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| Form Approved Through 8/31/2015 OMB No. 0925-0001 | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Department of Health and Human Services Public Health Services Grant Application Do not exceed character length restrictions indicated. | | | | | | | | | | | | **LEAVE BLANK—FOR PHS USE ONLY**. | | | | | | | | | | | | | | | |
| Type | | | | | Activity | | | | | Number | | | | | |
| Review Group | | | | | | | | | | Formerly | | | | | |
| Council/Board (Month, Year) | | | | | | | | | | Date Received | | | | | |
| 1. TITLE OF PROJECT *(Do not exceed 81 characters, including spaces and punctuation.)*  (example is 28 characters): UAB Diabetes Research Center | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION  NO  YES  *(If “Yes,” state number and title)* | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number: | | RFA-??-??-?? | | | Title: | | Diabetes Research Center (P30) | | | | | | | | | | | | | | | | | | | | |
| **3. PROGRAM DIRECTOR/PRINCIPAL INVESTIGATOR** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3a. NAME (Last, first, middle) | | | | | | | | | | | | 3b. DEGREE(S) | | | | | | | | | 3h. eRA Commons User Name | | | | | | |
| W. Timothy Garvey | | | | | | | | | | | | MD | | |  | | | |  | | garveyt | | | | | | |
| 3c. POSITION TITLE  Professor and Chairman | | | | | | | | | | | | 3d. MAILING ADDRESS *(Street, city, state, zip code)*  1675 University Boulevard  Webb 616  Birmingham, AL 35294-3360 | | | | | | | | | | | | | | | |
| 3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT  Nutrition Sciences | | | | | | | | | | | |
| 3f. MAJOR SUBDIVISION  School of Health Professions | | | | | | | | | | | |
| 3g. TELEPHONE AND FAX *(Area code, number and extension)* | | | | | | | | | | | | E-MAIL ADDRESS: | | | | | | | | | | | | | | | |
| TEL: | (205) 996-7433 | | | | | FAX: | | (205) 975-4065 | | | | garveyt@uab.edu | | | | | | | | | | | | | | | |
| 4. HUMAN SUBJECTS RESEARCH | | | | | | | | | 4a. Research Exempt | | | If “Yes,” Exemption No. | | | | | | | | | | | | | | | |
| No  Yes | | | | | | | | | No  Yes | | |  | | | | | | | | | | | | | | | |
| 4b. Federal-Wide Assurance No. | | | | | | | | | 4c. Clinical Trial | | | | | | | | | 4d. NIH-defined Phase III Clinical Trial | | | | | | | | | |
| FWA00005960 | | | | | | | | | No  Yes | | | | | | | | | No  Yes | | | | | | | | | |
| 5. VERTEBRATE ANIMALS  No  Yes | | | | | | | | | | | | 5a. Animal Welfare Assurance No. | | | | | | | | | | A3255-01 | | | | | |
| 6. DATES OF PROPOSED PERIOD OF  SUPPORT *(month, day, year—MM/DD/YY)* | | | | | | | | | | | 7. COSTS REQUESTED FOR INITIAL  BUDGET PERIOD | | | | | | | | | 8. COSTS REQUESTED FOR PROPOSED  PERIOD OF SUPPORT | | | | | | | |
| From | | | | Through | | | | | | | 7a. Direct Costs ($) | 7b. Total Costs ($) | | | | | | | | 8a. Direct Costs ($) | | | | 8b. Total Costs ($) | | | |
| 3/1/2013 | | | | 2/28/2018 | | | | | | | $69,925 | 102,440 | | | | | | | | 349,625 | | | | 512,200 | | | |
| 9. APPLICANT ORGANIZATION | | | | | | | | | | | | 10. TYPE OF ORGANIZATION | | | | | | | | | | | | | | | |
| Name | | | The University of Alabama at Birmingham | | | | | | | | | Public: **→**  Federal  State  Local | | | | | | | | | | | | | | | |
| Address | | | 1530 3rd Avenue South, AB 1170  Birmingham, AL 35294-0111 | | | | | | | | | Private: **→**  Private Nonprofit | | | | | | | | | | | | | | | |
| For-profit: **→**  General  Small Business  Woman-owned  Socially and Economically Disadvantaged | | | | | | | | | | | | | | | |
| 11. ENTITY IDENTIFICATION NUMBER  1636005396A6 | | | | | | | | | | | | | | | |
| DUNS NO. | | | | 063690705 | | | | | Cong. District | | | | | AL-007 | |
| 12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE | | | | | | | | | | | | 13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION | | | | | | | | | | | | | | | |
| Name | | | Lynn W. Stedman, MBA | | | | | | | | | Name | | Lynn W. Stedman, MBA | | | | | | | | | | | | | |
| Title | | | Director, Office of Sponsored Programs | | | | | | | | | Title | | Director, Office of Sponsored Programs | | | | | | | | | | | | | |
| Address | | | 1530 3rd Avenue South, AB 1170  Birmingham, AL 35294-0111 | | | | | | | | | Address | | 1530 3rd Avenue South, AB 1170  Birmingham, AL 35294-0111 | | | | | | | | | | | | | |
| Tel: | (205) 934-5266 | | | | | | FAX: | | | (205) 975-5977 | | Tel: | (205) 934-5266 | | | | | | | | | | FAX: | | (205) 975-5977 | | |
| E-Mail: | | | ogca@uab.edu | | | | | | | | | E-Mail: | | ogca@uab.edu | | | | | | | | | | | | | |
| 14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. | | | | | | | | | | | | SIGNATURE OF OFFICIAL NAMED IN 13.  *(In ink. “Per” signature not acceptable.)* | | | | | | | | | | | | | | | DATE |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Program Director/Principal Investigator (Last, First, Middle): | | | | | | | | | Garvey, W. Timothy | | | | | |
|  | | | | | | | | | | | | | | |
| PROJECT SUMMARY (See instructions): | | | | | | | | | | | | | | |
| This proposal will continue the progress of the DRTC, first established at UAB in 2008, and the transition  to a DRC. The immediate goal of the center is to promote excellence in diabetes research. Over the past 4  years, the DRC has galvanized the UAB research community around the study of diabetes resulting in an  increase in membership from 115 to 159, and a 32.5% increase in extramural research funding. Through  these efforts, the center ultimately endeavors to decrease diabetes morbidity/mortality, and to provide an  outstanding environment for training and career development in diabetes research. Our specific aims are to:  1. Facilitate and enhance diabetes research by sponsoring research core facilities expressly required by  our investigator base. The five research cores cover a broad translational spectrum: Bioanalytical REDOX  Biology, Islet Cell Biology, Animal Physiology, Human Biology, and Interventions & Translation Cores.  2. Augment diabetes research via a pilot & feasibility grant program that will emphasize innovation,  translation, and career development of highly promising junior investigators.  3. Sponsor an integrated Enrichment Program that promotes a cohesive environment for an outstanding  multi-disciplinary investigator base, which will enhance learning, collaboration, collegiality, and innovation.  4. Build upon the progress achieved over our first 4 years by responding to the evolving needs of our  investigators and through leadership that impels new ideas and lines of investigation.  5. Emphasize research, training, and outreach that are responsive to the needs of our trainees, achieve  better outcomes for our patients, and lessen the high burden of diabetes in our community and nation.  6. Leverage the resolve of UAB leadership, substantial institutional commitments, and generous  philanthropy from our community to further impel the development of a pre-eminent center of diabetes  research excellence in the heart of the Deep South.  Our DRC is located in a community with the highest rates of diabetes in the US, and unites investigators  around common themes to study diabetes in the context of cardiometabolic disease. | | | | | | | | | | | | | | |
| RELEVANCE (See instructions): | | | | | | | | | | | | | | |
| The UAB DRC is the only NIDDK diabetes center located in the Deep South, at the 'Diabetes Belt' epicenter  characterized by the highest rates of diabetes in the US. The Center has developed a comprehensive  strategy for new discoveries and a strong environment for training the next generation of research leaders.  Thus, the UAB DRC endeavors to lessen the burden of patient suffering and high social costs of diabetes. | | | | | | | | | | | | | | |
| PROJECT/PERFORMANCE SITE(S) (if additional space is needed, use Project/Performance Site Format Page) | | | | | | | | | | | | | | |
| **Project/Performance Site Primary Location** | | | | | | | | | | | | | | |
| Organizational Name: | | | | The University of Alabama at Birmingham | | | | | | | | | | |
| DUNS: | | 063690705 | | | | | | | | | | | | |
| Street 1: | | 1675 University Boulevard | | | | | | | | Street 2: |  | | | |
| City: | Birmingham | | | | | | | County: | | Jefferson | | | State: | AL |
| Province: | | |  | | Country: | | USA | | | | | Zip/Postal Code: | | 352943360 |
| Project/Performance Site Congressional Districts: | | | | | | AL-007 | | | | | | | | |
|  | | | | | | | | | | | | | | |
| **Additional Project/Performance Site Location** | | | | | | | | | | | | | | |
| Organizational Name: | | | |  | | | | | | | | | | |
| DUNS: | |  | | | | | | | | | | | | |
| Street 1: | |  | | | | | | | | Street 2: |  | | | |
| City: |  | | | | | | | County: | |  | | | State: |  |
| Province: | | |  | | Country: | |  | | | | | Zip/Postal Code: | |  |
| Project/Performance Site Congressional Districts: | | | | | |  | | | | | | | | |

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| Program Director/Principal Investigator (Last, First, Middle): | | | | Garvey, W. Timothy | | | | |
|  | | | | | | | | |
| SENIOR/KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below.  Start with Program Director(s)/Principal Investigator(s). List all other senior/key personnel in alphabetical order, last name first. | | | | | | | | |
| Name | | eRA Commons User Name | | | Organization | | Role on Project |
| Garvey, W. Timothy, MD | | Garveyt | | | UAB | | Principal Investigator |
| Frank, Stuart, MD | | Sfrank | | | UAB | | Associate Director |
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| OTHER SIGNIFICANT CONTRIBUTORS | | | | | | | | |
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| **Human Embryonic Stem Cells** | **No** | | **Yes** | | | | | |
| **If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list:** <http://stemcells.nih.gov/research/registry/eligibilityCriteria.asp>. *Use continuation pages as needed.*  If a specific line cannot be referenced at this time, include a statement that one from the Registry will be used. | | | | | | | | |
| **Cell Line** | | | | | | | | |
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 Page 3 Form Page 2-continued

Number the following pages consecutively throughout   
 the application. Do not use suffixes such as 4a, 4b.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Program Director/Principal Investigator (Last, First, Middle): | Garvey, W. Timothy | | | | |
| The name of the program director/principal investigator must be provided at the top of each printed page and each continuation page. | | | | | |
| RESEARCH GRANT | | | | | |
| TABLE OF CONTENTS | | | | | |
|  | | | *Page Numbers* | | |
| Face Page | | |  | 1 |  |
| Description, Project/Performance Sites, Senior/Key Personnel, Other Significant Contributors, and Human Embryonic Stem Cells | | |  | 2-5 |  |
| Table of Contents | | |  | 6-11 |  |
| Detailed Budget for Initial Budget Period | | |  | 12 |  |
| Budget for Entire Proposed Period of Support | | |  | 13 |  |
| Budgets Pertaining to Consortium/Contractual Arrangements | | |  | 14 |  |
| Biographical Sketch – Program Director/Principal Investigator (*Not to exceed four pages each*) | | |  | 15 |  |
| Other Biographical Sketches (*Not to exceed four pages each –* *See instructions*) | | |  | 16-18 |  |
| Resources | | |  | 19-20 |  |
| Checklist | | |  | 21 |  |
|  | | |  | | |
| Research Plan | | |  | 22-27 |  |
|  | | |  | | |
| 1. Introduction to Resubmission Application, if applicable, or Introduction to Revision Application,  if applicable \* | | |  |  |  |
| 2. Specific Aims \* | | |  |  |  |
| 3. Research Strategy \* | | |  |  |  |
| 4. Inclusion Enrollment Report (Renewal or Revision applications only) | | |  |  |  |
| 5. Bibliography and References Cited/Progress Report Publication List | | |  |  |  |
| 6. Protection of Human Subjects | | |  |  |  |
| 7. Inclusion of Women and Minorities | | |  |  |  |
| 8. Targeted/Planned Enrollment Table | | |  |  |  |
| 9. Inclusion of Children | | |  |  |  |
| 10. Vertebrate Animals | | |  |  |  |
| 11. Select Agent Research | | |  |  |  |
| 12. Multiple PD/PI Leadership Plan | | |  |  |  |
| 13. Consortium/Contractual Arrangements | | |  |  |  |
| 14. Letters of Support (e.g., Consultants) | | |  |  |  |
| 15. Resource Sharing Plan (s) | | |  |  |  |
|  | | |  | | |
| Appendix *(Five identical CDs.)* | |  | | Check if  Appendix is  Included | |
| \* Follow the page limits for these sections indicated in the application instructions, unless the Funding Opportunity Announcement specifies otherwise. | | | | | |

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|  |  |  |  |
| --- | --- | --- | --- |
| Program Director/Principal Investigator (Last, First, Middle): | Garvey, W. Timothy | | |
|  | | | |
| DETAILED BUDGET FOR INITIAL BUDGET PERIODDIRECT COSTS ONLY | | FROM | THROUGH |
|  |  |

List PERSONNEL *(Applicant organization only)*

Use Cal, Acad, or Summer to Enter Months Devoted to Project

Enter Dollar Amounts Requested *(omit cents)* for Salary Requested and Fringe Benefits

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| NAME | ROLE ON PROJECT | Cal.  Mnths | Acad.  Mnths | Summer  Mnths | | INST.BASE SALARY | SALARY REQUESTED | FRINGE BENEFITS | | TOTAL |
| Garvey, W. Timothy | PD/PI | 2.4 |  |  | | 100,000 | 20,000 | 5,400 | | 25,400 |
| Frank, Stuart | Co-Investigator | .3 |  |  | | 100,000 | 2,500 | 675 | | 3,175 |
| Gaga, Lady | Admin. | 12 |  |  | | 25,000 | 25,000 | 8,350 | | 33,350 |
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| SUBTOTALS | | | | | | | 47,500 | 14,425 | | 61,925 |
| CONSULTANT COSTS | | | | | | | | | |  |
| EQUIPMENT *(Itemize)* | | | | | | | | | |  |
| SUPPLIES *(Itemize by category)* | | | | | | | | | |  |
| TRAVEL  NIH Diabetes Center Meeting | | | | | | | | | | 4000 |
| INPATIENT CARE COSTS | | | | | | | | | |  |
| OUTPATIENT CARE COSTS | | | | | | | | | |  |
| ALTERATIONS AND RENOVATIONS *(Itemize by category)* | | | | | | | | | |  |
| OTHER EXPENSES *(Itemize by category)*  Apolipoprotein Peptide Mimetics | | | | | | | | | | 4000 |
| CONSORTIUM/CONTRACTUAL COSTS | | | | | DIRECT COSTS | | | |  | |
| SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)* | | | | | | | | | $ | 69,925 |
| CONSORTIUM/CONTRACTUAL COSTS | | | | | FACILITIES AND ADMINISTRATIVE COSTS | | | |  | |
| TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD | | | | | | | | | $ | 69,925 |

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| Program Director/Principal Investigator (Last, First, Middle): | | | Garvey, W. Timothy | | | | | |
|  | | | | | | | | |
| BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD DIRECT COSTS ONLY | | | | | | | | |
| BUDGET CATEGORY TOTALS | INITIAL BUDGET PERIOD *(from Form Page 4)* | 2nd ADDITIONAL YEAR OF SUPPORT REQUESTED | | 3rd ADDITIONAL YEAR OF SUPPORT REQUESTED | 4th ADDITIONAL YEAR OF SUPPORT REQUESTED | | 5th ADDITIONAL YEAR OF SUPPORT REQUESTED | |
| PERSONNEL: *Salary and fringe benefits. Applicant organization only*. | 61,925 | 61,925 | | 61,925 | 61,925 | | 61,925 | |
| CONSULTANT COSTS |  |  | |  |  | |  | |
| EQUIPMENT |  |  | |  |  | |  | |
| SUPPLIES |  |  | |  |  | |  | |
| TRAVEL | 4,000 | 4,000 | | 4,000 | 4,000 | | 4,000 | |
| INPATIENT CARE COSTS |  |  | |  |  | |  | |
| OUTPATIENT CARE  COSTS |  |  | |  |  | |  | |
| ALTERATIONS AND RENOVATIONS |  |  | |  |  | |  | |
| OTHER EXPENSES | 4,000 | 4,000 | | 4,000 | 4,000 | | 4,000 | |
| DIRECT CONSORTIUM/ CONTRACTUAL COSTS |  |  | |  |  | |  | |
| SUBTOTAL DIRECT COSTS  *(Sum = Item 8a, Face Page)* | 69,925 | 69,925 | | 69,925 | 69,925 | | 69,925 | |
| F&A CONSORTIUM/ CONTRACTUAL COSTS |  |  | |  |  | |  | |
| TOTAL DIRECT COSTS | 69,925 | 69,925 | | 69,925 | 69,925 | | 69,925 | |
| TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD | | | | | | $ | | **349,625** |
| JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.  **W. Timothy Garvey, MD; Director of the DRC.**  **1. Commitment and Effort Allocation.** (2.4 calendar months) is requested for Dr. Garvey as DRC  Director. Personal Statement: Ever since serving as Associate Director of the DRTC at Indiana University (1989-1994) as an Assistant Professor, it has been a long-term career goal of mine to establish a new DRTC at an institution where the NIH funding will have optimal impact to enhance diabetes research among an outstanding investigator base. In fact, that is one reason why I was recruited and decided to move to UAB in 2003. I began writing our application for a new DRTC at UAB in late 2006, and I can remember trying to simultaneously write and listen to the audiocast of the World Series, won that year by my team the St. Louis Cardinals. It was extremely gratifying to be able to successfully launch our new DRTC in April 2008. In less than 4 years, we are now writing the competitive renewal application for our center as we comply with the directives of becoming a DRC. I took great comfort in the fact that the St. Louis Cardinals again won the World Series in 2011 and I take this as a good omen. The serious point here is that I view my role as the Director of a DRC as the culmination of my professional life, and a role that will merit my full commitment in achieving our stated goals and specific aims. I am a physician-scientist and diabetologist who has engaged  **\*\*\*CONTINUE ON A PHS 398 CONTINUATION PAGE\*\*\*** | | | | | | | | |

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OMB No. 0925-0001/0002 (Rev. 08/12 Approved Through 8/31/2015)

* **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: W. Timothy Garvey, MD

eRA COMMONS USER NAME: GARVEYT

POSITION TITLE: Professor

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE  *(if applicable)* | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Washington University, St. Louis, MO | B.A. | 1974 | Biology |
| St. Louis University, St. Louis MO | M.D. | 1978 | Medicine |
| Washington University/Barnes Hospital | Residency | 1981 | Internal Medicine |
| U of Colorado and U of California San Diego | Fellowship | 1984 | Endocrinology & Metab |

1. **Personal Statement**

Dr. Garvey is an internationally recognized expert in insulin resistance, adipocyte and muscle cell biology, obesity, Metabolic Syndrome, and Type 2 Diabetes, bringing basic technologies to the study of humans. His work has advanced our understanding of cardiometabolic disease, the role of the glucose transport system in insulin resistance, and effective strategies for diabetes prevention.

Dr. Garvey is a dedicated mentor for our next generation of clinicians, basic scientists, and physician scientists.  He has mentored 13 junior faculty with NIH K01, NIH K23, RWJF, Fogarty, and COBRE awards; 15 post-doctoral fellows on NIH T32 and other training grants; 9 clinical fellows pursuing research careers; two MD/PhD students in the Medical Scientist Training Programs; 20 graduate students as primary mentor in PhD Degree programs; 21 medical students during summer research rotations; and 25 undergraduate research experiences.  All of the junior faculty members and many of the pre-doctoral and postdoctoral fellows have gone on to become successful independent researchers. As PI of the NIH-funded Diabetes Research Center at UAB, he has helped enhance the intellectual environment at UAB for junior scientists and trainees alike.

**B. Positions and Honors**

**Positions and Employment**

1984 - 1989 Instructor & Assistant Professor, Department of Medicine, University of California, San Diego

1989 - 1993 Associate Professor of Medicine, Physiology and Biophysics, Indiana University

1993 - 1994 Professor of Medicine, Physiology and Biophysics, Indiana University School of Medicine, and Chief, Section of Endocrinology, Indianapolis VAMC, Indianapolis, IN

1994 - 2003 Director, Division of Endocrinology, Diabetes, and Medical Genetics, Medical University of South Carolina, and Staff Physician at Charleston VAMC

2003 -present Chairman and Professor, Department of Nutrition Sciences, University of Alabama at Birmingham, and Staff Physician/GRECC investigator at Birmingham VAMC

2008 -present Director, UAB Diabetes Research Center (DRC)

**Other Experience and Professional Memberships**

Member: ADA; Endocrine Society; TOS, AACE, FASEB, ASCI; AAP. Study Sections: ADA 1992-1995 and 2005-2008; JDRF 1994-1997; American Federation for Aging Research 2004-2012; VA Merit Review Endocrine Section 1996-2000; NIH Metabolism Study Section 1998-2002; member and chairman of multiple NIH ad hoc; Chairman, DSMB for NHLBI Vascular SCCOR 2005-2015; Chair ADA Sci & Med Mtgs Oversight Com 2006-8; AACE Board of Directors 2013-2016; Chair AACE Obesity Scientific Committee 2013-present

**Honors and Awards**

Alpha Omega Alpha Honor Medical Society, 1977; Alpha Sigma Nu Jesuit Honor Society, 1978; Wendell Griffith Prize in Biochemistry, St. Louis U., 1978; Pfizer Postdoctoral Fellowship Award, 1984; Pfizer Scholars Award, 1987; 1988; American Society for Clinical Investigation, 1994; Pfizer Visiting Professor, 1999-2000, Association of American Physicians, 2002. Charles E. Butterworth, Jr.,MD, Professorship at UAB, 2006. UAB Excellence in Mentoring Award, 2011; FACE designation from the Amer Assoc Clin Endocrinologists, 2014.

**C. Contribution to Science (selections from over 200 publications)**

1. **Glucose Transport**

By studying molecular parameters in muscle and fat tissue from metabolically characterized individuals, the Garvey laboratory has made important observations regarding the pathogenesis of human insulin resistance.  He has been a principle contributor to our understanding of the role of the glucose transport system and glucose transporter proteins in human insulin resistance. In cultured cell and rodent models, and in human muscle and adipose biopsies, he has elucidated defects in glucose transporter expression and in GLUT4 vesicle trafficking and translocation as causes for insulin resistance.

**Garvey WT**, Huecksteadt TP, Birnbaum MJ. Suppression of an insulin-responsive glucose transporter gene in

diabetes mellitus. Science 125-2341-2349, 1989.

**Garvey, W.T**., L. Maianu, T.P. Huecksteadt, M.J. Birnbaum, J.M. Molina, and T.P. Ciaraldi. Pretranslational

suppression of a glucose transporter protein causes cellular insulin resistance in non-insulin-dependent diabetes

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1. **Glucose-Induced Insulin Resistance and Role of Tribbles Homolog 3**

The Garvey lab pioneered in the demonstration that high glucose induces insulin resistance in human patients and in cultured cell models. Working with Dr. Steve Marshall, there was the demonstration that glucose-induced insulin resistance required glucose metabolism via the hexosamine biosynthetic pathway; however, until recently the mechanisms by which flux through this pathway mediated insulin resistance were unknown. More recently the lab identified TRIB3 in microarray analyses as differentially expressed in human muscle and that levels of this pseudokinase, which binds and blocks phosphorylation of AKT, are correlated with fasting glucose and insulin resistance. In cultured cells and mice, TRIB3 is induced by glucose with dependency on the hexosamine pathway, impairs insulin-stimulated glucose transport, and modulates glucose toxicity in STZ-induced diabetic mice.

**Garvey, W.T,** J.M. Olefsky, J. Griffin, R.F. Hamman, and O.G. Kolterman. The effect of insulin treatment on

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Zhang W, Liu J, Tian L, Liu Q, Fu Y, **Garvey WT**. [TRIB3 Mediates Glucose-Induced Insulin Resistance Via a Mechanism that Requires the Hexosamine Biosynthetic Pathway.](http://www.ncbi.nlm.nih.gov/pubmed/23990361) Diabetes. 62:4192-4200, 2013

1. **Role of Adiponectin in Cardiometabolic Disease**

The Garvey lab has elucidated the role of adiponectin in both the metabolic and vascular components of cardiometabolic disease. The lab first discovered that it was the large molecular weight complex of adiponectin (duodecamer) rather that the smaller complexes (hexamers and trimers) that was most highly correlated with insulin resistance, lipids, and abdominal fat in humans. In cultured cells and genetically-manipulated mice, the lab proved that adiponectin functions as an autocrine/paracrine factor in adipose tissue to modulate insulin-sensitive glucose transport, lipid storage capability, and inflammatory status. Dr. Fu and Dr. Garvey showed that adiponectin also impaired macrophage foam cell formation by inducing genes that promote lipid efflux and suppressing genes that mediate lipid uptake. In mice, augmentation of adiponectin action in macrophages, by macrophage-specific overexpression of adiponectin R1 receptors, produced a lean, diabetes-resistant, atherosclerosis-resistant model with diminished macrophage infiltration in adipose. The data indicate that adiponectin action in macrophages links metabolic and vascular disease in insulin resistant patients.

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syndrome trait cluster. Diabetes 55:249-259, 2006. PMID:16380500

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mediating the risk of metabolic and cardiovascular disease. Curr Opin Lipidol, 18:263-270, 2007

Fu Y, Luo N, KleinRL, **Garvey WT**. Adiponectin Promotes Adipocyte Differentiation, Insulin Sensitivity, and

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Tian L, Luo N, Klein RL, Chung BH, **Garvey WT**, Fu Y. Adiponectin Reduces Lipid Accumulation by in

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1. **Genetics of Diabetes and the UCP3 Gene Mutation Affecting Substrate Metabolism**

Dr. Garvey has participated in genetic studies of diabetes, obesity, and cardiovascular disease risk in the Pima Indians, T1DM patients in the DCCT, and in Gullah-Speaking African Americans lining on the Sea Islands of South Carolina. In the Gullahs, he led Project SuGAR, anddemonstrated extremely low Caucasian admixture, and went on to identify chromosomal markers linked to diabetes, obesity, and lipid/lipoprotein subclasses measured by NMR spectroscopy. He discovered a UCP3 polymorphism present in 10% of Gullahs that altered fuel preference towards carbohydrate and away from fat as a metabolite for resting energy expenditure. This polymorphism would predictably promote fat storage under conditions of a high fat diet, and was associated with severe obesity in the Gullahs. The Garvey lab has also examined differential gene expression in muscle using cDNA microarrays in comparing insulin sensitive and resistant humans.

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Brown, A.M., Dolan, J.W., Willi, S.M., **Garvey, W.T**., and Argyropoulos, G. Endogenous mutations in human uncoupling protein 3 alter its functional properties. FEBS Letters, 464:189-193, 1999.

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Norman, R.A., D.B. Thompson, C. Bogardus, T. Foroud, **W.T. Garvey**, P. Bennett, E. Ravussin, and the Pima Diabetes Genes Group. Genome wide search for genes influencing percent body fat in Pima Indians: Suggestive linkage at chromosome 11q22. American Journal of Human Genetics. 60:166-173, 1997.

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Klein RL, McHenry MB, Lok KH, Hunter SJ, Le N-A, Jenkins AJ, Zheng D, Brown WV, Lyons TJ, **Garvey WT**, and DCCT/EDIC Research Group. Apolipoprotein C-III Protein Concentrations and Gene Polymorphisms in Type 1 Diabetes: Associations with Lipoprotein Subclasses. Metabolism 53:1296-1304, 2004.

Munoz J, Lok KH, GowerBA, FernandezJR, Hunter GR, Lara-CastroC, De Luca M, **Garvey WT**. A polymorphism in the transcription factor 7-like 2 (TCF7L2) gene is associated with reduced insulin secretion in non-diabetic women. Diabetes, 55:3630-3634, 2006.

1. **Diabetes Prevention and Medical Models of Obesity Management.**

Dr. Garvey has conducted clinical trials involving recently approved weight loss medications, and this has led to an appreciation that these new tools now enable a more robust medical model for obesity management. Dr. Garvey was a leading contributor and author in the AACE Position Statement designating Obesity as a disease and the proposition to the AMA which designated Obesity as a disease in May, 2013. Dr. Garvey was the chief architect of the Complications-Centric Model for Care of the Overweight/Obese Patient, an algorithm that emphasizes the use of weight loss therapy to treat obesity-related complications as the primary goal of treatment, as opposed to the BMI as the main determinant of treatment indications and success.  Dr. Garvey developed Cardiometabolic Disease Staging, which allows clinicians to quantitatively assign risk for Type 2 Diabetes and cardiovascular disease mortality as a guide for intensity of weight loss therapy, within the context of a complications-centric approach.  This work is widely applicable and relevant to policy-making regarding the prevention of diabetes. Thus, Dr. Garvey is a national leader in the development of medical models for the management of obesity and diabetes prevention.

**Garvey WT**, Ryan DH, Henry R, Bohannon NJ, Toplak H, Schwiers M, Troupin B, Day WW. [Prevention of Type 2 Diabetes in Subjects With Prediabetes and Metabolic Syndrome Treated with Phentermine and Topiramate Extended-Release.](http://www.ncbi.nlm.nih.gov/pubmed/24103901) Diabetes Care, 37:912-921, 2014

**Garvey WT**. New Tools for Weight Loss Therapy Enable a More Robust Medical Model for Obesity Treatment: Rationale for a Complications-Centric Approach. Endocrine Practice, 6:1-31, 2013

Guo F, Moellering DR, **Garvey WT.**  The Progression of Cardiometabolic Disease: Validation of a New Cardiometabolic Disease Staging System Applicable to Obesity.  Obesity, 22:110-118, 2014 PMC3866217

Mechanick JI, Garber AJ, Handelsman Y, **Garvey WT**. [American Association of Clinical Endocrinologists' position statement on obesity and obesity medicine.](http://www.ncbi.nlm.nih.gov/pubmed/23047927) Endocrine Practice, 18(5):642-648, 2012

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**Garvey WT**, Ryan DH, Bohannon NJ, Kushner RF, Rueger M, Dvorak RV, Troupin B. [Weight-loss therapy in type 2 diabetes: effects of phentermine and topiramate extended release.](http://www.ncbi.nlm.nih.gov/pubmed/25249652) Diabetes Care 37:3309-3316, 2014

**D. Research Support** ACTIVE

**Merit Review Research Grant, Garvey (PI)** 04/01/15 to 03/31/19

Department of Veterans Affairs “Mechanisms of Insulin Resistance in Diabetes”

This proposal assesses molecular mechanisms contributing to glucose-induced insulin resistance in diabetes with an emphasis of the role of tribbels homolog 3 in insulin action and systemic metabolism

**P60 DK-079626, Garvey (PI)** 4/1/13 to 2/28/18

NIH/NIDDK “UAB Diabetes Research Center”

This center grant enhances infrastructure for diabetes related research by funding core facilities and pilot

projects, through programs in community based research and disease prevention and control, and by

promoting enrichment activities and training programs relevant to diabetes.

**P30 DK-56336, Allison (PI)** 6/1/12 to 5/31/17

NIH/NIDDK “Nutrition and Obesity Research Center”

This center grant enhances infrastructure for nutrition related research by funding core facilities and pilot projects.

Dr. Garvey does not receive funds that directly support his individual research from this center grant.

Role: Dr. Garvey is Associate Director of the center.

**U01 DK098246 George Washington U, Lachin (PI)** 4/1/12 to 3/31/20

The Glycemia Reduction Approaches for Diabetes: A Comparative Effectiveness (GRADE) Study.

This is a multi-center, NIDDK-sponsored clinical trial with Dr. Garvey as PI at the UAB site

**DCRI/Astra Zeneca , Garvey (PI).** 4/26/10 to 7/26/15

BCB109. EXCSEL Study. A Randomized, Placebo Controlled Clinical Trial to Evaluate Cardiovascular Outcomes After Treatment with Exenatide Once Weekly in Patients with Type 2 Diabetes Mellitus.

This is an industry-initiated clinical trial. Role: Garvey is PI at the UAB site.

**Pfizer/Merck, Garvey (PI)** 1/22/15 to 1/21/16

Randomized, Double-Blind, Placebo-Controlled. Parallel-Group Study to Assess Cardiovascular Outcomes Following Treatment with Ertugliflozin (MK-8835/PF-04971729) in Subjects With Type 2 Diabetes Mellitus and Established Vascular Disease

This is an industry-initiated clinical trial. Role: Garvey is PI at the UAB site.

**Sanofi, Garvey (PI).** 4/1/14 to 8/1/15

A Randomized, 30-Week, Active-Controlled, Open Label, 2- Treatment Arm, Parallel-Group, Multicenter Study Comparing the Efficacy and Safety of the Insulin Glargine/Lixisenatide Fixed Ratio Combination to Insulin Glargine With or Without Metformin in Patients with T2DM

This is an industry-initiated clinical trial. Role: Garvey is PI at the UAB site.

**COMPLETED**

**RO1 DK083562, Garvey (PI).** 08/01/09 – 07/31/13

NIH/NIDDK “NR4A Orphan Receptors and Insulin Resistance”

This proposal will examine the role of NR4A orphan nuclear receptors in modulating insulin sensitivity in

cultured cells, transgenic mice, and humans, and will develop rationale for NR4A3 as a novel target for

treatment of insulin resistance, Metabolic Syndrome, and Type 2 Diabetes.

**R01 DK38765, Garvey (PI)** 07/01/06-06/30/12

NIH/NIDDK “Mechanisms of Human Insulin Resistance”

1. This porposal studies the functional and molecular defects in mitochondria from skeletal muscle that
2. contribute to defects in lipid metabolism and insulin resistance in the Metabolic Syndrome, obesity, T2DM

**RO1 DK-078328, NIH/NIDDK. S. Adams (PI).** 8/4/09 - 9/30/2012

NIH/NIDDK “Identification of Muscle Specific Biomarkers of Fatty Acid Beta Oxidation”.

This project examines metabolomic profiles of lipids in insulin resistance and after exercise in subjects

carrying a slice donor polymorphism for the UCP3 gene. Role: Garvey is PI of the subcontract from USDA.

**OVERLAP**

The current funding and pending grant applications do not constitute any scientific or budgetary overlap.

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| --- | --- |
| Program Director/Principal Investigator (Last, First, Middle): | Garvey, W. Timothy |
|  | |
| RESOURCES | |
| Follow the 398 application instructions in Part I, 4.7 Resources. | |
| **Offices and Conference Rooms.** The university allocated the entire 12th floor at the top of the new Richard C. and Annette N. Shelby Interdisciplinary Biomedical Research Building for programmatic diabetes research space assignment (total 23,326 sq ft). This contains the space used by the Administrative Core of the DRC as well as the UAB Comprehensive Diabetes Center in the area outlined in red below. The administrative space amounts to 4,100 sq ft, and includes 10 offices, a spacious reception area, an executive meeting room, and a conference room where lectures and journal clubs in the DRC Enrichment Program, and meetings of the various DRC Committees, take place. There are offices for Eva Gilliam, the Administrative Coordinator of the DRC, and Dr. Meredith Preuss, PhD, the Administrative Director of the UCDC, as well as offices for the respective directors, Drs. Garvey and Shalev. This space was occupied in mid 2008. The remaining space on the 12th floor is research space programmatically committed to diabetes, and houses laboratories for Drs. Garvey, Shalev, Tse, Fu, Ramanadham, and X Wang (office only), as well as the DRC Islet Biology Core. Two laboratories are still unoccupied and will accommodate additional new diabetes faculty currently being recruited. The blueprint for the 12th floor with administrative space outlined in red, and a picture of the Shelby Bldg, are shown below.    **Computers and Furnishings.** All administrative space and Dr. Garvey’s office is well outfitted with modern office furniture, desk top and laptop (with docking station) computers, a full array of updated software, printers. Internet communications, and audio/visual communications. The executive conference room and the large conference room are outfitted with remotely controlled mounted LCD projectors and screens driven by computers with internet connections.  **BioAnalytical Redox Biology Core Laboratory**  The BARB core recently moved to the Biomedical Research Building II (BMR2) in BMR2 546 and 572 (***Figure 1***). This space comprises 750 ft2 of well equipped, dedicated laboratories for BARB core activities, which represents a 200 ft2 increase from its previous location in Volker Hall. An additional 148 ft2 of renovated space have been designated as office space (***Figure 1***) for Dr. Moellering, providing a total of ~950 ft2 of space (laboratories + Dr. Moellering’s office) designated for BARB core activities, resulting in an overall net increase of ~450 ft2 for core functions. This space is located on the same floor as Dr. Ballinger’s and Dr. Darley-Usmar’s laboratories and office space, is newly renovated, and represents a significant improvement in laboratory and office space for the BARB core. It also confirms significant institutional commitment for BARB core activities. Institutional support for this relocation was provided by the department of Pathology and the Center for Free Radical Biology (i.e., a UAB University-Wide Interdisciplinary Research center – UWIRC).    **Figure 1:** BARB Core Lab space is bordered in red, office space for Dr. Moellering is bordered in green. Dr. Ballinger and Dr. Darley-Usmar’s laboratories are located adjacent to the BARB Core lab. Dr. Moellering’s office is also located within the same office suite as Drs. Ballinger and Darley-Usmar.  **Animal**. A UAB animal care facility is located in the ground floor of BMR2. This facility is a PHS approved pathogen free animal facility to house rodents and rabbits. Additionally, a BMR2 541 is a designated animal necropsy room, conveniently located a short distance down the west hallway of BMR2 from the BARB core. **Clinical.** N/A  **Computer.** 4 IBM compatible, Pentium II computers with Windows XP operating systems are available, including one computer located within Dr. Moellering's office (BMR2 536) and 2 computers designated for exclusive BARB core use in rooms BMR2 546 and 572. A Dell laptop computer is also available within the core that runs the Synergy II Multimode microplate reader.  **Office.** Drs. Ballinger, Darley-Usmar, and Moellering have newly renovated office space in BMR2 530, 508 and 536, respectively, which are all located within the same office suite.  **Library.** Our department has an excellent journal collection, as well as an interlibrary loan system. Lister Hill Medical Library maintains an extensive collection of biomedical journals. Medline searches are available from our personal computers as well as by departmental librarian and Medical Center Library. In addition, we have on-line subscriptions to many journals including: *Am J Physiol, Cell, Nature, J Biol Chem, J Clin Invest* and *PNAS*.  **Major Equipment located within the BARB Core:**  **Dr. Douglas Moellering.**  ***Figure 2*** shows the Mitochondrial Isolation Station located within the BARB core. This custom piece of equipment was designed and developed by Drs. Douglas Moellering and Carlos Krumdieck. Use of this apparatus allows isolation of mitochondrial preparations that produce high quality and consistently reproducible results. The financial support for the design and build of this equipment was provided by Nutrition Sciences.  Figure 2: Custom mitochondrial isolation station with: (A) homogenizer drive motor attached to a chart recorder; (B) a modified water-jacketed cooled homogenization chamber with mortar and pestle, and; (C) a cooled circulating water bath. (D) shows a tracing from the chart recorder whereas the enlarged image of (B) shows the (1) modified pestle; (2) clear homogenization chamber, and; (3) inlet and outlet for circulation of cooled water. The lower right panel is an enlarged image of the modified pestle (1) showing (a) flexible tubing; (b) a modified peak cap, and; (c) a peak ring which prevent unequal sheer during tissue homogenization.  ***Figure 3*** below shows the Oroboros Oxygraph 2K High Resolution Respirometer with TIP (titration injection pump) hardware (Austria) and DATLAB 4.0 software and IBM compatible, Pentium II computer with Windows XP operating system (provided by WT Garvey in the Department of Nutrition Sciences through a grant from the Veteran’s Administration Research Service). This equipment allows quantification of mitochondrial bioenergetics from isolated mitochondria and permeabilized tissues.    **Figure 3:** Left panel shows Dr. Moellering preparing the Oroboros Oxygraph 2K High Resolution Respirometer with a IBM compatible, Pentium II computer with Windows XP operating system for an experiment. The right panel shows a larger view of the Oroboros Oxygraph.    ***Figure 4*** is of the Seahorse XF24-3 extracellular flux analyzer (Billerica, MA) with O2/H+/CO2 three analyte ready detection capability, integrated automated drug delivery, temperature adjustable measurement chamber, color LCD touch screen & integrated computer, windows based data acquisition & display, and excel-based desktop analysis software (a joint purchase between the DRC, the department of Pathology, the Center for Free Radical Biology, and the Center for Nutrient-Gene Interaction). This equipment represents a “break through” for cellular bioenergetics measurement, allowing simultaneously quantification of anaerobic (glycolytic) and aerobic (mitochondrial) energy metabolism in cells. The XF24 creates a transient, 7-μl chamber in specialized microplates that allows for the determination of oxygen and proton concentrations in real time. Rates of oxygen consumption can also be measured across several samples at a time. Additionally, reagents can be added automatically via 4 injection ports within the Seahorse Flux Pak cartridges, enabling the researcher to observe the effects of pharmaceutical or compounds of interest upon cellular bioenergetics.  **Figure 4: Left panel** shows the Seahorse XF24-3 extracellular flux analyzer with O2/H+/CO2 three analyte ready detection capability, integrated automated drug delivery, temperature adjustable measurement chamber, color lcd touch screen & integrated computer, windows based data acquisition & display, and excelbased desktop analysis software. **Right panel** shows Ms. Kelley Johnston, the BARB core laboratory research assistant, performing data analysis on a XF-24 experiment.    ***Figure 5*** shows the Synergy II Multimode microplate reader (Biotek, VA) with Dell laptop computer, the Beckman DU800 spectrophotometer (Beckman Coulter) with kinetic package software and IBM compatible, Pentium II computer with Windows XP operating system and Storm 840 PhosphoImaging System (Amersham) with ImageQuant 2. These items are provided by the DRC (Synergy II Multimode microplate reader and the DU800) and the Pathology (Storm 840). These Synergy II and DU800 are required for multiple enzymatic assays and can be used in quantification assays of molecules of interest (e.g. ATP, lipid peroxides, etc). The Storm 840 is used to quantify immunoblots and DNA damage gels.  **Figure 5:** Left – Synergy II Multimode microplate reader; middle – Beckman DU800 spectrophotometer; right – Storm 840 Phospho  Imaging System    Also located within the BARB core are: a Zeiss Stemi 2000 stereomicroscope fitted with a Nikon digital camera system, Revco ThermoFisher -80 oC freezer, -20oC freezer, 4oC refrigerator, 37oC incubator (for the XF24 cell culture),vortex mixers, refrigerated/heated water bath, analytical balance, microprobe pH meter, stir/hot plates, rotating shaker, table top centrifuge and a microcentrifuge. Full access is also available to the equipment located within Drs. Ballinger and Darley-Usmar laboratories that are adjacent to the core. A walk through cold room (4°C), ice machine, Sorvall high speed centrifuge, a Densitometer (Molecular Dynamics), a Stratagene Eagle Eye gel imaging system, milli-Q water system and autoclave are located in common use areas in BMR2.  **Dr. Scott W. Ballinger**  **Laboratory.** Dr. Ballinger has 1,402 ft2 of well-equipped laboratory space in the Biomedical Research Building II (BMR2), rooms 572, 574 independent of the BARB core. BMR2 572 also houses an additional 280 ft2 dedicated for BARB core activities.  **Animal.** Dr. Ballinger currently has space (room 180C5) in the UAB animal care facility located in BMR2, that houses his mouse colonies. This facility is a PHS approved pathogen free animal facility to house rodents and rabbits.  **Clinical**  N/A  **Computer.** 5 IBM compatible, Pentium II computers with Windows XP operating systems are available, including one computer with MetaMorph imaging software. 4 are located within Dr. Ballinger's laboratories and the other is in Dr. Ballinger's personal office (BMR2 530).  **Office.** Dr. Ballinger has a newly renovated office in BMR2 530 with assigned secretarial support, in the same office suite and Drs. Moellering and Darley-Usmar.  **Library.** Our department has an excellent journal collection, as well as an interlibrary loan system. Lister Hill Medical Library maintains an extensive collection of biomedical journals. Medline searches are available from our personal computers as well as by departmental librarian and Medical Center Library. In addition, we have online subscriptions to many journals including: *Am J Physiol, Cell, Nature, J Biol Chem, J Clin Invest* and *PNAS*.  **Major Equipment: Located within Dr. Ballinger’s laboratory**  Dr. Ballinger has a fully equipped laboratory with high and low speed table-top centrifuges, horizontal and vertical gel electrophoresis units, Hoeffer protein gel apparati, assorted power supplies, gradient gel mixers (Hoefffer, BioRad), Eppendorf microcentrifuges, a Eppendorf refrigerated microcentrifuge, a BioRad semi-dry  Electroblotting system, shaking water baths, 4 Perkin Elmer 2400 PCR machines, 3 Perkin Elmer 2700 PCR machines, a PCR workstation, a biological safety cabinet and a tissue culture hood, 2 cell culture incubators, a SoftMax plate reading spectrophotometer (Molecular Devices), a CytoFluor 4000 plate reading fluorometer, a StrathKelvin Polarograph, Savant gel dryers, a tissue disrupter, a Savant speed Vac, a Misonix sonicator, a Zeiss Stemi 2000 stereomicroscope fitted with a Nikon digital camera system, 3 -80 oC upright freezers, 2 - 20oC freezers, 2 4oC refrigerators.  A walk through cold room (4°C), ice machine, Sorvall high speed centrifuge, a Densitometer (Molecular Dynamics), a Stratagene Eagle Eye gel imaging system, milli-Q water system and autoclave are located in common use areas in BMR2.  **Dr. Victor Darley-Usmar**  **Laboratory.** Dr. Darley-Usmar has laboratories of approx. 1720 ft2 located in the Biomedical Research Building II (BMR2 - 542 and 547), adjacent to the BARB core. They are fully equipped to perform tissue culture, biochemical and molecular biological experimentation. Equipment includes spectrophotometers, refrigerated desk-top centrifuge and biorad electrophoresis system.  **Computer.** All offices are have a PC connected via ethernet to internet, Medline, laser & color printers. All Software necessary to process & analyze data (statistical & graphics) & word processing have been installed.  **Office.** Dr. Darley-Usmar has 274 ft2 office space located in BMR2 508 and expert secretarial support.  **Other.** Tissue culture facilities, cold & equipment rooms (housing ultracentrifuges) are within Dr. Darley-Usmar’s lab. Our department and university libraries maintain extensive & accessible collections of biomedical journals.  **Equipment.** Dr. Darley-Usmar has a fully equipped laboratory for chemical synthesis, cell culture and biochemical analysis. Equipment includes spectrophotometers and plate readers, a refrigerated desk top centrifuge, Biorad electrophoresis system, chemiluminescence detectors for NO and ROS measurements and 2 HPLC systems with Diode array. Communal tissue culture facilities, cold rooms and common equipment rooms are available  and used by the PI in BMR II adjacent to the laboratory. These laboratories are fully equipped for purification and analysis. The laboratory has two Seahorse XF24 extracellular flux analyzers and other equipment necessary for cellular and mitochondrial bioenergetics.  **Other.** Perkin-Elmer Lambda 3B UV/VIS scanning spectrophotometer interfaced with PC, Beckman TJ-6 Benchtop centrifuge, Fisher Model 59 Microfuge, Savant Speed/Vac, Boekel shaker/incubator, Vortex mixers, refrigerated/heated water bath, analytical balances (2), pH meter (2), stir/hot plates, IWT water deionization system, Modulab water purification system, dot blot apparatus, vacuum pump, gradient mixer, ISCO peristaltic pump, ISCO Retriever II fraction collector, Fisher Model FS9 ultrasonic bath, Brinkman Polytron PT 300 tissue homogenizer, three isoflurane and one Ethrane anesthetic vaporizers, illuminated magnifier, 2 leaded-glass shields, 4000V electrophoresis power supply, vertical electrophoresis gel tanks (3), Virtis vacuum dryer (Advantage) with stoppering assembly. Plate Reader: Perkin Elmer Victor2, with IR upgrade: combination instrument with capability for absorbance, fluorescence (including near infrared), and luminescence. A cold room (4°C) and autoclave are located on the same floor.  **Dr. Stephen Barnes**  **Laboratory.** Dr. Stephen Barnes has laboratory space of 800 sq. ft. on the 4th floor of the McCallum (MCLM) Building The total area of the Targeted Metabolomics and Proteomics laboratory (TMPL) adjacent to Dr. Barnes’ lab on the 4th floor of the MCLM building is 2,400 sq. ft. See TMPL website www.uab.edu/proteomics/massspec  **Computer.** Dr. Barnes has a 2011 Mac BookPro computer with a 100 Mps connection to the internet. It can operate under Mac OS 10.7 or Windows. There are many computers (Windows-based) in TMPL for the operation of the instruments and for data analysis – all at 100 Mps. UAB also has a wireless network for the MCLM and Kaul buildings.  **Office.** Dr. Stephen Barnes has an office (152 sq. ft) on the 4th floor of the McCallum Research Building next to proteomics/mass spectrometry laboratories.  **Other.** Dr. Barnes’ laboratory is equipped with incubators, laminar flow hoods, a BioRad plate reader, thermocyclers, refrigerators and freezers (-20oC and -80oC), water baths and a HP 1080 HPLC for sample fractionation as well as automated sample extraction devices and evaporators.  **Major Equipment**  Dr. Stephen Barnes directs the Targeted Metabolomics and Proteomics Laboratory. This group was established in 1993. It typically supports the research of 60-100 investigators on an annual basis. It is also supported by the NIDDK-funded UAB Skin Disease Research Center, and the NIDDK-funded O’Brien Acute Kidney Injury Center and by collaboration with P01, R01 and R21-funded investigators. It has the following instruments:  • **AB-Sciex 5600 Triple-Tof mass spectrometer**. This is the latest proteomics instrument from ABSciex. It detects 5-15 more identifiable and verifiable peptides in a LC-MSMS discovery experiment than the AB Sciex 4000Qtrap. Although it was purchased to carry out targeted, quantitative analysis of proteotypic peptides from proteins in signaling pathways, it is also used for small molecule peptidomics, lipidomics and metabolomics analysis because of its high mass resolution (30-40,000), mass accuracy (3-5 ppm) and speed (20 MSMS spectra per second). It is operated with an Eksigent Tempo nanoLC pump and Nanoflex Chip system.  • **ABI Sciex 4000Q-trap mass spectrometer**. This instrument is used for the analysis of complex metabolite mixtures. It has a PAL robot and an Eksigent pump for nanoLC. It is used for high sensitivity (10-100 amol) analysisin complex mixtures. It is also used to carry MSn experiments for complex small molecules, in particular parent ion scanning to discover lipids/metabolites with specific head groups.  • **ABI Sciex 4000 triple quadrupole mass spectrometer**. This instrument is well suited to the quantitative measurement of small molecules in biological fluids and tissues, offering sensitivities mostly in the range of 1-10 fmol injected although sensitivity depends on the analyte. For example, the sensitivity limits for 17β-estradiol and the anesthetic propofol are 500 fmol injected, whereas the dansy derivative of 17β-estradiol is 1.6 fmol. It has a Shimadzu Prominence fPLC with refrigerated autosampler.  • **ABI Sciex 3200 triple quadrupole mass spectrometer**. This instrument is well suited to the quantitative measurement of small molecules in metabolomics applications, offering sensitivities in the range of 5-25 fmol. It has a Shimadzu HPLC with autosampler and a Waters Acquity uPLC.  • **Two ThermoFinnigan 7 tesla LTQ-FT Fourier Transform ICR-mass spectrometers** including nanoLC and an Advion NanoMate™/Triversa. One of the LTQ-FT instruments is equipped with IRMPD and ECD. It also has a 2D-nanoLC Eksigent pump. To use these instruments, investigators should contact Dr. Matt Renfrow (6-4681; renfrow@uab.edu) in the Biomedical FT-ICR-MS laboratory that’s adjacent to Dr. Barnes office and laboratory.  TMPL is situated on the 4th floor of the McCallum Building, occupying 2,400 square feet of laboratory space and adjoining office space. The facility contains areas and computers for data processing by investigators and for teaching and consulting issues involving mass spectrometry. A feature of TMPL is that all aspects of experiments and the resulting data can be tracked using the GenoLogics Proteus Laboratory Information Management System (LIMS). For assistance in using the LIMS, Scott Sweeny (4-3462; sweeneyman@uab.edu) should be contacted.  **Animal Physiology Core Resources**  **Body Composition/Energy Metabolism (Nagy)**  The body composition/energy metabolism facility is located in Volker Hall Education and Research Tower. The main facility (1,300 ft2) consists of three contiguous rooms: Room G009 houses the *in vivo* micro-computed tomography system; room G008 houses the *ex vivo* micro-computed tomography instrument, two quantitative magnetic resonance (QMR) instruments; two dual-energy X-ray absorptiometers (DXA); and the faxitron; room G006 contains the soxhlet apparatus, drying ovens, muffle furnace, necropsy space, and prep space. Additionally two rooms (400ft2) are located in the basement of Volker Hall within the animal facility. These rooms house the 4 large environmental chambers that are used when temperature and humidity must be rigorously maintained, including the 2 for the calorimetry system, and also the voluntary wheel running cages. Two additional rooms are shared with the Human Physiology Core. These rooms are located in the Webb Nutrition Building and house the Lunar Prodigy DXA (clinical DXA that is also used for rats and dogs), and the Stratec XCT3000 peripheral quantitative computed tomography system (clinical pQCT that is also used for rats and dogs).  **Major equipment:**  Lunar Prodigy DXA    Lunar PIXImus and Norland  pDEXA Sabre small animal  DXA’s    **For Body Composition Analysis:** For carcass analysis, the lab utilizes two drying ovens, 12 Soxhlet extractors, a muffle furnace, analytical balance, and all miscellaneous items. *In vivo* body composition is obtained via 3 DXAs (GE-Lunar PIXImus, Madison, WI; Norland Pdexa Sabre, Ft. Atkinson, WI; and GE-Lunar Prodigy), the latter DXA is utilized for animals greater than 250g and is a shared resource with the Human Physiology Core (Core C), or 2 quantitative magnetic resonance instruments (EchoMRI, Houston, TX). *In vivo* imaging is obtained using the Imtek MicroCAT II (ImTek Inc., Knoxville,TN), while *ex vivo* 3-D imaging of bone is performed with the μCT40 (Scanco Medical, Bassersdorf, Switzerland) microcomputed tomography instruments. Three high-end computer workstations are available in the laboratory for processing and analyzing μCT data. The Imtek μCT allows the discrimination between visceral and subcutaneous fat in either anesthetized or dead animals. The Scanco μCT allows for the quantification of 3-D structure of trabecular and cortical bone with resolutions up to 6 μm in excised bones. A Faxitron Model MX-20 tabletop X-ray machine is used to take high-resolution digital radiographic images of small animals or excised bones. The Stratec XCT3000 pQCT allows for the *in vivo* determination of trabecular and cortical bone, as well as attenuation rates of muscle and bone marrow.  Rat QMR instrument    3-in-1 quantitative magnetic  resonance (QMR) instrument    Scanco 40 uCT    Imtek uCT    **For Energy Budget Studies:** The core has a complete indirect calorimetry system (TSE Systems GmbH, Bad Homburg, Germany) with 8 calorimetry cages, and 16 acclimation cages. In addition to measuring oxygen consumption and carbon dioxide production, this system also uses a grid of infrared beams to detect both locomotor, and fine motor activity as well as force transducers attached to the feeding apparatus to constantly measure food intake. These are housed within 2 large environmental chambers (Powers Scientific, 63 cu ft with up to 12 shelves each, capable of holding temperatures between 5-37˚C, and air exchange of 10-15 times per hour). All chambers have lights controlled by timers to allow for complete control of the photoperiod. Voluntary physical activity can also be measured using our wheel running system (Mini Mitter, Bend, OR), which measures wheel revolutions during the measurement period using the VitalView software. The core has 16 mouse and 16 rat wheel cages. For forced exercise, the core has a forced exercise / walking wheel bed that contains 20 wheels that can be set for different speeds and lengths of time.  **Animal Facilities:**  The body composition/energy metabolism facility is conveniently located directly above, and within, one of UABs largest animal facilities, greatly facilitating the transport of animals to the Core. In most cases, containment at UAB is at the level of the cage so most animals can readily be transported to and from the animal facilities. Great care is taken to sanitize all instruments and areas between animals. In the years that we have operated the facility we have never had a case of cross-contamination. For investigators who house their animals in barrier facilities, they are required to relocate their animals to a non-barrier facility for the proposed studies and animals are not returned to the barrier facility at the end of the experiment. These animals are typically housed in Volker Hall to facilitate ease of transport. Investigators housing animals in facilities other than Volker Hall have the option of transporting animals themselves (following strict Animal Resource Program procedures) or they can arrange for the Animal Resource Program to transport the animals for them at no charge.  TSE Lab animal system    **Cardiometabolic Facility (Yang)**  The Cardiometabolic facility is located on **the 4th floor** (~2,500 sq. ft.) of the Webb Building. These laboratory spaces include separate rooms for mouse surgery and mouse cardiac physiology.  **Major equipment:**  **For Glucose Homeostasis:**  For the hyperinsulinemic euglycemic clamp study, surgical microscope (Haloid lam cold-light source, AmScope), isoflurane vaporaizer anesthetic conduction system, MiniVent Mouse Ventilator (HUGO SACHS, Germany), single channel PHD 2000 Infusion/Withdraw dual syringe pump and independently regulated dua  channel CMA 402 syringe pump (HARVARD APPARATUS) are located in webb building room 418.    Images of the VEVO 770 echocardiographic system and work station.  **For *In vivo* cardiovascular**  **assessments using highresolution echocardiography:**  This subcore has a VEVO 770 high-resolution in vivo imaging (echocardiographic) system (VisualSonic Inc., Toronto, Canada) with an RMV 707B high frame rate scanhead for in vivo adult mouse cardiovascular imaging. The system is located at Webb building room 416. The system is equipped with Pulsed Wave Doppler, M-mode capture and analysis software, ECG kilohertz-based Visualization analytic software, advance Cardiovascular Package for tissue Doppler imaging, automated left ventricular analysis, integrated blood pressure for integrating blood pressure inputs with live high-resolution Vevo image data w/Pressure vol analysis, Anatomical M-Mode for MMode analysis in the anatomically correct plane with advanced cardiovacular measurements capability. In addition, this subcore will also utitize the micro-ultrasound imaging system (Vevo 2100, VisualSonic Inc., Toronto, Canada), which will enable assess the cardiovascular system in mice and rats with 30-microM resolution and physiology monitoring in real time. This capacity makes it possible to determine vessel morphology, calcium deposits, and blood flow analyese in addition to cardiac imaging.    Image of the pressure/volume measurement system for assessment of in vivo cardiac function and simultaneous systemic blood pressure.  **For *In vivo* cardiovascular assessments with catheterization and Blood pressure:**  A **Millar** Pressure-Volume conductance system for measurement of left ventricular volume and pressure in rats and in mice (Aria-1, MILLAR INSTRUMENTS) and The ADVantage™ PV system (SciSense) are located at the Webb building room 418. In the ADVantage PV system, a second pressure channel permits advanced protocols, such as simultaneous systemic blood pressure recordings with PV loops, or pulse-wave velocity studies. Other associated equipment includes isoflurane vaporaizer anesthetic conduction system, and the MiniVent Mouse Ventilator (HUGO SACHS, Germany).  **For Isolated working heart function:**    Images of the IHSR-isolated heart system (Harvard Apparatus).  The IHSR - Complete Isolated Langendorff and/or Working Heart Perfusion System for Small Rodents (Harvard Apparatus) is housed in the Webb building room 418. The IH-SR apparatus has been designed for experiments on the isolated heart of small rodents like rats or guinea pigs, and especially mice. The apparatus can be used for both Langendorff Heart and Working Heart mode. Both modes allow easy conversion between constant pressure and constant flow conditions. Mode changeover is performed through a few simple manipulations; no additional conversion of the apparatus required. The precision design simplifies system use and minimizes user error.  In working heart mode the left atrium is cannulated and the heart performs pressure-volume work. Atrial preload is set by a simple fluid column height adjustment. Measurable parameters in working heart mode include perfusion pressure, aortic flow, total cardiac output from left atrial flow, atrial preload pressure, LVP pressure via aortic cannulation or ventricular cannulation. Parameters that can be monitored in either Langendorff and working heart modes include ECG, and Monophasic Action Potential. A MICROX TX3 Fiberoptic oxygen meter is used to monitor myocardial oxygen consumption during the perfusion experiment. A custom made silicone membrane oxygenator is used in isolated working heart study of myocardial fatty acid and glucose metabolism.  **Imaging Facility (Zinn)**  The primary location is in the Volker Hall Education and Research Tower, a building centrally located within the UAB campus such that interactions with other colleagues in the Medical School and Basic Science Departments are convenient. The facility (~4000 square feet) includes 6 labs: Rooms G082G, G082G1, and G082H (radiotracer preparation, imaging, tissue harvest, *in vitro* assays, biochemistry, gel electrophoresis, centrifugations, etc.); Rooms B021 and B021A (*in vivo* Imaging Suite), Room G082J (ultrasonics research); Room G082K (tissue culture, flow cytometry); Room B054M (animal housing). Volker Hall Laboratories currently houses a gamma camera and a custom-built Leica Stereomicroscope for animal imaging. Additional rodent imaging capabilities in Volker Hall include: SPECT/CT system (GammaMedica X-SPECT) for 3-dimensional SPECT imaging in combination with X-ray CT, microPET/CT (GE Triumph), two IVIS-100 systems (Xenogen) for bioluminescence/fluorescence imaging, Vevo-6600 high frequency ultrasound imaging instrument (Visualsonics), SONIX RP ultrasound research system (Ultrasonix), time-domain fluorescence scanner (Explore Optix, GE/ART), and a Bruker 9.4T MR system.  **Major equipment:**  **For MRI/MRS:** The facility is currently equipped with a fully upgraded horizontal-bore ultra high field 9.4T system for small animals. The system is operated with Bruker Avance console and ParaVision software and is housed adjacent to our imaging suite in Volker Hall. Two SGI workstations are available for off-line data analysis and pulsed sequence development.  **For *In Vivo* Gamma-ray**  **Imaging:** Dual Heal SPECT  Gamma Camera (large animals); 2 Anger Technicare 420/550 Mobile Gamma Cameras; a full range of collimators for all 3 units; 2 NUMA PC-based acquisition systems; Small animal SPECT/CT dual head system (X-SPECT) with 1 mm 3D spatial resolution, in combination with X-ray CT at 50 μm resolution (Gamma Medica, Inc); and microPET/CT (GE Triumph). SPECT (large animals) with microSPECT/CT (below).  **For Light-based *In Vivo* Imaging**: Leica MZFL3 Stereomicroscope with Xenon Light Source for Excitation (including Near Infrared); Hamamatsu ORCA ER digital CCD camera (suitable for Near Infrared, Quantum Efficiency: 500 nm=70%; 600 nm=68%, 700 nm=50%, 800 nm=30%; 900 nm=15%); Diagnostic Instruments SPOT color CCD camera; OpenLab™ imaging and camera control software; appropriate filter sets for fluorescence (e.g. GFP, Cy5.5, Cy7, and others); Nuance spectral imaging camera; Xenogen IVIS system equipped for bioluminescence and fluorescence imaging. ART/GE’s time domain fluorescence instrument (Explore Optix) is equipped with 630 nm and 488 pulse lasers. A special chamber for maintaining mice under aseptic conditions is available. IVIS-100 system for Bioluminescence Custom Fluorescent Stereomicroscope    **For Ultrasound Imaging:** Vevo-6600 system with 20, 30, 40, and 55 MHz transducers; heated animal stage with EKG and temperature monitoring, and ultrasound guided injection system. The system is equipped to collect and analyze 3-dimensonal images using movement of the stage. SONIX RP system with a 4-15 MHz broadband linear array transducer and research software for customized scanning and data acquisition. Velmex three-axis precision positioning  system; 2 Tektronix 2-channel arbitrary function generator and 4-channel digital oscilloscope; 2 E&I broadband  power amplifiers; single element transducers; acoustic hydrophone and preamplifier; Ohmic Instruments  ultrasound power meter; Cole-Parmer precision flow pump and vascular flow phantom (ATS Labs).  **Radioisotope Measurement:** Packard Minaxi 5000 Series gamma counter interfaced with PC for data  acquisition, Ortec germanium detector interfaced with a PC for data acquisition (Canberra Genie PC system), 2  Biodex Atomlab 100 dose calibrators, Keithley Model 36150 integrating survey meter, 2 Geiger counters.  **Tissue Culture:** Four 6 ft. Laminar flow biosafety hoods, 6 CO2 incubators, Clay Adams clinical centrifuge,  Leica DM-IRB Inverted Research Microscope for Phase Contrast, Bright Field, and Fluorescence with Mercury  light excitation; appropriate filter sets for fluorescence. Diagnostic Instruments SPOT color CCD camera;  OpenLab™ imaging and camera control software; fluorescence filters (e.g. GFP, Cy5.5, Cy7, and others;  Accuri flow cytometry system.  **Refrigeration Equipment:** refrigerators (4), -20°C freezers (2), -80°C freezer (2), high capacity liquid nitrogen  storage container (Forma Scientific CryoPlus 1).  **Transgenic Mouse Facility (Kesterson)**  Dr. Kesterson has an 875 ft2 laboratory (KAUL 606) that is located next door to his office (KAUL 602A), and  dedicated tissue culture space located in KAUL 613. The main laboratory is fully equipped for molecular  biological, biochemical, and histological procedures. The PI has two approximately 500 ft2 dedicated animal  rooms (each with separate chambers for procedures) within a controlled access barrier area on the 1st floor of KAUL, located adjacent to the dedicated Transgenic Mouse Facilities that he directs. The transgenic facilities include: 2 additional 500 ft2 animal rooms plus 1100 ft2 of laboratory space equipped with two independent microinjection rigs for transgenic animal production. Additional spaced includes a dedicated tissue culture room and common equipment space (200 ft2 each KAUL 613 and 611, respectively), and office space provided for the co-Director/Coordinator of the facility (605 KAUL).  **Major equipment:**  **Molecular Biology & Tissue Culture Labs:**  MJChromo4 Real Time PCR machine, Molecular Dynamics STORM phosphorimager, MJ dyad 2x96 well PCR machine, MJ PTC100 and Bio-Rad iCycler PCR thermal cyclers, Savant DNA110 Speed Vac, 4 microcentrifuges, Eppendorf 5810R refrigerated centrifuge, BTX ECM 630 Electroporator, 2 refrigerator/freezers and 3 freezers (2@-20oC and 2@-80oC), Hitachi U1100 spectrophotometer, 2 tissue culture incubators (Nuaire), 4 liquid N2 tanks, Cryoplus 4 tank, Nikon E600 eclipse microscope equipped with fluorescent imaging and Spot Digital camera, sliding microtome (Microm) for routine sectioning of mouse brains; hybridization oven (Northern Blots), bacterial incubators, BIORAD 3000 power supplies, horizontal gel boxes.  Funded by a NIH Shared Instrument Grant ($200K Kesterson, PI), the **AutoGenprep 965** is a state-of-the-art fully automated high throughput robotic instrument that will isolate and purify DNA from mouse tissues and ES cells (plasmids/BACs too). This instrument will allow high throughput isolation of DNA from mouse tail biopsies (384 samples / 4 hrs).  **Microinjection labs:**  2 Leitz/Leica Laborlux S Nomarski DIC microscopes, 4 Leitz micromanipulators, 3 Meiji dissecting microscopes, 2 Harvard Apparatus automatic injector systems, Leitz Defonbrune microforge with Leitz microscope head, Sutter P-87 horizontal pipet puller, Kopf 720 vertical pipet puller, FTS system S programmable freezer, 2 anti-vibration tables, Bio-Cool model BCIV40 controlled-rate cryopreservation freezer, Piezoelectric Drill.  **Human Physiology Core**  **Overview**  The majority of the Core (Analytical and Body Composition/Energy Metabolism components) is located in the  Webb Nutrition Sciences Building, with the Vascular Laboratory component a short walk away in the Community Health Building. The Webb components consist of three suites of laboratories located on the second, third, and fourth floors of the Webb Nutrition Sciences Building. Webb 218 and 224 (150 sq ft each) house the iDXA, the Prodigy, and the BodPod. Webb 306 (400 sq ft) houses the pQCT and the PeaPod. Webb 317 (800 sq ft) houses the analytical laboratory. Webb 412 A-B (~800 sq ft; a suite of four rooms) houses the whole-room indirect calorimeter; an office for Mr. Petri, who operates the room calorimeter; a kitchen facility that is used to store and prepare food for study participants who stay in the calorimeter; and a room dedicated to the resting metabolic monitors. The suite is connected to a shower facility. A research participant parking area is located adjacent to the Webb Building. These components are located in close proximity to each other and to the Director’s office (423 Webb). The Vascular Laboratory is housed in the Hypertension Research Clinic, 115 Community Health Service Building (CHSB), which is located two blocks from the Webb Building. This laboratory is conveniently located near the offices of Drs. Calhoun and Dudenbostel, who conduct the cardiovascular testing.  **Analytical Laboratory**  The analytical laboratory of the Human Physiology Core is an 800 sq.-ft. laboratory located on the 3rd floor of the Webb Nutrition Sciences Building that is staffed by four full-time technicians. It is equipped with automated analyzers for assessment of lipids and glucose (StanBio SIRRUS), and insulin and other protein hormones (TOSOH); and instrumentation necessary for conducting ELISA (BioTek ELx405 micro-plate washer, BioTek Synergy HT plate reader) and RIA (Perkin Elmer Wizard 1470 5-head Automatic Gamma Counter). A multiplex analyzer (Meso Scale Discovery SECTOR imager 2400; Gaithersburg, MD) is available for performing determinations of hormone and cytokines. The laboratory also contains general supplies, pipetting devices, a refrigerator, -80oC and -20oC freezers, two refrigerated centrifuges, water baths, a shaker, a rotating extractor, and an ALPCO microplate rotator. A water distillation and filtration system, cold rooms, and an ice machine are located adjacent to the laboratory, and are available for use in hormone/substrate analysis. Agilent Model 6890 GC System and Model 5973N Mass Selector Detector are used to perform the GCMS analysis for stable isotopes of glucose and amino acids. A Thermo Scientific isotope-ratio mass spectrometer (Thermo Electron North America LLC, West Palm Beach, FL) is used for analysis of stable isotopes of hydrogen and oxygen (doubly-labeled water; DLW).    Gamma Counter  **Analytical Laboratory: Major Equipment**    MSD multiplex analyzer  **Perkin Elmer Wizard 1470 5-head Automatic Gamma Counter**. The gamma counter allows for rapid quantification of  RIA tubes. With five “heads” (counting chambers), the instrument can count five test tubes simultaneously, permitting rapid through-put. The sample bed holds up to 500 test tubes, thus easily accommodating most of our large assays. The StatLIA software performs routine data reduction. The instrument is used for all 125I-based RIAs and IRMAs.  **Meso Scale Discovery SECTOR imager 2400** (Gaithersburg,  MD). This multiplex analyzer is available for performing determinations of hormone and cytokines. The Mesoscale Discovery (MSD) multiplex method is an ELISA (Enzyme-linked immunosorbant assay) that uses electrochemiluminescence as the signal to detect binding events. Conducting the MSD-based assay is similar to conducting any ELISA in that the sample is pipeted into a 96-well plate that has been prepared in advance with a capture antibody. In the case of multiplex determinations, the well can have up to 10 capture antibodies that are arrayed in discrete spots. Each spot is coupled to a unique electrode. The addition of the detection antibody with signal conjugate completes the circuit, and generates a luminescent (light) signal. The signal images are then captured by the SECTOR® Imager 2400 reader, and transmitted to a computer for data reduction and report generation. Because the signal (light) is not coupled to the stimulation mechanism (electricity), background “noise” is minimal, which allows for a highly sensitive assay. Because only labels near the electrode are excited and detected, the assay can be conducted without wash steps, which minimizes technician time and enables high throughput. Amplifying substances in the buffers, along with multiple excitation cycles, increase signal intensity. Thus, the MSD system offers sensitive analyses with a greater dynamic range than other ELISA and RIA approaches.  **BioTek Synergy HT plate reader and BioTek ELx405 micro-plate washer.** These instruments support the  laboratory’s ELISA effort. The plate reader analyzes signals in the visible and fluorescent light ranges. The  plate washer can store multiple custom programs for specific wash profiles. The custom programs permit  details such as the number and volume of each wash to be specified.    ELISA Plate Reader    ELISA Plate Washer  **TOSOH.** The TOSOH immunoassay analyzer allows for rapid automated, high throughput of many common protein and steroid hormones. The Human Physiology Core uses the TOSOH daily for insulin and C-peptide. The instrument also is used routinely for analysis of estradiol and testosterone. A large number of other analytes are available. The TOSOH uses the same assay principle as an ELISA, which is a sandwich-type immunoassay with signal being directly proportional to analyte concentration. The instrument is calibrated according to each lot of reagent. The calibration produces a standard curve that is then used to analyze the unknown samples. The TOSOH can be loaded with up to 25 samples at one time. The Core has used the TOSOH for the past 6 years, and noted it to have excellent precision. Due to the large number of insulin determinations performed by the Core (approximately 6000/yr), the TOSOH has greatly improved turn-around time and freed staff to perform other tasks that previously were devoted to insulin RIA.    TOSOH immunoassay analyzer  **SIRRUS analyzer.** The SIRRUS automated chemistry analyzer (Stanbio, Boerne, TX) is a flexible platform that can be easily customized to analyze a broad array of molecules using standard colorimetric assays. The Human Physiology Core uses the SIRRUS daily for analyses of glucose, cholesterol (total, HDL-C, and LDL- C), triglycerides, free fatty acids, and CRP. The Core has used the SIRRUS for the past 7 years. Precision is excellent. The SIRRUS can be configured to assess up to 36 analyses simultaneously, and can conduct up to 400 tests per hour. For one “run,” up to 45 “patient” (serum) samples can be loaded into the instrument. HDLand LDL-cholesterol can measured directly, without sample pre-treatment. Glucose is analyzed using the glucose oxidase method. Total cholesterol is analyzed with the cholesterol oxidase method. HDL-cholesterol is analyzed using a two-reagent system. First, LDL, VLDL, and chylomicrons are stabilized with cyclodextrin and dextrin sulfate, leaving the HDL particles exposed. Second, enzymes are used that react with the HDL cholesterol and produce the reaction product detected by the instrument. Similarly, LDL-cholesterol is analyzed using a two-reagent system. First, HDL, VLDL, and chylomicrons are bound with a detergent, and organic and inorganic phosphoric acid, leaving the LDL particles exposed. Second, enzymes are used that react with the LDL cholesterol and produce the reaction product detected by the instrument. Triglycerides are assessed with the glycerylphosphate (GPO) method. Free fatty acids (FFA) are measured by enzymatic, colorimetric methodology.The SIRRUS is calibrated weekly. Control sera of low and high substrate concentration are analyzed with each group of samples, and values for these controls must fall within accepted ranges before samples are analyzed.  **Agilent Model 6890 GC System**. The Core houses instrumentation necessary for determining isotope enrichment of biological samples for in vivo metabolic studies (glucose, amino acids): Agilent Model 6890 GC System, Model 5973N Mass Selector Detector, Dell computer; DCNE Intel Pentium 4HT Optiplex GX620, Hewlett-Packard Laser Jet 4050 printer.  **The Body Composition/Energy Metabolism Laboratory**  The Body Composition/Energy Metabolism Laboratory (2nd, 3rd, and 4th floors, Webb) is designed for stateof  the art analysis of human body composition and energy metabolism. It houses two Lunar dual energy X-ray absorptiometers (Prodigy and iDXA; Lunar Radiation Corp. Madison, WI) used for determining total andregional body composition. It also houses a BOD POD (Life Measurement, Inc, Concord, CA), which determines body volume using air-displacement plethysmography, which can be used to calculate body composition using published multi-compartment equations. A PEA POD is available for use in determining body composition in infants. A Peripheral Quantitative Computed Tomography (pQCT) instrument (XCT 3000®; Stratec, Germany) is located on the third floor of the Webb Building. Energy metabolism is assessed using indirect calorimetry. A whole-room indirect calorimeter is available for extended measurements, and two metabolic carts (VMAX ENCORE 29N; VIASYS Respiratory Care, Yorba Linda, CA) are available for assessment of resting energy expenditure.  **Body Composition/Energy Metabolism Laboratory: Major Equipment**  **Dual-Energy X-ray Absorptiometry (DXA):** The Core houses two instruments (Prodigy and iDXA; GE-Lunar Radiation Corp. Madison, WI). The iDXA was acquired in 2008 in response to investigator need for an instrument capable of use with larger patients. The iDXA table can accommodate patients up to 450 lbs, and has a wider scanning area than the Prodigy. Although some studies still use the Prodigy, it is being phased out, and all new studies use the iDXA. The iDXA is connected to a desk-top computer and printer.  **Magnetic Resonance Imaging (MRI) and computed tomography (CT):** MRI and CT scanning are conducted on clinical scanners in the Departments of Radiology and Cardiology at UAB, which are located within or adjacent to UAB Hospital, ~2 blocks from the Webb Building. The Department of Radiology offers MRI scans on a Philips 1.5 Tesla Ingenia Omega HP; Cardiology uses a Philips Intera 3 Tesla scanner (Philips Medical Systems, Best, The Netherlands). CT scanning is available through Radiology (GE HiLight/Advantage scanners, Milwaukee, WI). Magnetic Resonance Spectroscopy (MRS) also is available through Cardiology. Scanning is not offered as a DRC Core service; rather, each investigator makes his/her own arrangements with the appropriate departmental personnel, and arranges for faculty in Radiology/Cardiology to provide assistance with determining appropriate acquisition parameters. The Core provides scan analysis using SliceOmatic software. Analyses are performed using a Dell desktop computer located in room 423 of the Webb Building. A dedicated Mac mini (433 Webb), equipped with Osirix software, also is used for scan analysis. Core personnel also assist investigators with making necessary contacts with staff and faculty in Radiology and Cardiology.    MRI of thigh tissue. The figure shows subcutaneous (SAT), perimuscular (PMAT), and intermuscular (IMAT) adipose tissue.  **Peripheral Quantitative Computed Tomography (pQCT):** The XCT 3000® (Stratec, Germany) is a fully automated system for the determination of bone density and muscle composition. It consists of a specially developed X-ray tube; a series of miniature-semiconductor-crystals; microcontrollers to transfer the results and axis positions; and a computer. The absorption of X-rays by a given tissue yields an absorption profile. The raw data are corrected for dead time by beam hardening. By mathematical folding of many absorption profiles from different angular positions, a cross sectional image can be calculated which represents the original object. This method is called filtered back projection. Each point of the image (voxel) corresponds to an attenuation coefficient with the dimension of 1/cm. The attenuation coefficient is characteristic for a given X-ray energy for a given material. For assessment of bone, calibrations are conducted with phantoms of a specific hydroxyapetite concentration. The attenuation coefficients of tissue are then transformed to density values (mg/cm3) based on the phantom data. The calibration takes only the mineral portion of bone into account. For soft tissue, the attenuation of the tissue is used as an index of fat infiltration of skeletal muscle. Scans are obtained at 66% of the calf length, proximal to the terminal end of the tibia. This site was chosen based on published data indicating that this is the region of the calf with the largest circumference and lowest variability. Tissues are separated according to density thresholds. Fat, muscle, and cortical bone are measured with mineral equivalent densities of 0, 80, and 1200 mg/cm3, respectively. Thus, fatty infiltration of skeletal muscle will be detected as a shift in mineral equivalent density of the muscle from 80 to 0 mg/cm3. Images of the cross-sectional area are analyzed using the Stratec analysis software version 5.5D (Orthometrix, Inc.). All images are analyzed by one technician.    Stratec Peripheral Quantitative  Computed Tomography (pQCT)  **Indirect Calorimetry (resting):** Two open-circuit metabolic monitors are available for assessment of resting energy expenditure (REE) and substrate oxidation (Vmax ENCORE 29N Systems, SensorMedics Corporation, Yorba Linda, CA). Each unit interfaces with a laptop computer and printer.  **The Vascular Laboratory**  The Vascular Laboratory is housed in the Hypertension Research Clinic, 115 Community Health Service Building (CHSB). The clinic consists of approximately 3500 sq. ft. including four patient examination rooms, a  atient waiting area, office space, a conference room, and a double-locked medication storage room. The Vascular Laboratory consists of a separate dedicated room within this facility.  **The Vascular Laboratory:**  **Major Equipment**  **Endothelial function.** Brachial artery images are obtained on by ultrasound with use of a 7.5-MHz linear  array ultrasound probe (Acuson 128XP/10, Siemans, Malvern, PA ). Recorded images are then analyzed on a variable speed high resolution medical VCR (SONY SVO-9500MD, Sony USA, New York, NY) and color video monitor (SONY Trinitron PVM 14L1, Sony USA, New York, NY).      Endothelial function assessed with flow-mediated dilation.  **Pulse wave velocity and central aortic augmentation index.** Vascular indices are obtained by applanation tonometry with use of a high-fidelity micromonometer (SphymgomCor Vx, AtCor Inc., Sydney, Australia). **Thoracic impedance** values are obtained by high fidelity sensors placed on the neck and chest (BioZ ICG Monitor, CardioDynamics, San Diego, CA).  **Ambulatory Blood Pressure Monitoring.** Five ambulatory blood pressure units (Spacelabs model 90207, Spacelabs Healthcare, Issaquah, WA) are available exclusively for research purposes. The units are programmable and each monitor has four different arm cuffs (pediatric, small adult, medium, large adult). The recorded data are downloaded from the monitors into a dedicated desk top computer. Data are then analyzed with proprietary software (Spacelabs Healthcare, Issaquah, WA).  **Office Space and Computers**  All investigators have individual office space and access to computers, printers, and the internet. Specific locations are: Gower (4th floor Webb), Calhoun (4th floor Biomedical Research Building), Granger (4th floor School of Health Professions Building), and Eto (3rd floor Webb Building).  **Targeted Metabolomics and Proteomics laboratory (TMPL)**  The TMPL will be used for the developmental component of the project period, which is assessment of steroid hormones by liquid chromatography / mass spectrometry. Stephen Barnes, PhD, iserves as Director of the TMPL, and co-Director of the DRC REDOX Biology Core. He will collaborate with the Human Physiology Core and oversee implementation of these assays. The TMPL web site is: www.uab.edu/proteomics/massspec  Dr. Barnes’ office and the TMPL facility are located in adjacent spaces in the McCallum Research Building, which is one block from the Webb Building. Established in 1993, the laboratory typically supports the research of 60-100 investigators on an annual basis. The TMPL occupies 2,400 square feet of laboratory space and adjoining office space, and contains computers for data processing, teaching, and consulting, and a GenoLogics Proteus Laboratory Information Management System (LIMS) for data tracking. The TMPL has the following major equipment:  • **AB-Sciex 5600 Triple-Tof mass spectrometer**. This is the latest proteomics instrument from ABSciex. It detects 5-15 more identifiable and verifiable peptides in a LC-MSMS discovery experiment than the AB Sciex 4000Qtrap. Although it was purchased to carry out targeted, quantitative analysis of proteotypic peptides from proteins in signaling pathways, it is also used for small molecule peptidomics, lipidomics and metabolomics analysis because of its high mass resolution (30-40,000), mass accuracy (3-5 ppm) and speed (20 MSMS spectra per second). It is operated with an Eksigent Tempo nanoLC pump and Nanoflex Chip system.  • **ABI Sciex 4000Q-trap mass spectrometer**. This instrument is used for the analysis of complex metabolite mixtures. It has a PAL robot and an Eksigent pump for nanoLC. It is used for high sensitivity (10-100 amol) analysisin complex mixtures. It is also used to carry MSn experiments for complex small molecules, in particular parent ion scanning to discover lipids/metabolites with specific head groups.  • **ABI Sciex 4000 triple quadrupole mass spectrometer**. This instrument is well suited to the quantitative measurement of small molecules in biological fluids and tissues, offering sensitivities mostly in the range of 1-10 fmol injected although sensitivity depends on the analyte. For example, the sensitivity limits for 17β-estradiol and the anesthetic propofol are 500 fmol injected, whereas the dansyl derivative of 17β-estradiol is 1.6 fmol. It has a Shimadzu Prominence fPLC with refrigerated autosampler.  • **ABI Sciex 3200 triple quadrupole mass spectrometer**. This instrument is well suited to the quantitative measurement of small molecules in metabolomics applications, offering sensitivities in the range of 5-25 fmol. It has a Shimadzu HPLC with autosampler and a Waters Acquity uPLC.  • **Two ThermoFinnigan 7 tesla LTQ-FT Fourier Transform ICR-mass spectrometers** including nanoLC and an Advion NanoMate™/Triversa. One of the LTQ-FT instruments is equipped with IRMPD and ECD. It also has a 2D-nanoLC Eksigent pump.  The laboratory also is equipped with incubators, laminar flow hoods, a BioRad plate reader, thermocyclers, refrigerators and freezers (-20oC and -80oC), water baths and a HP 1080 HPLC for sample fractionation as well as automated sample extraction devices and evaporators.  **RESOURCES and FACILITIES**  **I. Division of Preventive Medicine.**  The Interventions & Translation Core (ITC) is housed in the Medical Towers Building in space assigned to the Division of Preventive Medicine in the Department of Medicine. The Division of Preventive Medicine (DOPM) is dedicated to medicine and the health of the public through research, teaching, and dissemination and translation of knowledge for improved health outcomes. It includes over 20 faculty and a total staff of some 280. From its inception in 1967, the Division of Preventive Medicine has played a key role in the many groundbreaking trials contributing to the knowledge of medical and health systems, behavioral aspects of disease, epidemiology, prevention, control, and disease outcomes. Special concern with health disparities and a desire to promote women’s health guide many Division activities. A research-oriented division, we also have active programs for the training of post doctoral fellows and clinical scholars. The Division’s research infrastructure also includes a research clinic with approximately 6,000 participant visits per year.  The DOPM is also home to two University-wide centers – the UAB Minority Health and Health Disparities research Center and the UAB Center for Outcomes and Effectiveness Research and Education. It also houses the Health Services and Comparative Effectiveness Research T-32 Fellowships. The DOPM is located in the Medical Towers Building. Communications equipment and connections, internet connections, and computers for staff, and fellows are supported through institutional commitments from the Division of Preventive Medicine (DOPM) and Department of Medicine (DOM) and institutional funds available to the Center for Outcomes and Effectiveness Research and Education (COERE) through UAB’s University-wide Interdisciplinary Research Centers program, as well as through extramural research and training dollars. The DOPM provides intranet service (including wi-fi connection), servers, software access, and IT support.  The Division also has sufficient conference space for meetings; 1 large 900 sq ft conference room with adjoining kitchen facilities, and 2 large 500 ft conference rooms. Parking is available on the 2nd and 3rd floors of the Medical Towers Building, as well as a gated lot behind the building.   1. **DOPM Research Clinic.** The DOPM Clinical facilities are located on the 7th floor of the MT Building, at the southern edge of the UAB campus. The clinic is an attractive area especially designed for clinical trials containing all the necessary facilities for participant assessments. With approximately 10,000 participant visits per year, the DOPM Clinic is equipped specifically for research with a reception area, large waiting room, 22 exam rooms, and 5 smaller rooms for patient interviews; phlebotomy, processing, a locked medical record room; and staff offices, all totaling over 17,000 square feet. The clinic facilities space is extremely flexible and can be allocated as needed for the study. The newly renovated laboratory contains a separate phlebotomy and processing areas, equipped with centrifuges (ambient & refrigerated) refrigerators, ultra low-temperature freezers, ice machine, centrifuges, a urine processing area with hood for preparing blood and urine specimen for submission to other labs for analyses. Additional low-temperature freezers, with alarm and back-up systems, and our specimen shipping area are located in a secured section of the first floor.   The DOPM has clinical equipment, located in the 7th floor clinic include: an MRI, ONI, Inc, OrthOne 1.0 Tesla superconducting extremities magnet with circumferential coil; a Hologic QDR 4500W dexa (dual x-ray bone densitometer); two biphasic automated external defibrillators (AED); 3 ultrasounds,1 for trans-vaginal testing and 2 for carotid ultrasounds; resting ECG machines and flexible sigmoidoscopy equipment. Our graded exercise testing labs have one Q stress and one Q4000 model ECG monitor with Q55 treadmills for exercise testing. We have a Sensormedics 2300 metabolic cart that can be used for resting energy expenditures or maximum oxygen consumption testing. The x-ray system, located on the first floor of the MT Building, is a Quantom radiographic system (Q-Rad Odyssey High Frequency system) with AGFA computed radiography capability for imaging.  The DOPM Nutrition Unit is located on the 1st floor, facilitating lifestyle intervention trials where assessment staff, located in the DOPM research clinic on the 7th floor, must be masked to intervention assignment. The facility contains offices for a staff of 12. The space was specially designed for lifestyle intervention studies and contains a demonstration kitchen that opens onto a small conference room with seating for up to 16 participants. An adjacent larger conference room can seat up to 25 participants. The interdisciplinary team of exercise physiologists, health behaviorists, psychologists and nutritionists are highly trained and experienced in conduct of a number of dietary intervention and/or exercise promotion programs, with integrated behavioral strategies, including the use of Motivational Interviewing techniques for group- and individual-based sessions.  **B. DOPM Video Conferencing Resources.** The Division has two high definition capable polycom HDX 7000 systems with dual 42" lcd displays. PowerPoint slideshows can be incorporated into a videoconference. Making use of the bridging facilities available to us we can connect up to 38 sites (connecting from compatible systems). Using this system, telephone conference calls can be joined to a conference. Conferences can also be recorded.  **C. DOPM Computer Resources.** Data, Information, Statistics Core (DISC). DISC is a central component of the Division’s research infrastructure. It includes a team of 13 faculty biostatisticians, Information Systems (IS), Data Management (DM) and Statistical Computing (SC) Units, all with a focus on data security and quality assurance  **Within the *IS Unit:***  • Network Operations: The Division occupies five floors in an off-campus building and typically includes some 250 personnel and over 275 computer work stations. Connectivity across the floors is handled by inter-connected gigabyte routers on each floor. Connectivity outside the building is handled by the UAB fiber optic backbone and is standardized on IP v4 and v6. We operate a Microsoft Windows 2003/2008 Active Directory redundant managed network made up of 22 rack mounted servers in a secure room within Division space in the Medical Towers building. These tend to be organized in clusters or a loadbalanced arrangement.  • SQL Cluster: a two node redundant cluster with an off-site virtual node. This system utilizes dual-core /dual-processor running Microsoft SQL 2008 and has a storage capacity of 2 TB.  • Exchange System Cluster a 4 node redundant mirror with an off-site Stand-by Continuous Replication system. This system utilizes dual-core /dual-processor running Microsoft Exchange 2008 and has a storage capacity of 4 TB.  • File Storage System Cluster a 2 node mirrored cluster with an off-site mirrored stand-by system. This system utilizes dual-core /dual-processor running Microsoft Enterprise Server 2008 with a storage capacity of 15 TB.  • DICOM Image System Cluster a 2 node virtual server with an off-site mirrored stand-by system. This system utilizes dual-core /dual-processor running Microsoft Enterprise Server 2008 with a storage capacity of 4 TB.  • Network load balanced Windows Servers for load-balancing and redundancy include; IIS and Sharepoint web servers for internet based web services; Terminal servers for remote access; Encryption Server utilizing Microsoft Bit Locker; Hyper-V Windows Virtualized Server technology for improved maintenance of legacy applications, development platform testing and server management for virtualization include; Print Server to manage printers for 35 network printers including 12 color systems, 11 network copy machines; FAX Server with OCR automation; Applications Server for testing and development environments; License Server to manage applications; Verity Tele-Forms server for data collection and standardized form printing; Office Communication server for collaboration and conferencing; Team Foundation server for development support.  • Statistical Software Cluster: Cluster a 2 node network load balanced servers along with the software packages; SPSS, Stata, PASS, SAS (Add VERSION), BMDP, NCSS, StatXact, MapInfo, NQuery Advisor, DBMSCopy, S-Plus 2000, P-Pharm 1.5.1, Kinetica 2000, Mathematica, EpiInfo 6.0, Cart, Rancode, Scientific Work Place 2.5, PASS, EquivTest, LISrel 8.0, IMSL, SUDAAN, Costart.  • Server storage system utilizes HP MSA 1000 Fiber channel array based solution currently consisting of 15 terabytes of storage space with a maximum capacity of over 60 terabytes of storage space. Each of the clustered servers has redundant fiber connections for failover. These systems are powered by 10 APC3000 208 volt UPS for continuous operation during power outages.  • Security and Compliance: the Division uses a software based management system for updates that includes Forefront, MacAfee, NOD32, COMODO and Ghost Firewall and Microsoft Antigen SPAM protection with daily automated updates for virus protection for the Divisions data files, mail, and active network monitoring to ensure HIPAA, FISMA and NIST compliance at all times. All personnel undergo certification process to maintain up-to-date training. This system is connected to the University of Alabama at Birmingham main network through a fiber backbone and is monitored for outages at all times by a staff of 10 trained personnel and an additional 5 support personnel.  • Disaster Recovery: An off-site system includes in functionality a mirror each system with a maximum of 24 hour lag time. Systems included in the mirror are a hardware based SQL; Exchange; File servers; DICOM Image; Microsoft Hyper-V Server Share-point; Terminal Server; Encryption Server; Print Server FAX Server; Applications Server; License Server; Statistical Core. The Division mirrored server storage system utilizes HP MSA 1000 Fiber channel based solution currently consisting of 15 terabytes of storage space with a maximum capacity of over 48 terabytes of storage space. These systems are powered by 8 Libert 110 volt UPS for continuous operation during power outages. These systems are monitored 24-hours/day 7 days/week and backed up daily using Veritas with an automated 72 tape (400 GB/Tape) LTO library and a 36 tape (800 GB/Tape) LTO library. The tapes are stored in an offsite storage vault with a quarterly data protection sent to a geographically separate salt-mine. Rotation is 90 days with a daily snapshot of up to 6 weeks duration to a mirror and a quarterly tape based permanent underground off-site archive.  • Personnel: An eleven person team provides technical, user and desktop support. The user support desk is open from 7AM until 6PM, Monday through Friday and handles about 100 user support request a week. A seven person team builds, deploys and manages applications written in Microsoft Visual Studio .NET using Microsoft Team Foundation Server. Management includes scope of work, design, testing, deployment and maintenance, for a complete programming life cycle.  • Software resources available include but are not limited to Microsoft Windows Vista, Microsoft Windows XP, 2000 Server, 2003 Server, Linux, Microsoft SQL, Exchange, FoxPro, Borland DBase & Paradox, Microsoft Excel, SPSS, Stata, PASS, SAS, BMDP, NCSS, StatXact, MapInfo, NQuery Advisor, DBMSCopy, Harvard Graphics, CorelDraw, Ethnograph, WordPerfect, Endnote, Microsoft Office including Outlook 2003 and 2007, Star Office, DICOM image software to include Desacc Digital Jacket, Personnel Server, DICOM Gateway, Verity Tele-Forms, MacAfee Virus protection, NOD32, COMODO Firewall, Ghost Firewall and Microsoft Desktop Firewall, TeleForm 10.2, Cytel StatXact 8, StatXact Procs for SAS, Cytel LogXact 8, East 5, MathType 6, Rightfax Business Server 11.0., S-Plus 2000, PPharm 1.5.1, Kinetica 2000, Mathematica, EpiInfo 6.0, Cart, Rancode, Scientific Work Place 2.5, PASS, EquivTest, LISrel 8.0, IMSL, SUDAAN, Costart, Scientific Word 3.0, Wusage 7.1, Omni Page Pro v10.0, Macromedia DreamWeaver 8.0, Fireworks 8.0, Microsoft GeneSpring 6.0, JRUN 3.0, JRE 3.1, Tomcat 6.0, SUN Fortran Suite, Adobe Acrobat.  **Within the *DM Unit:***  • The *DM Unit* handles data entry systems and data entry, data curation team certified by CABig, data editing and error reporting, and data archiving. This unit includes, in addition to the Director, three full time programmers and a data entry staff and typically creates datasets that are then accessed and analyzed by the SC Unit. The DM unit also includes three NCI-CaBig certified data curators. All personnel are HIPAA and IRB certified.  • Off-site web-based and off-site and on-site PC-based data entry systems are carefully planned and validated before implementation. Programmers are familiar with a variety of languages and programs including SQL, C+, Visual Basic, Microsoft Access, Visual Studio, MedQuest, HTML, Java, and ASP.  • On-site PC-based data entry is via dual screen procedures. All data entry staff are trained and certified as per the requirements for each project. A 10% random sample is typically reentered, with up to 100% reentry when appropriate. An error report is produced and used for corrective action as required.  • The unit provides progress reports detailing the data collection process including counts and other aggregate information. Written documentation regarding the collected data is also created within this group, including data dictionaries, data receipt logs, and data release logs. Data files are archived as are transmission records and dataset documentation. Data management systems are operated in a secure environment. This system provides a clear audit trail to reflect access and changes to data.  **Within the *SC Unit:***  • The *SC Unit* includes, in addition to the Director*,* six master’s level biostatisticians that typically work in SAS, STATA, NCSS, PASS, SPSS, and MapInfo and handles statistical computing needs for the Division’s many projects. The group works closely with faculty biostatisticians to perform statistical reviews and analyses for projects and manuscripts. All analysts are experienced in the management and analysis of large clinical and administrative datasets and have expertise in quality assurance and complex statistical analysis techniques. Unit computers are routinely upgraded and optimized to handle large amounts of data and several statistical packages and current versions of software utilized.  **II. Minority Health and Health Disparities Research Center (MHRC)**  The UAB Minority Health and Health Disparities Research Center (MHRC) is a comprehensive educational, research, and community-outreach center focused on eliminating the health inequalities experienced by racial and ethnic minorities locally, regionally, and nationally. Under the theme of building trust, sharing power, and eliminating racial bias and discrimination, the center accomplishes its mission by fostering partnerships with academic schools and centers, historically black colleges and universities, state agencies, community organizations, and grassroots groups and serves as an infrastructure that supports interdisciplinary research on minority health and health disparities.  The priorities of MHRC are encompassed within three programs: Research, Training/Career Development, and Community Outreach. The Research Program links investigators to develop a conceptual framework for health disparities research. It identifies research priorities and multidisciplinary funding opportunities, provides investigators with scientific expertise and feedback during the research, and funds pilot research projects.  The Training and Career Development Program provides training in health disparities research with emphasis on genetic admixture, cultural competency, bioethics, risk assessment, behavioral, and community-based participatory research principles. The Community Outreach Program links UAB schools, centers, and investigators with the community to facilitate the dissemination of evidence-based interventions and knowledge in a culturally appropriate fashion.  The center’s three programs are supported by three cores: Genetics, Bioethics, and Recruitment and Retention. The Genetics Core supports the Research Program and the Training and Career Development Program by providing to researchers seminars and workshops on using genetic methodology to understand and characterize health disparities along with statistical analysis and consultation in genetic admixtures. The Bioethics Core supports the Training Program by conducting ongoing education for researchers on ethical issues and cultural sensitivity and by developing guidelines for addressing ethical and social issues in genetic research. With this focus, the Bioethics Core seeks to determine barriers to working with minority communities in conducting health disparities research. The Recruitment and Retention Core supports the Research Program by providing strategies for recruitment and retention of minority participants in research studies through FACES, the Facility for Access to Clinical Enrollment Services. Decades of work building trust within the community provides access to grassroots organizations, service groups, health-care professionals, and local businesses.  As a University-wide Interdisciplinary Research Center, the MHRC is supported by ten UAB schools and  has 200 faculty members, 16% of which African American and 15% Hispanic. Such university-wide  participation facilitates MHRC’s involvement in interdisciplinary activities and ensures the accomplishment of  its purpose to serve as an infrastructure that supports university-wide interdisciplinary research on health  disparities.  **III. Healthsmart**  Healthsmart, a downtown store-front wellness center, is MRHC’s newest core facility, opened on March 15, 2011. It promotes UAB in the community, supports the University through community outreach, facilitates the integration of research and service, and disseminates evidence-based practices. In collaboration with faculty and students from the SOM, SON, SHP, SOPH, SOD, and SOO, HealthSmart offers: 1) Health evaluations, risk assessments, and free preventive screenings (vision, blood sugar, cholesterol, blood pressure, body fat, and other health tests); 2) Counseling sessions with nurses, exercise physiologists, and nutritionists to set goals; 3) Physical activity demonstrations and fitness classes; 4) Nutrition demonstrations; 5) Lunch & Learn talks—health education discussion groups led by health-care professionals; 6) Health e-Answers computer workstations providing personal health profiles and access to online health-risk assessments and health resources; 6) Health education tools—brochures and videos explaining chronic diseases and health risks; and 7) Chances to enroll in UAB research studies. In just 4 months HealthSmart has provided 1,300 such services to nearly 700 individuals. In the next cycle, a user charge-back plan will be developed for utilizing the facility.  **IV. Center for Outcomes Effectiveness, Research and Education (COERE)**  The UAB’s Center for Outcomes, Effectiveness Research and Education (Director, K. Saag) was established in 1998 and is a multidisciplinary University-wide Interdisciplinary Research Center. The COERE’s mission is to maintain and continuously enhance a successful program of research on improving the quality and outcomes of health care in Alabama and across the nation. To accomplish this mission, the COERE 1) uses interdisciplinary teams to test innovations that promote evidence-based practice, reduce inequities in care for under-served and minority populations, and improve quality of life and functional outcomes for patients; 2) develops and tests innovative methods with application to important questions in the delivery of health care; 3) trains and mentors students, fellows and faculty in these methods; and 4) serves as a resource to UAB faculty, health care systems, related organizations, government, and philanthropy to further disseminate outcomes research knowledge and expertise.  The COERE offers integrated scientific expertise and experience in health services and outcomes and effectiveness research. This expertise includes: quality measurement and improvement, implementation research, patient-based outcomes assessment, pharmacoepidemiology, epidemiological/population-based health services research, retrospective claims data analysis, and economic evaluation and modeling (decision analytic modeling, cost-effectiveness and cost-benefit analysis). This expertise is currently supported by a Methods Unit of faculty-level biostatisticians, epidemiologists and masters level program managers, statisticians and data managers and coordinated through focused Work Groups in methodological areas of expertise and interest (e.g., health informatics, economic evaluation and modeling, implementation sciences, use of large data bases in HSR, pharmacoepidemiology) and certain disease focused areas of interest (e.g., cardiometabolic disorders, including diabetes; musculoskeletal disorders; HIV-AIDS). Within and across these focus areas are the cross-cutting themes of health disparities, quality improvement, and patient safety. Through this intellectual infrastructure the COERE supports UAB faculty by providing: 1) assistance in the design and analysis of outcomes and effectiveness research studies; 2) assistance in the use of patient- and provider- level data for outcomes studies; 3) assistance in the development of research ideas and grant applications; and 6) mentoring of faculty and students in outcomes and effectiveness research. Since being formalized as a University-Wide Interdisciplinary Research Center, COERE leadership has been instrumental in attracting over $283M in extramural grant support for interdisciplinary research and training in health services and outcomes research at UAB. Through its work in statistical and methodological innovations in quality measurement and improvement, COERE has become a national resource to the health care industry. An example of this is our work in developing and disseminating the Achievable Benchmarks of Care (ABC™). In the area of training, COERE has established an excellent track record in mentoring junior faculty to facilitate their training in clinical health services and outcomes research and in 2003 was awarded a highly competitive 5-Year National Research Services Award Institutional Training Grant (T32), the *UAB Health Services & Outcomes Research Training Program*, from the Agency for Healthcare Research and Quality (AHRQ).  The UAB Health Services and Outcomes Research Training Program (AHRQ T32) is a collaborative effort between the COERE, UAB Lister Hill Center for Health Policy (LHC), and the UAB Schools of Medicine, Public Health and Health Professions. This is a combined predoctoral and postdoctoral training program that builds on UAB's rich collaborative research environment and health services research training capacity through targeted synergies between existing programs and infrastructure. The program prepares investigators to pursue careers focused on translating research into practice and policy (TRIPP) and contributing to the knowledge base that is required to do so. Predoctoral trainees obtain a PhD in Health Services Administration- Health Services Research. Postdoctoral trainees (MDs or other doctoral trained clinicians) obtain the MSPH in Outcomes Research. The cornerstone of the training program is the mentored research experience, which draws from the strengths of the UAB faculty, who are national and international leaders in what the NIH Roadmap designates as Phase 2 Translational Research (T2). The mentored research experience is also enhanced through the program's access to a large pool of mentors with excellent track records in AHRQ and NIH funding and through our innovative and highly successful "mentor-in-training" component.  **V. Center for Clinical and Translational Science (CCTS)**  The Center for Clinical and Translational Science (CCTS) is a research center of the University of Alabama at Birmingham (UAB). One of three autonomous institutions within The University of Alabama System, UAB is the only four-year, public university in the state’s largest metropolitan area. The vision of the Center for Clinical and Translational Science (CCTS) is to transform the institutional environment by building productive and efficient interdisciplinary research teams through educational ingenuity, regulatory reorganization, resource coordination, and methodological innovation. Its mission is to develop a transformative infrastructure that spans the spectrum from preclinical research to bench-to-bedside translation to community implementation. The CCTS was developed in response to the National Institutes of Health’s request for applications for Clinical and Translational Science Awards (CTSAs). The Center was officially approved by the University of Alabama Board of Trustees on February 3, 2006 and funded by the NIH on May 19, 2008. The CTSA initiative grew out of the NIH commitment to restructure the clinical research enterprise, one of the key objectives of theNIH Roadmap for Medical Research. Funding for the CTSA comes from redirecting existing clinical and translational programs, including Roadmap funds. When fully implemented in 2012, the initiative is expected to provide more than $500 million over five years to 60 academic health centers. The CCTS is committed to developing current and future clinical and translational researchers and research teams through a Training Academy which integrates successful training programs with new initiatives. The CCTS Training Academy includes all CCTS trainees, investigators, and faculty mentors. The CCTS offers a broad range of degree and non-degree (certificate) training programs for clinical and translational researchers and research team members.  • The CCTS Professional Skills Training Program (PSTP) is designed to provide practical assistance in the areas of scientific writing (such as the development of grants and scientific manuscripts), scientific presentations, career development, and leadership.  • Degree programs include the Master of Science in Public Health (MSPH) in Clinical and Translational Science and the Master of Science or MD/MS in Biomedical Sciences in CTS.  • Certificate programs include the 20-hour Vocabulary of Clinical and Translational Science, the 50-hour Clinical and Translational Science Training Program, and the Research Coordinator Training Program.  • Two competitively selected training mechanism are available: 1) The CCTS Mentored Career Development Program (KL2 Scholars) is for junior faculty in a clinical or related discipline. Scholars, selected through a competitive application process, receive KL2 Clinical and Translational Science career development support for up to five years with protected time for both formal training and hands on research. Scholars enroll in an educational program, usually the MSPH in Clinical and Translational Science, which include the CTS core curriculum. In parallel, they enter a research apprenticeship with a primary mentor who has an excellent training record and commits to extended close interaction with the Scholar. The overall goal of this training program is to impart knowledge, experience, and perspective to a network of junior scientists who will emerge as independent investigators. Training culminates in lead author manuscripts and an extramurally-funded research grant submission (e.g., R01). 2) Through the CCTS Pre-doctoral Training Program (TL1 Trainees) eligible individuals will have funded, protected time to acquire competencies necessary to conduct clinical and translational research. CCTS TL1 Trainees will dedicate full-time effort to pursue a translational science-related doctoral degree. In addition to completing the Core curriculum and other curricular requirements, Trainees will ultimately complete a dissertation that will culminate in the submission of manuscripts for publication and a grant application.  **VI. Facility for Access to Clinical Enrollment Services (FACES)**  FACES is a UAB’s Comprehensive Cancer Center (CCC) shared facility. The FACES team includes data managers and analysts, project planners and coordinators, telephone interviewers, and community outreach personnel. The strong community outreach and educational services of FACES help overcome barriers to participation in underrepresented populations. By using innovative recruitment techniques and culturally appropriate recruitment materials, we are able to successfully engage participants from minority communities. More than 10 years work building trust within the community provides access to grassroots organizations, service groups, healthcare professionals, and local businesses.  The facility 1) provides CCC researchers with diverse recruitment services (designing recruitment strategies, recruiting subjects, developing recruitment materials and advertisements, etc.); 2) provides and maintains the necessary linkage between CCC researchers and the surrounding communities, including potential research subjects, community-based organizations, community leaders, and community health-care providers; 3) disseminates culturally appropriate information regarding techniques for recruitment and retention of minority subjects suitable for UAB investigators; and 4) establishes and maintains an information system with a Recruitment Data Base comprised of a Mass Mailing System, a Recruitment Tracking System, and a Health Profile System to identify subjects with certain health profiles of interest to UAB investigators.  FACES has completed various recruitment activities for 21 cancer-related studies and has recruited and enrolled more than 19,000 participants in these studies, 27% of whom were AA. FACES focuses its efforts on refining minority population recruitment strategies, especially for population-based studies. It developed stateof- the-art information and tracking system, finalized the operational procedures, and reinforced partnerships with community organizations and health-care providers. Having in place a centralized database, an infrastructure, and expertise with general and minority-specific recruitment strategies provides critical support for investigators so they don’t have to build recruitment staffs for each new study.  From the primary focus of population-based studies, FACES now is expanding its focus to develop recruitment strategies for therapeutic trials. The facility is working with UAB clinicians and community healthcare providers to develop efficient methods of reaching potential participants for therapeutic trials. One example of such recent effort is the pilot project IMPaCT, which employs Patient Navigators to educate, enroll, and support patients in cancer treatment trials.  **VII. TUSKEGEE UNIVERSITY**  Tuskegee University, a historically black university, is an independent and state-related institution of higher education. Its programs serve a student body that is coeducational as well as racially, ethnically, and religiously diverse. With a strong orientation toward disciplines which highlight the relationship between education and work force preparation in the sciences, professions and technical areas.  • **National Center for Bioethics in Research and Health Care**  The Tuskegee National Center for Bioethics in Research and Health Care is the nation’s first bioethics center devoted to engaging the sciences, humanities, law, and religious faiths in the exploration of the core moral issues that underlie research and medical treatment of African Americans and other underserved people. The Tuskegee University National Center for Bioethics in Research and Health Care was established in January 1999. The Bioethics Center was developed as a partial response to the apology of President William J. Clinton for the United States Public Health Service Study on Syphilis conducted at Tuskegee, in Macon County, Alabama from 1932 to 1972. The negative legacy of this study has been cited as a contributing hindrance to the full participation of African Americans and others in taking advantage of medical care and scientific research. It is the aim of the Tuskegee University National Center to transform the burden of this negative legacy. The Tuskegee University National Center for Bioethics in Research and Health Care works with local, regional, national and international communities, to address ethical and human rights issues in science, technology and health, particularly as they impact people of color.  The Center’s goals are to: 1. Promote racial and ethnic diversity in the field of bioethics and in public debates about bioethical issues; 2. Conduct research and publish scholarship on bioethics and underserved populations; 3. Educate students, scholars, media, and the public about bioethical issues of importance to underserved populations; 4. Foster effective, respectful, and mutually beneficial community partnerships to address inequities in health and health care, to increase public education about bioethics, and to develop training programs; 5. Advocate public policies that improve the health and health care of all Americans, particularly the underserved.  **VIII. COMMUNITY-BASED PARTNERS**  **A. YMCA**  Established in 1884, the YMCA of Birmingham is a nonprofit dedicated to strengthening communities through youth development, healthy living and social responsibility. Across Jefferson and Shelby Counties, 13 Ys engage more than 40,000 men, women and children – regardless of age, income or background – to nurture the potential of children and teens, improve the nation’s health and well-being, and provide opportunities to give back and support neighbors. With long-standing relationships and physical presence the YMCA is able to not just promise, but to deliver lasting personal and social change.  The YMCA's Diabetes Prevention Program helps those at high risk adopt and maintain healthy lifestyle and reduce their chances of developing type 2 diabetes. The Program is based on the landmark Diabetes Prevention Program funded by the National Institutes of Health (NIH) and the Center for Disease Control and Prevention (CDC), which showed that by eating healthier, increasing physical activity and losing a small amount of weight, a person with pre-diabetes can prevent or delay the onset of type 2 diabetes by 58%. In a classroom setting, a training lifestyle coach helps participants change their lifestyle by learning about healthy eating, physical activity, and other behavior changes over the course of 16 one-hour sessions. Topics covered include nutrition, getting started with physical activity, overcoming stress, staying motivated, and more. After the initial 16 core sessions, participants meet monthly for up to a year for added support to help them maintain progress.  **B. American Diabetes Association (ADA)**  The mission of the American Diabetes Association (ADA) is to prevent and cure diabetes and to improve the lives of all people affected by diabetes. The ADA funds research to prevent, cure and manage diabetes; delivers services to hundreds of communities; provides objective and credible information; and gives voice to those denied their rights because of diabetes. Advocacy plays an integral role in ADA’s mission. Diabetes Advocates around the country fight to increase funding to prevent, treat and cure diabetes; improve access to health care and eliminate discrimination against people with diabetes at school, work and elsewhere in their lives. The ADA’s Alabama/Mississippi Chapter, headquartered in Birmingham, AL, is committed to educating the public about how to stop diabetes and support those living with the disease.  **C. Lakeshore Foundation**  Lakeshore Foundation is a non-profit 501c3 organization that promotes independence for persons with physically disabling conditions and provides opportunities to pursue active, healthy lifestyles. LakeshoreFoundation offers a wide range of fitness, recreation, athletic and education programs to children and adults who experience diagnostic conditions including spinal cord injuries, cerebral palsy, multiple sclerosis, stroke, amputation, and visual impairment. The Foundation also serves persons who have been diagnosed with arthritis, diabetes, chronic pain, cardiac conditions, and many other related disorders.  Lakeshore Foundation is located on a 45-acre campus in Homewood, Alabama. In 2001, due to growing community need, Lakeshore Foundation opened one of the nation's premiere fitness, recreation and education facilities for persons with physically disabling conditions. A highly trained and experienced staff of more than 80 full and part-time employees provide programs in this state of the art facility which includes an aquatics center with two pools, a fieldhouse with three hardwood courts and a 200-meter track, a ten lane marksmanship range; 6,000 square foot fitness center and The Fred Sington Community Room.  In addition to these amenities, the Lakeshore Foundation campus is home to an outdoor tennis facility with eight championship lighted hard courts, the Birmingham office of the Alabama Department of Rehabilitation Services (ADRS), the National Multiple Sclerosis Society, Alabama Chapter and the HealthSouth Lakeshore Rehabilitation Hospital.  Lakeshore Foundation and UAB are developing a world-class research program in rehabilitative science– the Lakeshore Foundation/UAB Research Collaborative. On January 3, 2012, Dr. James Rimmer, PhD, was recruited from the University of Illinois to assume the Lakeshore Foundation Endowed Chair in Health Promotion and Rehabilitation Sciences and to serve as the director of this collaborative. Dr. Rimmer is a member of the NIH National Center for Medical Rehabilitation Research advisory board, and the Centers for Disease Control and Prevention’s Health Disparities Advisory Committee to the Director of CDC. He directs two federally funded centers which will transfer to UAB — the National Center on Physical Activity and Disability <http://www.ncpad.org/>, and the Rehabilitation Engineering Research Center on Interactive Exercise Technologies and Exercise Physiology for People with Disabilities <http://www.rectech.org/> . Dr. Rimmer has an interest in the impact of diabetes and obesity as disabling conditions, and their impact o in patients with other disabling conditions. Dr Rimmer will serve on the Advisory Board. | |

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| Program Director/Principal Investigator (Last, First, Middle): | | | | | | | | | | | | | Garvey, W. Timothy | | | | | | | | | | | | | | | |
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| CHECKLIST | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **TYPE OF APPLICATION** *(Check all that apply.)* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| NEW application. *(This application is being submitted to the PHS for the first time.)* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| RESUBMISSION of application number: | | | | | | | |  | | | | | | | | | | | | | | | | | | | | |
| *(This application replaces a prior unfunded version of a new, renewal, or revision application.)* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| RENEWAL of grant number: | | | | |  | | | | | | | | | | | |  | | | | |  | | | | | | |
| *(This application is to extend a funded grant beyond its current project period.)* | | | | | | | | | | | | | | | | | | | | | |  | | | | |  | |
| REVISION to grant number: | | | | |  | | | | | | | | | | |  | | | | | |  | | | | |  | |
| *(This application is for additional funds to supplement a currently funded grant.)* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CHANGE of program director/principal investigator. | | | | | | | | | | | | |  | | | | | | | | | | | | | | | |
| Name of former program director/principal investigator: | | | | | | | | | | |  | | | | | | | | | | | | | | | | | |
| CHANGE of Grantee Institution. Name of former institution: | | | | | | | | | | |  | | | | | | | | | | | | | | | | | |
| FOREIGN application | Domestic Grant with foreign involvement | | | | | | | | | | | | | | List Country(ies) Involved: | | | | | | | |  | | | | | |
| INVENTIONS AND PATENTS *(Renewal appl. only)*  No  Yes | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| If “Yes,” | | | | | | | | | | | | | | Previously reported  Not previously reported | | | | | | | | | | | | | | |
| **1. PROGRAM INCOME *(See instructions.)***  All applications must indicate whether program income is anticipated during the period(s) for which grant support is request. If program income is anticipated, use the format below to reflect the amount and source(s). | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Budget Period | | | | Anticipated Amount | | | | | | | | | | | | | | Source(s) | | | | | | | | | | |
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| **2. ASSURANCES/CERTIFICATIONS *(See instructions.)***  In signing the application Face Page, the authorized organizational representative agrees to comply with the policies, assurances and/or certifications listed in the application instructions when applicable. Descriptions of individual assurances/certifications are provided in Part III and listed in Part I, 4.1 under Item 14. If unable to certify compliance, where applicable, provide an explanation and place it after this page. | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **3. FACILITIES AND ADMINSTRATIVE COSTS (F&A)/ INDIRECT COSTS.** See specific instructions. | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| DHHS Agreement dated: | | 09/25/2014 | | | | | | | | | | | | | | | | | No Facilities And Administrative Costs Requested. | | | | | | | | | |
| DHHS Agreement being negotiated with | | | | | | |  | | | | | | | | | | | | | | | | | | Regional Office. | | | |
| No DHHS Agreement, but rate established with | | | | | | | | | |  | | | | | | | | | | | | | | | Date |  | | |
| CALCULATION\* *(The entire grant application, including the Checklist, will be reproduced and provided to peer reviewers as confidential information.)* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| a. Initial budget period: | | | Amount of base $ | | | | | | 69,925 | | | x Rate applied | | | | | | | | 46.5 | | | | | % = F&A costs $ | | | 32,515 |
| b. 02 year | | | Amount of base $ | | | | | | 69,925 | | | x Rate applied | | | | | | | | 46.5 | | | | | % = F&A costs $ | | | 32,515 |
| c. 03 year | | | Amount of base $ | | | | | | 69,925 | | | x Rate applied | | | | | | | | 46.5 | | | | | % = F&A costs $ | | | 32,515 |
| d. 04 year | | | Amount of base $ | | | | | | 69,925 | | | x Rate applied | | | | | | | | 46.5 | | | | | % = F&A costs $ | | | 32,515 |
| e. 05 year | | | Amount of base $ | | | | | | 69,925 | | | x Rate applied | | | | | | | | 46.5 | | | | | % = F&A costs $ | | | 32,515 |
|  | | | | | | | | | | | | | | | | | | | | | | | | TOTAL F&A Costs $ | | | | 162,575 |
| \*Check appropriate box(es): | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Salary and wages base | | | | | | Modified total direct cost base | | | | | | | | | | | | | | | Other base *(Explain)* | | | | | | | |
| Off-site, other special rate, or more than one rate involved *(Explain)* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Explanation *(Attach separate sheet, if necessary.):* | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| **4. DISCLOSURE PERMISSION STATEMENT:**  If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?  Yes  No | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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***Mailing address for application***

*Use this label or a facsimile*

**All applications and other deliveries to the Center for Scientific Review must come either via courier delivery or via the United States Postal Service (USPS.) Applications delivered by individuals to the Center for Scientific Review will not be accepted.**

**Applications sent via the USPS EXPRESS or REGULAR MAIL should be sent to the following address:**

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| **CENTER FOR SCIENTIFIC REVIEW**  **NATIONAL INSTITUTES OF HEALTH**  **6701 ROCKLEDGE DRIVE**  **ROOM 1040 – MSC 7710**  **BETHESDA, MD 20892-7710** |

**NOTE: All applications sent via a courier delivery service (non-USPS) should use this address, but CHANGE THE ZIP CODE TO 20817**

**The telephone number is 301-435-0715. C.O.D. applications will *not* be accepted.**

**A special label for responding to RFAs is not required.**