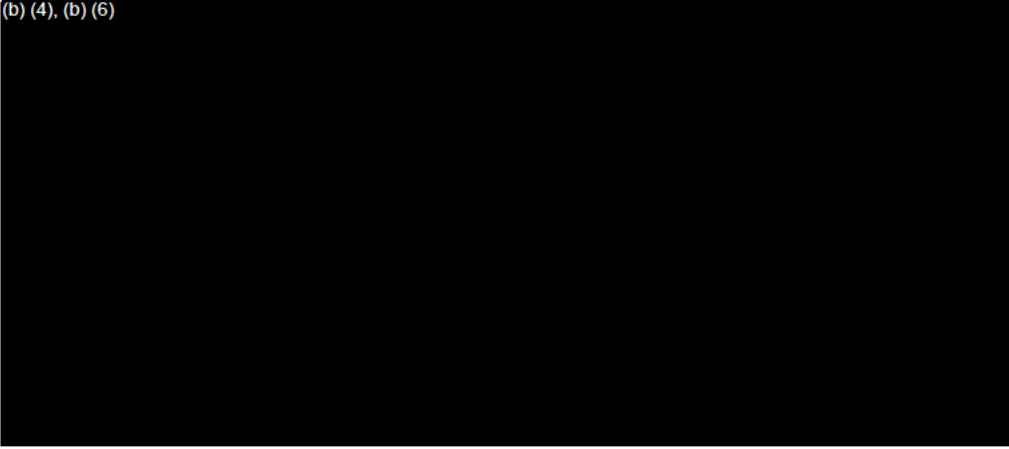
Total Award Amount (including Indirect Costs): \$105,000

Person-Month(s) (or Partial Person-Months) Per Year Committed to the Project:

Year	Person-months per year committed
2019	(b) (4), (b) (6)
2020	
2021	
2022	

(b) (4), (b) (6)

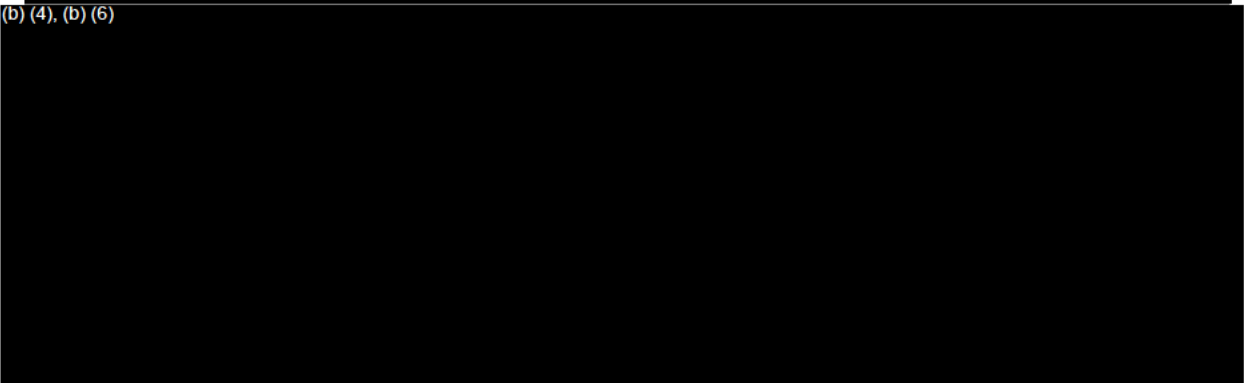
(b) (4), (b) (6)



(b) (4)

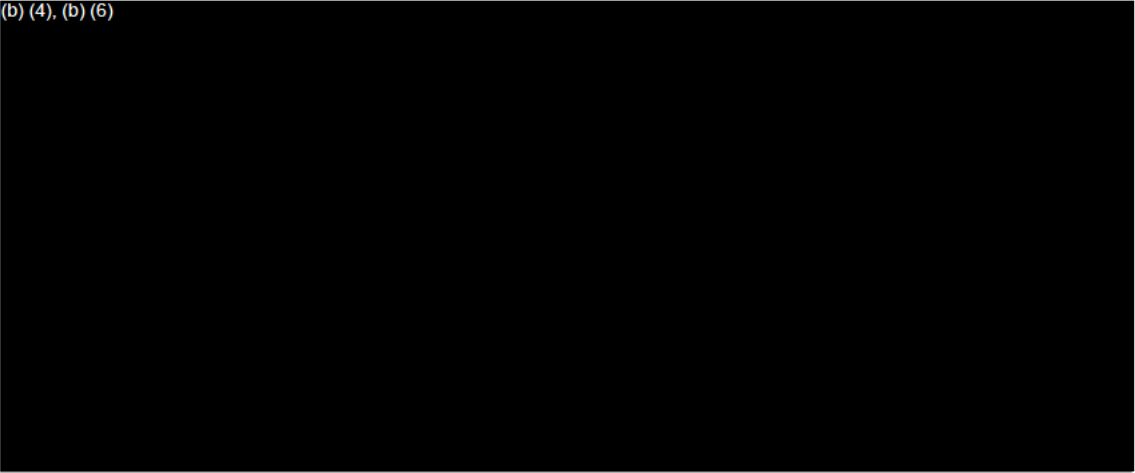


(b) (4), (b) (6)



CPS-3 of 5

(b) (4), (b) (6)



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**PROJECT/PROPOSAL PENDING SUPPORT**

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1. Project/Proposal Title: The effects of dietary emulsifiers on fat digestion in dairy cows.

Proposal/Award Number (if available):

Source of Support: USDA Federal Capacity Funding (Hatch)

Primary Place of Performance: Cornell University

Project/Proposal Support Start Date (if available): 2021/10

Project/Proposal Support End Date (if available): 2024/09

Total Award Amount (including Indirect Costs): \$90,000

Person-Month(s) (or Partial Person-Months) Per Year Committed to the Project:

Year	Person-months per year committed	
2021	(b) (4), (b) (6)	
2022		
2023		
2024		

2. Project/Proposal Title: Collaborative Research: Revisiting the homeorhetic mechanisms of lactation: The role of ceramide

Proposal/Award Number (if available):

Source of Support: NSF IOS

Primary Place of Performance: Cornell University



(b) (6)



3. Project/Proposal Title: Effects of serine palmitoyltransferase inhibition on insulin sensitivity and milk production in dairy cows

Proposal/Award Number (if available):

Source of Support: USDA NIFA AFRI

Primary Place of Performance: Cornell University

Project/Proposal Support Start Date (if available): 2021/01

Project/Proposal Support End Date (if available): 2023/12

Total Award Amount (including Indirect Costs): \$500,000

Person-Month(s) (or Partial Person-Months) Per Year Committed to the Project:

Year	Person-months per year committed
2021	(b) (4), (b) (6)
2022	
2023	

**NSF CURRENT AND PENDING SUPPORT**

**OMB-3145-0058**

\*PI/co-PI/Senior Personnel Name: Michelle Kortenaar

NSF ID:

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**\*Required fields**

**Note:** NSF has provided 10 Project/Proposal and 10 in-kind contribution entries for users to populate. Please leave any unused entries blank.

**Project/Proposal Section:**

Current and Pending Support includes all resources made available to an individual in support of and/or related to all of his/her research efforts, regardless of whether or not they have monetary value.<sup>[1]</sup> Information must be provided about all current and pending support, including this project, for ongoing projects, and for any proposals currently under consideration from whatever source<sup>[2]</sup>, irrespective of whether such support is provided through the proposing organization or is provided directly to the individual. Concurrent submission of a proposal to other organizations will not prejudice its review by NSF, if disclosed.<sup>[3]</sup>

Please enter your support entries so they are grouped together based on the "Status of Support" and are in the order of Current, Pending, Submission Planned, and Transfer of Support from top to bottom

[1] If the time commitment or dollar value is not readily ascertainable, reasonable estimates should be provided.

[2] For example, Federal, State, local, foreign, public or private foundations, non-profits, industrial or other commercial organizations or internal funds allocated toward specific projects.

[3] The Biological Sciences Directorate exception to this policy is delineated in PAPPG Chapter II.D.2.

**Projects/Proposals**

(b) (4), (b) (6)

2.\*Project/Proposal Title : Investigating the Impact of Head Start Family Interactions on Children's STEM Process Skills during Family Events at Two Science Centers

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available): 2005594

\*Source of Support: NSF

\*Primary Place of Performance : Ithaca, NY

Project/Proposal Start Date (MM/YYYY) (if available) : 09/2020

Project/Proposal End Date (MM/YYYY) (if available) : 08/2022

\*Total Award Amount (including Indirect Costs): \$ 297,336

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1. 2021	(b) (4), (b) (6)	4.	
2. 2022		5.	
3.			

CPS- 2 of 12

**Projects/Proposals**

3.\*Project/Proposal Title : Migration and Survival of Exoplanets near Magnetized Young Stars

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available): 2009820

\*Source of Support: NSF

\*Primary Place of Performance : Ithaca, NY

Project/Proposal Start Date (MM/YYYY) (if available) : 08/2020

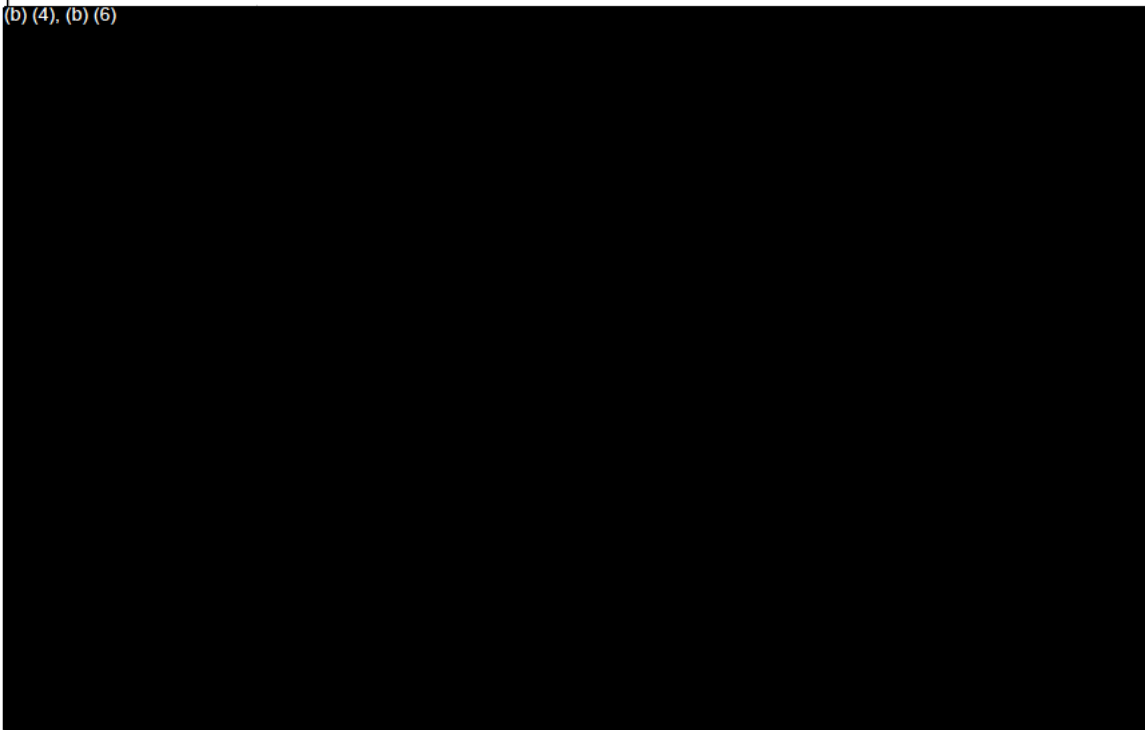
Project/Proposal End Date (MM/YYYY) (if available) : 07/2023

\*Total Award Amount (including Indirect Costs): \$ (b) (4)

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1. 2021	(b) (4), (b) (6)	4.	
2. 2022		5.	
3. 2023			

(b) (4), (b) (6)





**Projects/Proposals**

(b) (4), (b) (6)

6.\*Project/Proposal Title : Collaborative Research: Grounding Institutional Partnerships in Structures for Broader Impacts Design

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available): 1610039

\*Source of Support: NSF

\*Primary Place of Performance : Ithaca, NY

Project/Proposal Start Date (MM/YYYY) (if available) : 03/2017

Project/Proposal End Date (MM/YYYY) (if available) : 02/2028

\*Total Award Amount (including Indirect Costs): \$ 768,530

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1. 2021	(b) (4), (b) (6)	4.	
2.		5.	
3.			

CPS- 4 of 12

**Projects/Proposals**

7.\*Project/Proposal Title : Life on the Edge

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support: NASA

\*Primary Place of Performance : Ithaca, NY

Project/Proposal Start Date (MM/YYYY) (if available) : 10/2016

Project/Proposal End Date (MM/YYYY) (if available) : 09/2021

\*Total Award Amount (including Indirect Costs): \$ 1,250,000

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1. 2021	(b) (4), (b) (6)	4.	
2.		5.	
3.			

8.\*Project/Proposal Title : Explore Science: Destination Moon

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support: NASA

\*Primary Place of Performance : Ithaca, NY

Project/Proposal Start Date (MM/YYYY) (if available) : 01/2021

Project/Proposal End Date (MM/YYYY) (if available) : 12/2023

\*Total Award Amount (including Indirect Costs): \$ 998,433

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1. 2021	(b) (4), (b) (6)	4.	
2. 2022		5.	
3. 2023			

**Projects/Proposals**

(b) (4), (b) (6)

**10.\*Project/Proposal Title :**\*Status of Support :    ☐ Current    ☐ Pending    ☐ Submission Planned    ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

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**In Kind Contributions**


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\*Required fields

**In-Kind Contribution Section:**

Current and Pending Support also includes in-kind contributions (such as office/laboratory space, equipment, supplies, employees, students). If the in-kind contributions are intended for use on the project being proposed to NSF, the information must be included as part of the Facilities, Equipment and Other Resources section of the proposal and need not be replicated in the individual's Current and Pending Support submission. In-kind contributions not intended for use on the project/proposal being proposed that have associated time obligations must be reported below. If the time commitment or dollar value is not readily ascertainable, reasonable estimates should be provided.

Please enter your support entries so they are grouped together based on the "Status of Support" and are in the order of Current to Pending from top to bottom

1.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$



**In Kind Contributions**2.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

3.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**4.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

5.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**6.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

7.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**8.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

9.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**

10.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$



NSF CURRENT AND PENDING SUPPORT

OMB-3145-0058

\*PI/co-PI/Senior Personnel Name: Amanda Davis

NSF ID: (b) (4), (b) (6)

**\*Required fields**

**Note:** NSF has provided 10 Project/Proposal and 10 in-kind contribution entries for users to populate. Please leave any unused entries blank.

**Project/Proposal Section:**

Current and Pending Support includes all resources made available to an individual in support of and/or related to all of his/her research efforts, regardless of whether or not they have monetary value.<sup>[1]</sup> Information must be provided about all current and pending support, including this project, for ongoing projects, and for any proposals currently under consideration from whatever source<sup>[2]</sup>, irrespective of whether such support is provided through the proposing organization or is provided directly to the individual. Concurrent submission of a proposal to other organizations will not prejudice its review by NSF, if disclosed.<sup>[3]</sup>

Please enter your support entries so they are grouped together based on the "Status of Support" and are in the order of Current, Pending, Submission Planned, and Transfer of Support from top to bottom

[1] If the time commitment or dollar value is not readily ascertainable, reasonable estimates should be provided.

[2] For example, Federal, State, local, foreign, public or private foundations, non-profits, industrial or other commercial organizations or internal funds allocated toward specific projects.

[3] The Biological Sciences Directorate exception to this policy is delineated in PAPPG Chapter II.D.2.

**Projects/Proposals**

1.\*Project/Proposal Title : Collaborative Research: Revisiting the homeorhetic mechanisms of mammalian lactation: The role of ceramide

\*Status of Support : ☐ Current ☒ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support: National Science Foundation

\*Primary Place of Performance : SUNY Cortland

Project/Proposal Start Date (MM/YYYY) (if available) : 08/2021

Project/Proposal End Date (MM/YYYY) (if available) : 07/2025

\*Total Award Amount (including Indirect Costs): \$ 200,806

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##) (b) (4), (b) (6)	Calendar Year (YYYY)	Person Months (##.##) (b) (4), (b) (6)
1. 2021		4. 2024	
2. 2022		5. 2025	
3. 2023			

2.\*Project/Proposal Title :

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

**Projects/Proposals**

3.\*Project/Proposal Title :

\*Status of Support : ☒ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

4.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☒ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

**Projects/Proposals**

5.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☒ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

6.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☒ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

**Projects/Proposals**

7.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☒ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

8.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☒ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			



**Projects/Proposals**

9.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

10.\*Project/Proposal Title :

\*Status of Support : ☐ Current ☐ Pending ☐ Submission Planned ☐ Transfer of Support

Proposal/Award Number (if available):

\*Source of Support:

\*Primary Place of Performance :

Project/Proposal Start Date (MM/YYYY) (if available) :

Project/Proposal End Date (MM/YYYY) (if available) :

\*Total Award Amount (including Indirect Costs): \$

\*Person-Month(s) (or Partial Person-Months) Per Calendar Year Committed to the Project

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

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**In Kind Contributions**


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\*Required fields

**In-Kind Contribution Section:**

Current and Pending Support also includes in-kind contributions (such as office/laboratory space, equipment, supplies, employees, students). If the in-kind contributions are intended for use on the project being proposed to NSF, the information must be included as part of the Facilities, Equipment and Other Resources section of the proposal and need not be replicated in the individual's Current and Pending Support submission. In-kind contributions not intended for use on the project/proposal being proposed that have associated time obligations must be reported below. If the time commitment or dollar value is not readily ascertainable, reasonable estimates should be provided.

Please enter your support entries so they are grouped together based on the "Status of Support" and are in the order of Current to Pending from top to bottom

1.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**2.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

3.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**4.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

5.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**6.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

7.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$



**In Kind Contributions**8.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

9.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**In Kind Contributions**

10.\*Status of Support : ☐ Current ☐ Pending

\*Source of Support :

\*Primary Place of Performance :

\*Summary of In-Kind Contributions :

Time Commitment - Month(s) (or Partial Person-Months) Committed Per Calendar Year

If the time commitment is not readily ascertainable, reasonable estimates should be provided.

*Calendar Year (YYYY)	*Person Months (##.##)	Calendar Year (YYYY)	Person Months (##.##)
1.		4.	
2.		5.	
3.			

\*Dollar Value of In-Kind Contribution: \$

**Collaborative Research:  
Revisiting the homeorhetic mechanisms of lactation: The role of ceramide.**

**Data Management Plan**

McFadden will be responsible for all experimental documentation, samples, and data (Aim 1 through 3); albeit, Davis will be responsible for coordinating REU involvement and sharing affiliated data with McFadden. McFadden and Davis will co-manage broader impact information.

**1. Data and materials produced**

Following IACUC approval, research data collected during animal care and use will include feed intake and refusals, body weights, rectal temperatures, milk produced, and general health observations and veterinary interventions. These data will be recorded using a laboratory notebook then copied into an Excel spreadsheet within 30 d of collection. A similar approach will be utilized to record all methodology utilized to perform analyses and culture primary myotubes (e.g., cell counts, treatment and media formulations, and viability tests). All other data including feed and milk composition, colorimetry, mass spectral, immunoblotting, ELISA, and enzyme activity data will be immediately recorded within Excel spreadsheets the day of collection. For quality control, data will be entered by a graduate or REU student then validated by McFadden or Davis at least once per quarter. Excel spreadsheets will be saved as a comma-separated value (.csv) file. All data within .csv file format will be statistically analyzed using SAS and data outputs will be saved in Excel. Drafts and finalized scientific abstracts and manuscripts will be saved in Word (.docx) file format.

Research samples (feed, milk, plasma, lipoprotein fractions, tissue and cell pellets) collected will be immediately snap-frozen on dry ice and stored at -80°C until analysis. Weekly feed samples will be frozen and composited at trial completion. Plasma samples for each time point and treatment will be divided across 9 aliquots. A minimum of three milk and tissue aliquots will be stored. Tissue will be processed on dry ice in order to conserve tissue for future analyses. All laboratory freezers are linked to 24/7 temperature monitoring with e-alarms sent directly to McFadden via e-mail and cellular text messaging.

Documentation used for interactions with the Sciencenter and (b) (4) will be saved in Excel (.csv), Word (.docx), and Powerpoint (.pptx) file formats and stored on a virtual folder (i.e., Box) for shared access by McFadden and Davis. Course syllabus and electronic course evaluations are recorded and saved on the Cornell University College of Agriculture and Life Sciences website.

**2. Standards, formats and metadata**

Raw data files will include written observation logs, and mass spectral data (.mzML) and Excel spreadsheets as .csv files. To ensure data can be understood and properly reused by other researchers, we will document our work with readme metadata files (following the basic template and format suggested at <https://data.research.cornell.edu/content/readme>). These readme files will explain the timeframe of work, geographic locations, filenames, abbreviations and units of measure, relationships between files, statements of re-use and attribution, and researcher contact information. For all statistical files, we will save and share all syntax files as text, to provide details of reading in the file to the software, including any manipulations to the data and procedures used along with labels and formats.

### **3. Roles and responsibilities**

Although graduate or REU students will be responsible for establishing sample and data inventories, McFadden and Davis will be responsible for all data management during and after collection. McFadden and Davis will ensure that the data management plan is executed and maintained by meeting with students monthly to review adherence. Six months prior to the departure of student trainee, McFadden and Davis will meet with the student to ensure that samples and files are archived for future use. If a student departs the lab prematurely and unexpectedly, McFadden or Davis will immediately check to ensure security of all samples and data. Moreover, McFadden or Davis will ensure that trainees are adequately familiarized with the data management plan prior to their use of the data. If McFadden or Davis unexpectedly leaves, Dr. Thomas Overton (Cornell University Department Chair) or Dr. Patricia Conklin (SUNY Cortland Department Chair) will coordinate with remaining lab personnel and manage the data.

### **4. Dissemination methods**

After publication no later than two years past final data collection, McFadden and Davis will provide all data for public use by submitting excel .csv data sets to [eCommons@Cornell](mailto:eCommons@Cornell) (<http://ecommons.cornell.edu/>), a service of the CU Library that provides long-term access to a broad range of Cornell-related digital content of enduring value. Items in eCommons are openly accessible via the Internet, and are assigned a permanent identifier, making it easy to persistently reference data sets in publications or other documents. The CU Library is committed to the bit-level preservation of items deposited in eCommons. Additionally, peer-reviewed scientific abstracts and articles will be published in journals with open-access permissions including the *American Journal of Physiology Regulatory, Integrative and Comparative Physiology*. Complete lipidomic data findings will be published in the main narrative or as supplemental findings. Such approaches will enable the discovery and use of our data by the wider scientific community.

### **5. Policies for data sharing and public access**

McFadden and Davis will retain exclusive rights to the samples and data until the resulting peer-reviewed publication is generated or within two years of data production. Written evaluations of learning assessment will be copied, and filed within the office of McFadden and the Cornell University Department of Animal Science central storage located in Morrison Hall. Once publically available, data will be shared with a CC BY 4.0 statement which means the information is fully open and accessible to the public with attribution to the original data creators.

### **6. Archiving, storage and preservation**

During the course of research data collection, the project team will use Cornell's enterprise version of Microsoft's OneDrive, a cloud-based password-protected data storage and collaboration platform. OneDrive maintains data in an encrypted format, versioning, and customizable read/write permissions, allowing only authorized individual's access to the data. We will also maintain storage of all laboratory notebooks in a fire-proof cabinet within the office of McFadden (264 Morrison) or Davis (231 Bowers Hall). At experiment completion, all data will be copied and deposited to the CU eCommons repository.

*Should our proposed research generate additional data sets of value that we did not anticipate at the time of this proposal, we will consult with the CU Research Data Management Service Group (<http://data.research.cornell.edu/>) to determine an appropriate data management strategy.*

**Postdoctoral Mentoring Plan**

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**Data Not Available**



## H. REU supplement

### H.1. REU project aims

In order for the United States to expand economic prosperity and remain internationally competitive, broadening participation in the scientific workforce is essential<sup>[131]</sup>. Recruiting and retaining interested women and minorities are critical strategies to meet this goal<sup>[132]</sup>, and undergraduate research experiences are increasingly considered to be effective approaches to retain students on a scientific career pathway<sup>[133-136]</sup>. Participation in undergraduate research increases self-efficacy and career ambitions for underrepresented students in STEM and promotes entry to professional and academic STEM career tracks involving post-graduate study<sup>[137]</sup>. Recruiting underrepresented minorities and women for participation in our proposed REU is a means to expand participation and increase diversity in the scientific workforce and is in alignment with NSF's mission. We will recruit these students from SUNY Cortland, a university with no animal science program, to increase student interest in solving the pending world food crisis.

The goals of this REU supplement are to provide SUNY Cortland undergraduates (1) the opportunity to learn about how efficient nutrient utilization by domestic food animals can help achieve global food security and reduce environmental impact, (2) research experience so they can develop fundamental field and laboratory STEM skills, (3) communication training so they can educate the public about the importance of science, and (4) career planning for STEM fields including animal science. To accomplish these goals, REU students will engage in summer research and mentorship in the labs of Davis (b) (4)

(b) (4) will be used as a research and classroom location. Students will engage in performing research, journal clubs, professional development workshops, and science communication training. Students will communicate to the public how changes in nutrient utilization by livestock influences food production efficiency, environmental change, and food security at the Sciencenter museum (Ithaca, NY; (b) (4))

### H.2. Nature of undergraduate involvement

Each summer REU participants will execute an individual research project that will involve collecting samples, performing laboratory assays, and organizing, analyzing, and presenting their results. Students will spend approximately 5 hours each week participating in mentorship, education, and outreach activities that are integrated with the research. The major theme that will be conveyed is that improvements in efficiency of nutrient utilization in food animals improves food security and reduces environmental impact.

#### H.2.a. Research engagement and mentorship

Undergraduates will report to the SUNY Cortland or CU site under the guidance of Davis or McFadden, respectively. To facilitate effective mentor-mentee relationships, REU students will meet with Davis three times per week to outline expectations, check in on progress, and give feedback on both mentor and mentee performance. We understand that our REU students likely do not have much research experience at this stage of development, so our goal is to facilitate open communication where students feel free to ask questions and learn. McFadden and his graduate students will co-mentor REU students at every stage of development. Students will acquire transferrable skills through hands-on research experience and mentorship, which includes critical thinking, problem-solving, communication, collaboration, and independence. These skills will be acquired through various activities including experimental planning and design, animal care and handling (e.g., feeding, treating, and milking), collecting field data (e.g., feed intakes and milk yields), maintaining a cell culture system, sample collection and processing, benchtop colorimetry and immunological assays (e.g., plasma glucose and insulin, and Western blots), data organization using Excel, data analysis using SAS, and presentation of results using Microsoft PowerPoint.

In years 1 through 3 (Aim 1 and 2 of the Project Description), REU students will work to determine whether ceramide inhibits insulin action to partition glucose towards the mammary gland for the synthesis of milk and whether the homeorhetic actions of somatotropin (ST) involve ceramide-dependent mechanisms.

(b) (4) In years 3 and 4 (Aim 2 and 3 of the Project Description), students will work toward the above goals, while also learning cell culture techniques to determine whether ceramide mediates insulin resistance in myotubes. For each of these aims, students will be involved in the collection and analysis of at least one experimental block of samples for their project.

In addition, REU students will share the responsibility to estimate the environmental impact of the research (Project Description D.5.1.). REU students will calculate changes in milk production efficiency, and determine animal requirements, feed, land, and water requirements, methane and carbon dioxide production, and carbon footprint that would be required to produce an equivalent amount of milk in the experimental scenarios of Aim 1 and 2. Students will communicate their findings at weekly lab meetings, the (b) (4), and public events as described in this proposal.

### H.2.b. Classroom engagement

Under the guidance of Davis and McFadden, students will participate in either a journal club, professional development workshop, production farm visit, presentation, or community outreach event each week that will allow them to 1) understand the importance of sustainable agriculture for food security and environmental protection, 2) perform research using the scientific method, 3) effectively communicate science to the public, and 4) understand and plan for potential career options in STEM. Our classroom engagement and outreach event plan is detailed in Table 4.

**Table 4. Schedule of REU student engagement and public outreach<sup>1</sup>.**

Week	Activity	Details
1	Journal club Workshop	Comparative analysis of environmental impacts of agricultural production systems, agricultural input efficiency, and food choice <sup>[129]</sup> with Dr. Xingen Lei Introduction to Research Methods
2	Journal club	(b) (4), (b) (6)
3	Journal club Farm visit	(b) (4), (b) (6) (b) (4), (b) (6)
4	Journal Club	(b) (4), (b) (6)
5	Workshop	(b) (4)
6	Workshop	Analyzing and Presenting Data
7	Workshop Presentation	CV and Career Prep with Animal Science Graduate Student Association (b) (4)
8	Outreach	Ruminate with Ruminants at the Sciencenter (1 d in yrs. 1-3) or Capstone (b) (4)

<sup>1</sup>Davis and McFadden will be present at all events.


From reading and discussing papers, students will learn about ruminant biology and the homeorhetic control of lactation. This foundation of understanding will allow them to visualize how advancements in genetics, nutrition, and management influence these biological mechanisms and the efficient use of nutrients. Students will connect how improvements in nutrient efficiency over the past century have reduced the carbon footprint, enteric greenhouse gas emissions, and land and water use per unit of animal food produced. Lastly, students will also learn how use of biotechnology, like recombinant ST, can benefit these outcomes. Journal clubs will also teach undergraduates how to critique a scientific paper. The Introduction to Research Methods workshop will include a discussion of scientific method; experimental design; the rationale behind sample size, controls, and experimental bias; and how to collect and organize data within the context of their summer projects. The Analyzing and Presenting Your Data workshop will cover statistical analysis and scientific presentation to prepare the REU students for the poster presentation they will give at the (b) (4) (b) (4). (b) (4) has agreed to cover how to prepare a curriculum vitae (CV) and how to navigate academia to secure career placement in STEM fields including animal science. We will also lead a tour of (b) (4) to teach students how dairy production operates to optimize milk production efficiency. Students will participate in a Portal to the Public science communication training led by Sciencenter Youth Program Coordinators, as detailed in section E.3.a. of the Project Description.

### H.2.c. Community engagement

In the final week of the REU, undergraduates will educate the public about the importance of improving the efficiency of nutrient utilization to ensure food security and reduce environmental impact. In years 1-3, REU students will participate in *Ruminant with Ruminants* at the Sciencenter as described in the Project Description E.3.b. REU students will guide adults and children through a series of stations that demonstrate how increasing the efficiency of nutrient use by dairy ewes and cows decreases the required number of animals and amount of feed, land and water use, enteric methane and carbon dioxide emissions, and fossil fuels to produce a gallon of milk. Students will also showcase how recombinant ST biotechnology is a safe tool to control nutrient use in livestock and lower the environment impact. In year 4, REU participants will take the Sciencenter interactive exhibit to The Great New York State Fair, which is detailed in section E.3.b. of the Project Description. Each REU student will be responsible for co-managing the exhibit for 7 days (week 8 of the REU). As part of the Sciencenter and The Great New York State Fair exhibits, REU students will incorporate calculations of environmental impact parameters (e.g., milk production efficiency; feed, land, and water required; greenhouse gas production; and calculate carbon footprint;) generated from aims 1 and 2 (Project Description D.5.1.). Preparing for this exhibit will be a significant effort because it requires developing a historical timeline of innovations that have been utilized to increase milk production efficiency.

### H.3. PI experience involving undergraduates

(b) (4), (b) (6)



### H.4. Student selection

Our plan is to enroll 2 students in the REU program annually, which is justifiable because the proposed work is intensive. All procedures (e.g., feeding and milking ewes, collecting samples, performing biopsies and post-op care, performing clamps, processing samples, etc.) are time-sensitive and laborious. (b) (4)

The program will be advertised within the (b) (4) by hanging fliers and classroom announcements. We will recruit underrepresented minorities and females within the biology and biomedical sciences majors. Preference will be given to students who have completed one or two years of college in order to allow time for career planning and development after the experience. Finalists will be selected based on an application review and interviews by Davis, McFadden, the chairs of the CU Department of Animal Science and SUNY Cortland Biological Science Department (b) (4), (b) (6)

Students will be selected based on academic record, recommendations, background, and motivation. A waiting list of (b) (4) student replacements will be created in the event that an REU student withdraws from the program. We will invite past REU students to participate in the capstone event at (b) (4), (b) (6)