UNIVERSITY OF NORTHERN COLORADO

SPONSORED PROGRAMS
MAR 2 5 2016

Provost Fund for Faculty Scholarship & Professional Development
RESEARCH, DISSEMINATION & FACULTY DEVELOPMENT GRANT APPLICATION

Deliver or mail one paper copy of the completed application to Sherry May, Office of Sponsored Programs, Suite #25, Kepner Hall, or email a scanned copy to sherry.may@unco.edu, or fax to the attention of Sherry May at 970-351-1934. All submissions must include signatures (not typed or printed names), and must be received by 5:00 p.m. on the published deadline date.

The Research, Dissemination and Faculty Development program supports faculty scholarship and professional activity in the faculty's efforts to develop as teachers, researchers, scholars and artists. Please review the guidelines available on the OSP website.

Applicant Name: Laura Stewart
Email Address: laura.stewart@unco.edu
Dept/Div/School: School of Sport and Exercise Science
ORG: 46300
Campus Phone: 351-1891
Campus Address: Gunter Hall Room 2790
Bear Number: 801490536

☑ This is an individual application.
☐ This is a collaborative application with other UNC faculty. (List names of collaborators below; see RDFD guideline #2.)

UNC Collaborators:
Title of Project: T Cell and Cancer Project
Proposed Start Date: May 2016
Anticipated Completion Date: May 2017

Brief Summary of Proposed Project (Also attach a complete description following the RDFD Application Requirements, item #2):

There are currently 14 million cancer survivors living in the United States and this figure is projected to increase to 18 million in the next 10 years. Immune system dysfunction has emerged as one of the most significant causal factors related to cancer development and there are gaps in the literature related to T cell population shifts. The Rocky Mountain Cancer Rehabilitation Institute (RMCRI) has a phase program which groups survivors in terms of activity and stage of cancer recovery. The purpose of the present cross sectional study is to measure T cell subpopulations and the biomarkers associated with immune function at various phases of rehabilitative exercise training. Cancer survivors (N=24; RMCRI Phase 1-2 subjects n=12; RMCRI Phase 3-4 subjects n=12) enrolled in the exercise training program at RMCRI and will be asked to visit the center once to undergo basic descriptive measures and a blood sample. All blood samples will be analyzed for T cell populations, (naïve T cells (CD8, CD28, CD127), T regulatory cells (CD4, CD25, CD127) and senescent T cells (CD8, CD28, CD57)), using a flow cytometer. Circulating biomarkers (tumor necrosis factor alpha , interleukin 6, interleukin 7, interleukin 10 and transforming growth factor beta) will be measured with a flow cytometer and C-reactive protein will be measured with a microplate reader. Providing more information about the immune systems of the cancer survivors at RMCRI at all stages of disease and recovery allows for crucial insight that can have therapeutic, clinical, and rehabilitative applications in the future.

PROJECT SUPPORT

Provost Fund Request: $ 9999.50 — Should match the total of the first column on the project budget form
Other Funding Source: $ ____ — Source of Funding: ____
Other Funding Source: $ ____ — Source of Funding: ____
Other Funding Source: $ ____ — Source of Funding: ____
Total Anticipated Cost: $ 9999.50 — Should match the total of the third column on the project budget form

COMPLIANCE APPROVALS: *RDFD funds will not be released until necessary approvals have been secured and documentation provided to the FRPB.*

Does the project involve human subjects? ☑ Yes ☐ No
If yes, has it been approved by the IRB? ☐ Yes ☑ No
If yes, what was the approval date? ____

Does the project involve animal subjects? ☐ Yes ☑ No
If yes, has it been approved by the IACUC? ☐ Yes ☑ No
If yes, provide the approval #: ____

SIGNATURES (Proposals lacking required signatures will not be considered for funding.)

Applicant: [signature] Date: 3/21/2016
Director/Chair: [signature] Date: 3/21/2016
Dean: [signature] Date: 3/25/2016

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BUDGET FORM: *Please ensure that the sum of column 1 (Provost Funds requested) and column 2 (Other Sources) is equal to the amount in column 3 for each row; also ensure that each column sums correctly.*

All costs to be reimbursed to the applicant must be in compliance with UNC policies and procedures.

Budget Item	Requested from Provost Fund	Funds from Other Sources	Total Anticipated Project Cost
I. PERSONNEL Costs			
a. Salaries & Wages			
b. Fringe Benefits			
Personnel Subtotal			
II. CONTRACTUAL Costs			
a. Consultants			
b. Contracts			
Contractual Subtotal			
III. TRAVEL & CONFERENCE Costs			
a. Transportation			
b. Conference Registration			
c. Lodging			
d. Per diem or meals			
Travel Subtotal			
IV. EQUIPMENT Costs			
Equipment Subtotal			
V. OTHER Costs			
a. Materials & Supplies	9999.50		9999.50
b. Publication/Dissemination			
c. Printing/Copying			
d. Participant Support			
e. Communication			
f. Miscellaneous Other Costs			
Other Costs Subtotal			
VI. TOTAL PROJECT BUDGET	9999.50		9999.50

BUDGET JUSTIFICATION: Attach a budget narrative explaining in detail how the cost of each line item was determined and a narrative explanation for why the costs are necessary to the project and how the costs were determined

Examples:

Salaries & Wages – PI Smith @ .05 effort X 2 months plus graduate student hourly @ $12/hour X 4 hrs/wk X 16 wks, plus narrative

Transportation – Roundtrip airfare on SW Airlines from Denver to Washington D.C. @ $248 plus rental car @ $95/day X 3 days, plus narrative

OTHER ATTACHMENTS (See RDFD Proposal Guidelines):

- Description of Project, Workshop or Training Activity to be funded
- Current CV no longer than 3 pages

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A. NEED FOR AND SIGNIFICANCE OF THE PROJECT

1. Value and potential impact of the research project

There are currently 14 million cancer survivors living in the United States and, even when the current advances in cancer treatment are combined with the expansion of the aging population, this figure is projected to increase to 18 million in the next 10 years (11). Immune system dysfunction has emerged as one of the most significant causal factors related to cancer development. Cell-mediated immunity is the strongest means by which the immune system eliminates cancer cells (1,3,10).

Tumors are able to develop in the human body in part due to their ability to suppress the immune system (1,10). Transforming Growth Factor-β (TGF-β) and interleukin 10 can be secreted by tumors to convert naïve CD4+ cells into T regulatory cells (5, 10). T regulatory cells can suppress the cytotoxic capabilities of cell-mediated immunity that would ordinarily kill cancer cells (1,5,10). T regulatory cells are normally found in healthy individuals at approximately 5% of all CD4 expressing lymphocytes in the body, as they are needed for proper immune balance to protect the body from autoimmune disease and excessive inflammation (6,7,10). At the time of a cancer diagnosis, T regulatory cell levels rise to levels of 20-25% of all CD4 expressing lymphocytes in the body (10). This rise in T regulatory cells demonstrates the necessity of immunosuppression for tumor development. Immunosuppression is so critical to tumor development that an inverse correlation exists between amount of T regulatory cells in the body and survival (5), (10).

Naïve T cells (CD8+ CD28+) are the pool from which effector T cells that fight cancer may be drawn (1,3,8,10). The larger the naïve T cell pool, the larger capacity the immune system has to recruit cells to eliminate cancer cells through cell-mediated immunity. CD28 membrane protein binding is essential for this process (1). One means by which this immunity is suppressed in tumor development is through binding of PD-1 and CTLA-4 receptors on the membranes of naïve and effector T cells (1,4). T regulatory cells can secrete ligands that competitively bind CTLA-4 and PD-1 leaving the CD28 receptor unbound and the naïve T cell inactivated, thus unable to fight cancer (1).

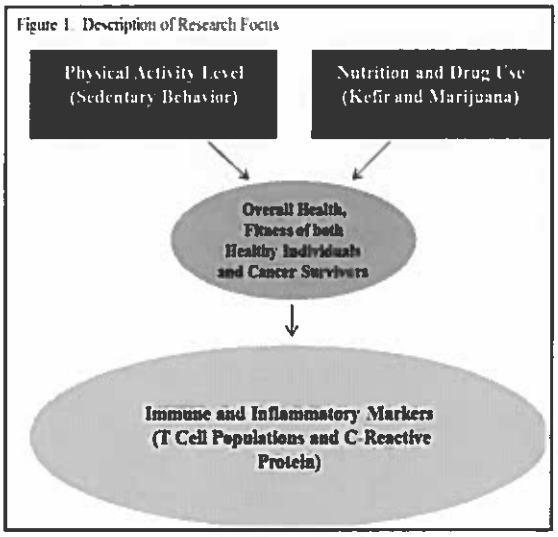
Cancer diagnosis has been demonstrated to increase with age (3,8,10). CD57+ T cells are known as functionally senescent (9). These T cells have a limited response to exposure to antigen, and a reduced replicative capacity, as well as significantly shortened telomeres as compared to other T cells (8,9). Thus, functionally senescent T cells are less able to actively eliminate diseased cells, such as cancer cells as compared to the rest of the T cell population (3,8,9). CD57+ senescent T cells are nearly undetectable in newborns, but accumulate with age (9). This has been proposed as a possible mechanism of increased cancer incidence with age (3,8,9). Due to the increased number of senescent T cells making up the available T cell population with age, and thymic involution, there is a subsequent decrease in available naïve T cells that can be activated to eliminate cancer cells (3,8). This reduction in the available naïve T cell population may be a form of immunosuppression occurring due to aging that can lead to availability for tumor growth (3,8,9).

Exercise training has been shown to help remove CD57+ senescent T cells from the blood, and the body fills the void with naïve T cells (3), (8). This increased proportion of naïve T cells induced by exercise training has been proposed as a means of protecting against cancer, and reversing the possible threat of tumor development made available by an aging immune system (3, 8). Increases in naïve T cell population have still been observed to occur from exercise training in a cancer population (2). The question then arises, if at the time of cancer diagnosis, the immune system was suppressed through a disproportionate increase in T regulatory cells, how is the naïve T cell population able to increase in those afflicted with cancer? The means by which this occurs remains to be elucidated.

2. Potential contribution to increased knowledge in area of investigation

The current scientific literature leaves gaps in the literature associated with immune system function in cancer patients. The Rocky Mountain Cancer Rehabilitation Institute (RMCRI) at UNC has a phase program which also groups survivors in terms of activity and stage of cancer recovery. Providing more information about the immune systems of the cancer survivors at RMCRI at all stages of disease and recovery allows for crucial insight that can have therapeutic, clinical, and rehabilitative applications.

3. Potential impact of the project on the applicant's continued area of research



This project has far reaching impact and will significantly influence my ability to proceed with my research mission. My research focus is presented in Figure 1. I am currently exploring questions that are related sedentary behavior and kefir in cancer human and animal models, respectively. I am also exploring the relationship between marijuana and health status. All of these studies involve measuring whole body responses. This project will allow me to begin exploring a mechanism (shifts in T cell populations and immune biomarkers) which will provide more depth to my applications for external funding. Whole body response based NIH applications are often rejected because of the lack of a proposed "mechanism of action."

B. DESIGN OF THE PROJECT

1. Goals and objectives are relevant and clearly specified

The overarching goal of this cross sectional project is to characterize the T cell populations and immune biomarkers in cancer survivors at different phases of cancer recovery at RMCRI. This project will also allow me to optimize protocols on the flow cytometer for the measurement of T cell subpopulations and immune cell biomarkers (CRP and cytokines).

2. Purpose of workshop or training is clearly stated

The purpose of the present study will be to measure T cell subpopulations and the biomarkers associated with immune function (C-reactive protein (CRP), tumor necrosis factor alpha (TNF-alpha), interleukin 6 (IL-6), interleukin 7 (IL-7), interleukin 10 (IL-10) and transforming growth factor beta (TGF-beta)) at various phases of rehabilitative exercise training. T cell subpopulations will be measured by expression of membrane proteins with a flow cytometer. The hypothesis of the present study is that there are more naïve T cells (CD8, CD28, CD127), less T regulatory cells (CD4, CD25, CD127) and senescent T cells (CD8, CD28, CD57), as well as lower concentrations of cytokines (IL-6, IL-7, TNF-alpha, IL-10 and

TGF-beta), and more interleukin 7 receptor expression on naïve T cells in cancer survivors further out from treatment (RMCRI Phase 3 and 4) when compared to clients early in cancer recovery (RMCRI phase 1 and 2).

3. Methodology is appropriate

Study Design : This study is cross sectional and quantitative in design. To summarize, male and female cancer survivors (N=24; RMCRI Phase 1-2 subjects n=12; RMCRI Phase 3-4 subjects n=12) enrolled in the exercise training program at RMCRI and will be asked to visit the center once. All clients at RMCRI all have had a previous cancer diagnosis at some point in their lifetimes. At RMCRI, all survivors are in 1 of 4 phases of cancer rehabilitation. Phase 1, clients are currently in chemotherapy or radiation treatments for cancer. Phase 2, clients are less than three months post-chemotherapy treatment or who are currently receiving other cancer treatments besides chemotherapy or radiation. Phase 3 consists of clients who are no longer on any cancer treatment, and are being physically rehabilitated to healthy levels of physical fitness. Phase 4 consists of clients who have been successfully physically rehabilitated and are utilizing exercise training to maintain healthy levels of physical fitness. In this project, we'll compare biomarkers associated with T cell activation as well as T cell phenotype in physically active participants in early (Phase 1 and Phase 2) vs. later (Phase 3 and Phase 4) in recovery from cancer. Participants will visit RMCRI once to undergo basic anthropometric measures and will provide a blood sample.

Data Collection Procedures: Subjects will report to the laboratory between 0630 and 1200 h following an overnight fast and having refrained from moderate to vigorous exercise for the previous 72 hours and no exercise for the previous 24 hours. During the study visit, the participant will review and sign the informed consent. Basic descriptive measures including height, weight, waist and hip circumference, body composition (via bioelectrical impedance (InBody 770 machine, or 7-site skinfolds) will be obtained. Then, subjects will provide a rested and fasted (for 12 hours) blood sample (25 mL total: 10 mL serum, 10 mL plasma, 5 mL whole blood) from a prominent forearm vein. All blood samples will be collected and a portion of the blood will be taken and analyzed for T cell populations (naïve T cells (CD8, CD28, CD127), less T regulatory cells (CD4, CD25, CD127) and senescent T cells (CD8, CD28, CD57)

using a flow cytometer (Accuri). Circulating biomarkers (IL-6, IL-7, IL-10, TGF-beta, TNF-alpha) and CRP will be evaluated using a multiplex bead assay on the flow cytometer (Ross Hall) and microplate reader (BioTek, Gunter Hall), respectively.

Data Analysis Procedures: All participant and data will be collected, entered into the jmp statistical program and differences between the groups (Phase 1 and Phase 2) vs (Phase 3 and Phase 4) will be determined using an analysed using a standard T Test.

4. Implications of expected findings are provided

The implications of this study are significant. This study will provide information about shifts in T cell populations related to phase of recovery and exercise training, which will be significant from a scientific standpoint. This funding will also allow us to optimize our flow cytometry and bead assay protocols which will help provide preliminary data to support a potential immune related mechanism of action in our kefir (rat chemotherapy model, the subject of our National Institutes of Health (NIH)-R21 application which is currently in review) and marijuana based projects (small human study underway). The ability to provide "T-cell population shifts" as a potential mechanism in these projects will make our external grant applications more competitive in the future.

5. Explanation of dissemination plan is clear

The preliminary results of this study will be submitted for presentation at the American College of Sports Medicine National Conference (deadline Nov 1, 2016) and I will follow up shortly thereafter with a manuscript that will be submitted to the *Journal of Applied Physiology* or *Brain, Behavior and Immunity.* All data will be used as pilot data for external grant applications (American Cancer Society and NIH).

C. Advancement of research, artistic or professional goals: individual/school/college/university

1. The degree to which the project, will contribute to advancing the applicant's goals

My research focus is outlined in figure 1 in the previous section. The current project is integral to my work because it will help me hone my skills in flow cytometry and optimize the assays needed for T cell phenotype analysis as well as use the multiplex software with the flow cytometer which will allow me to

measure a large number of cytokines (immune related proteins) in just one small sample. I will be able to use this technique and hypothesis as it relates to marijuana and kefir users in the future.

2. Project contribution to the mission/goals of the discipline, school, college, and to the university

This project helps support the discipline in the following ways:

a. *"student-centered university that promotes effective teaching"* – Although I will be supervising all aspects of this project, I have a research team led by a doctoral student (Craig Coronado) consisting of 12 undergrad students. Any student on this team will be permitted to observe or gain an experience in study participant interactions, sample collection and processing.

b. *"the advancement of knowledge, research"* – This project will advance knowledge in the area of cancer and exercise and allow students to gain a valuable research experience. It will also allow UNC and RMCRI explore mechanisms related to cancer recovery.

c. *"contribute effectively in a rapidly changing, technologically advanced society"* – By using the flow cytometer to analyze cell phenotypes and multiplex assay to measure cytokines, my doctoral students (and undergraduate student observers) will be exposed to cutting age technology (flow cytometry).

3. Adequacy of resources

RMCRI provides an ideal center for participant recruitment. This center uses the phase program for the administration of exercise programming. RMCRI also has private patient rooms so that we will be able to conduct the informed consent discussion, the descriptive evaluation (age, height, weight and body composition), as well as blood sample collection in private. The flow cytometer is housed in Ross hall and we are currently working with Dr.Gregory DeKrey in the School of Biological Science to optimize the machine for T cell phenotype and multiplex (cytokine) analysis.

a. The proposed budget is adequate to support the project, workshop or training

The budget of this project is adequate to support this project and there are no foreseeable limitations.

b. Any additional resources necessary to support the project (e.g., facilities, supplies, equipment, etc.) are available and adequate

RMCRI is available for use in this project and the resources (flow cytometer) in Ross Hall is adequate. The plate reader in Gunter Hall is also adequate and I have used this model to conduct CRP analysis.

4. Outcomes of previous internal funding

a. Results from previous UNC internal funding (RDFD, NPP, and SSI programs).

I received FRBP funding ($5,000.00) in Fall of 2015 for the Marijuana and Fitness Study (MariFit Study). We began recruitment for the project in mid-October and from mid-October until the end of the semester (mid-December) we were able to get 11 subjects through all 4 visits. While this was a good start, recruitment was a bit more difficult than anticipated. Consequently, I worked to obtain IRB approval to recruit non students in the Greeley and Evans areas and obtained approval from the university to provide a $25.00 gift card to study participants in the hopes that we would get more people to participate in our project. The assays (ELISAs) that were requested only allow us to run 40 samples (there are 40 sample wells in addition to control and standard curve wells) at one time. In other words, we have to run all samples in one batch. Our goal is to have 40 subjects by the end of the semester and I've assembled a team of 1 PhD student (Jonathan Lisano) and 12 undergraduate students to assist.

b. Conference presentations that have resulted from research supported by internal funds.

Abstracts with MariFit preliminary data were submitted on Jan 31, 2016 to Rocky Mountain American College of Sports Medicine for Presentation at the conference in Denver (April 8-9, 2016). **(undergrad students in italics and grad students underlined).** Both abstracts below have also been submitted to UNC for poster presentation at Research Day on campus.

Keegan Reeves*, Jonathon Lisano, *Andi Brownlow, Matthew Christensen, Telisha Quezada*, Kristina Phillips, Jeremy Smith, Laura Stewart. **Marijuana Use and Muscular Strength and Power in College Aged Students: An Exploratory Study.

Jonathon Lisano*, *Keegan Reeves, Andi Brownlow, Matthew Christiansen, Telisha Quezada*, Kristina Phillips, Colin Quinn, Jeremy Smith, Laura Stewart. **Chronic Marijuana Use May Be Associated with Decreased $FEV1_{max}$ but not VO_2max in Active Young Adults.

BUDGET and NARRATIVE BUDGET JUSTIFICATION

a. Completed the Provost Fund budget form (attached)

b. A detailed budget is outlines in Table 2 and a written summary is provided below.

Table 2: Detailed Budget (note prices are in USD; US Dollars)

Item	Source	Amount	Quantity	Catalog #	Price (USD)
Flow Cytometer Upgrade	BDBiosciences		1		5225
Flow Cytometry Supplies					
PE Mouse ant-human CD28	BDBiosciences	100 tests	2	555729	230
FITC Mouse anti-human	BDBiosciences	100 tests	1	555634	100
APC Mouse anti-human	BDBiosciences	100 tests	2	560845	414
FITC Mouse anti-human CD4 RTA T-4	BDBiosciences	100 tests	1	555346	100
PE Mouse anti-human CD25	BDBiosciences	100 tests	1	555432	175
APC-R700 Mouse anti-human CD127	BDBiosciences	50 tests	4	565185	940
Stain Buffer (BSA)	BDBiosciences	500mL	1	554657	95
Histopaque-1077	Sigma	100mL	1	10771-100ML	39.3
12 x75 Polypropylene Snap Cap Test Tubes	E & K Scientific	500/Case	1	607512-S	57.16
Trypan Blue Stain Solution	Fisher Scientific	100mL	1	ICN1691049	23.76
16% Paraforlmaldehyde Aqueous Solution	EMS	10 x10mL	1	15710	27
Lysing Buffer	BDBiosciences	100mL	1	555899	70
Cytokine Analysis Kits					
Human IL-7 Flex Set	BDBiosciences	100 tests	1	558334	253
Human IL-6 Flex Set	BDBiosciences	100 tests	1	558276	253
Human IL-10 Flex Set	BDBiosciences	100 tests	1	558274	253
Human TGF-Beta Single Plex Flex Set	BDBiosciences	100 tests	1	560429	253
Human TNF Flex Set	BDBiosciences	100 tests	1	560112	253
C-Reactive Protein ELISA	ALPCO	42 tests	1	30-9710s	470
Other Supplies and Reagents					
Blood Collection Supplies (Gloves, Needles, Tubes)	VWR				643
Absorbent Lab Paper	VWR	2 Rolls	1	51138500	125.28
Total					**9999.5**

Written Budget Justification

Flow Cytometer Upgrade: The Accuri C6 Flow Cytometer located in the Imaging Suite in Ross Hall of the University of Northern Colorado is equipped to detect cell-surface proteins that have been stained with fluorescent antibodies. This upgrade is necessary to conduct all analyses related to this project. Total Cost: $5,225.00

T Cell Materials: Mouse anti-human antibodies are needed for the analysis of the different subpopulations (described in the proposal above) of T Cells for the study. Lysis buffer histopaque, trypan blue and staining buffer are also required for this analysis in preparation for analysis by the flow cytometer. Total Cost: $2,271.22

Cytokine Analysis by Luminex Bead Assay and ELISA: Bead assays are quickly becoming the standard in cancer-related immunological research for cytokine analysis. This provides both a time and long-term cost benefit for research. Testing for several cytokines at once through use of Luminex bead assay flex sets is what makes the varied cytokine analysis of the present study possible. Total Cost: $1735.00

Blood collection supplies: Gloves, needles, tubes are needed for sample collection and processing. Total Cost: $768.28

Project Total Cost: $9,999.50

CURRENT CIRRICULUM VITAE

LAURA KATHLEEN STEWART
University of Northern Colorado
School of Sport and Exercise Science/Rocky Mountain Cancer Rehabilitation Institute
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E-mail: Laura.Stewart@unco.edu

Education

Postdoctoral Fellow
NIH – T-32 Botanical Research Training Program
Adipocyte Signaling Laboratory/Botanical Research Center
Pennington Biomedical Research Center, Baton Rouge, LA
August, 2005 – August, 2007

Doctor of Philosophy
Interdisciplinary Program in Exercise Physiology and Nutrition
Department of Health and Kinesiology
Purdue University, West Lafayette, IN
Conferred: May, 2005

Master of Science (Health Promotion)
Department of Health and Kinesiology
Purdue University, West Lafayette, IN
Conferred: August, 2000

Magna Cum Laude Bachelor of Science (Exercise Science)
Major: Wellness Management/ Emphasis: Cardiac Rehabilitation
Colorado State University, Fort Collins, CO
Conferred: August, 1998

Bachelor of Science (Biology)
University of Mary Washington, Fredericksburg, VA
Conferred: May, 1996

Faculty Appointments

University of Northern Colorado	Associate Professor	Exercise Phys	2015-Present
Louisiana State University	Associate Professor	Exercise Phys	2013-2014
	Assistant Professor	Exercise Phys	2007-2013
Pennington Biomedical Research Center	Adjunct	Associate Professor	2007-Present

Recent Selected Peer Reviewed Research Publications (Out of 30 Publications Total)

Bolded= Stewart or graduate student ***UNC Affiliated Publication**

1. ***O'Brien KV, Stewart LK, Forney LA**, Aryana KJ, Prinyawiwatkul W and Boeneke CA. The effects of postexercise consumption of a kefir beverage on performance and recovery during intensive endurance training. (2015). Dairy Science. Aug. 19. Epub doi 10.3168/jds.2015-9392.
2. *Hengan TM, Cefalu WT, Ribnicky DM, Noland RC, Dunville K, Campbell WW, **Stewart LK, Forney LA**, Gettys TW, Chang JS, and Morisson CD. In vivo effects of dietary quercetin and quercetin-rich red onion extract on skeletal muscle mitochondria, metabolism, and insulin sensitivity. (2015). Genes and Nutrition. Jan. 10(1):451. doi: 10.1007/s12263-014-0451-1.

3. *Hengan TM, **Stewart LK,** Forney L, Sparks L, Johannsen NM and Church TS. PGC1α -1 Nucleosome Position and Splice Variant Expression and Cardiovascular Disease Risk in Overweight and Obese Individuals. (2014). PPAR Research. Dec 28. Epub. doi: 10.1155/2014/895734

4. **Hengan TM**, Lenard NR, Gettys TW, and **Stewart LK**. Dietary quercetin supplementation in mice increases skeletal muscle PGC1α expression, improves mitochondrial function and attenuates insulin resistance in a time-specific manner. (2014) PLoS One. Feb 21;9(2):e89365. doi: 10.1371/journal.pone.0089365. eCollection 2014.

5. **Forney L,** Earnest C, **Henagan T, Johnson L, Castleberry T,** and **Stewart LK**. Vitamin D status, adiposity and athletic performance measures in college-aged students. Journal of Strength and Conditioning Research. (2014). Mar;28(3):814-24. doi: 10.1519/JSC.0b013e3182a35ed0.

6. Hasek, B, Boudreau A, Shin J, Feng D, Hulver M, Vann N, Laque A, **Stewart LK**, Stone KP, Wanders D, Ghosh S, Pessin J, and Gettys TW. Remodeling the integration of lipid metabolism between liver and adipose tissue by dietary methionine restriction in rats. (2013). Diabetes. 62(10): 3362-72.

Book Chapters and Book Reviews

Carson RL and **Stewart LK**. Book Chapter. (2015) "Promoting Physical Activity as a Major Goal." Book Chapter in Moving and Learning: Elementary Physical Education for the Future. ISBN: 978-7-5041-9155-7

Flynn MG and **Stewart LK.** Book Chapter. (2013) "Exercise, Nutrition and Aging." Book Chapter in Gerontology: Perspectives and Issues. ISBN-10: 0826109659

Henagan TM, Daray L, Stewart LK. Book Chapter. "CRP and Exercise" in C-Reactive Protein-New Research. (2009). Nova Publishers. ISBN: 978-1-6069237-8.

Stewart LK. Obesity Management. February, 2008. Book Review of Slow Fat Triathlete: Liver Your Athletic Dreams in the Body You Have Now, by Jayne Williams. Marlow Publishing, New York, 2004.

Selected Recent Research Presentations/Abstracts (Out of 35 Total)

1. ***Forney LA**, Johannsen NM, Barkemeyer AK, Dietrich MA, Henagan TM and **Stewart LK**. Optimal vitamin D status is associate with healthier immune indices in untrained but not trained females. Poster Presentation at Experimental Biology 2015.

2. *Scott VP, **O'Brien KV,** Boeneke CA, **Stewart LK, Forney LA** and Henagan TM. Exercise- and Kefir-induced Internalization of the Anti-inflammatory Melanocortin 3 Receptor in Monocytes. Poster Presentation at Experimental Biology 2015.

3. ***Davis GR,** Fuller S, **Daray L,** Nelson AG, Stephens J, Datri J and **Stewart LK.** The effects of marathon training versus combined training on plasma adiponectin and c-reactive protein in healthy young females. NSCA National Conference 2015

4. **O'Brien KV**, Boeneke CA, Aryana KJ, **Stewart LK**, Prinyawiwatkul W, and Forney L. The effects of post exercise consumption of a kefir beverage on performance and recovery during intensive endurance training. Poster presentation. American Dairy Science Association Annual Meeting. June 2014

Selected External and Internal Funded Grants (out of 7 total)

Stewart LK (PI). FRBP. Marijuana Use and Fitness (MariFit) Study. ($5,000.00). Data Collection Underway.

Stewart, LK (PI) . Impact of Carbohydrate on Exercise Performance. Gatorade Sport Science Institute. ($57,000). July 2008 – January 2009. Complete.

Stewart, LK (PI). An Evaluation of Quercetin-Induced Changes In Inflammatory Biomarkers (QUICK study). Dean's Circle. May 2013. Complete.

Stewart LK (PI). Vitamin D, Body Composition, Inflammation and Performance. ($8,000). Dean's Fund. December 2010 – December 2012. Complete.

Stewart LK (PI). Changes in physical activity and dietary habits during endurance training. ($1,500). LSU-Chandler Fund. January 2010 – June 2010. Complete.

Stewart LK (PI). Are Melanocortin Receptors The Key To Understanding the Anti-Inflammatory Effects of Exercise? ($10,000). LSU-Board of Regents Pfund. December 2009 - December 2010. Complete.

Stewart, LK (PI). Phenolic Flavonoids and Metabolic Syndrome: Mechanisms for Protective Effects of Quercetin. ($33,000). Pennington Biomedical Research Center. Botanical Research Center Pilot Study Program. May 2008 – July 2009. Complete.

Professional Honors

University of Northern Colorado
Sponsored Research Fellows Program (2016)

Louisiana State University:
Mary Ethel Baxter Lipscob Memorial Endowed Professorship in the College of Human Sciences (Awarded Summer 2013)
LSU Flagship Faculty Recognition, LSU (Fall, 2010)
LSU Tiger Athletic Foundation Teaching Award (Spring 2010)
Delta Gamma Favorite Professor, LSU, (Spring 2008 and Fall 2008).
Adjunct Professor Appointment, Pennington Biomedical Research Center (2007-Present).

References

1. Abbas, K.A., Lichtman, A.H., Pillai, S. (2015). *Cellular and Molecular Immunology* (8th Ed.). Philadelphia, PA: Elsevier Saunders.
2. American Physiological Society (APS). (2012, October 10). Exercise could fortify immune system against future cancers. Retrieved July 15, 2015 from www.aps /releases/2012/10/121010161843.htm
3. Bigley, A.B., Spielmann, G., LaVoy, E.C. and R.J. Simpson. (2013) Can exercise-related improvements in immunity influence cancer incidence and prognosis in the elderly? Maturitas.(76)1, 51-56.
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Letter of Support

UNIVERSITY of
NORTHERN COLORADO

College Natural and Health Sciences
School of Biological Sciences

March 21, 2016

Faculty Publications and Research Board
Research, Dissemination and Faculty Development program

Re: Dr. Laura Stewart, FRPB RDFD application

Dear Review Committee,

It is my pleasure and honor to write this letter of support for Dr. Laura Stewart's application for funding. As a supporter, I am committing my time to train Dr. Stewart and her students on the use of our flow cytometer for purposes of analyzing human cells and human cytokines, and for purposes of interpreting the flow cytometry data that will be generated. I have provided space in my research laboratory in Ross Hall for use by Dr. Stewart and her students for preparing samples prior to analysis with the flow cytometer. My qualifications for acting in this capacity include 30 years of experience as a research immunologist, expertise in the use of flow cytometry for research and teaching purposes, specific experience using the current Accuri flow cytometer in Ross Hall, eight peer-reviewed primary research publications that include flow cytometry data, and numerous presentations including flow cytometry data or the use of flow cytometers for research or teaching purposes.

The study that Dr. Stewart is proposing will examine the status of human cancer patient immune systems and the influence of exercise on that status. As Dr. Stewart has outlined so well in her application, balancing the effectiveness of immune surveillance and tolerance to self is critical throughout life, but no more so when cancer arises. Defeating cancer requires discriminating between normal and abnormal cells within the body, and then killing the cells that are abnormal. The fact that so many persons develop lethal forms of cancer is evidence of how often anticancer immunity fails. As Dr. Stewart described, part of the reason anticancer immunity may fail is a tipping of the balance too far toward tolerance of self (as evidenced by increased numbers of T regulatory cells). Another part of the reason may be the existence of a bottleneck: there is only so much room in the body for immune cells, and filling that space with seemingly unresponsive senescent T cells may limit the production of a more diverse population of T cells with greater potential for recognizing and destroying the cancer.

The work that Dr. Stewart is proposing is important and has significant potential to advance our understanding of anticancer immunity. I urge you to fully fund her proposal.

Sincerely,

G.K. DeKrey

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