

2.2 BACKGROUND

Rationale and Need for the Research Training Program

Life expectancies of women and men in developed countries continue to increase^{1, 2} in conjunction with persistently high, and in many cases rising, incidences of chronic disease (e.g., heart disease³, diabetes⁴, obesity³, arthritis⁵) and cancer⁶. This is the great irony of healthcare today—and one that comes with a price. While advances in medical technologies, symptom management strategies, and surgical procedures extend life-span, co-morbidities and chronic states of functional impairment and pain compromise one's health-span. In short, diseased individuals are now living for extended periods with an impaired health related quality of life (HRQoL). Unfortunately this adverse state is suffered by millions of individuals afflicted by an array of chronic diseases including neuromotor impairment (e.g., Parkinson's disease), chronic musculoskeletal (e.g., arthritis, myositis) disease, cardiopulmonary (e.g., heart failure, COPD) disease, and metabolic (e.g., diabetes, obesity) disease. The same is experienced by the cancer survivor who—via advanced diagnostic, surgical, and medical care—"defeats cancer" but often suffers chronic fatigue, reduced functional capacity, and deleterious changes in body composition including losses of muscle mass and concomitant increases in visceral adiposity. Further, estimates of economic burden attributed to chronic diseases reach hundreds of billions annually in lost productivity and healthcare expenditures^{7, 8}. Overall this presents an incredible challenge as well as opportunity for rehabilitation scientists. In fact, **arguably the demand for advances in rehabilitation medicine has never been higher**. To meet this demand, **a new wave of cross-cutting, translational rehabilitation scientists is essential**. These investigators must be capable of driving evidence-based rehabilitation medicine by conducting experiments across multiple levels of scientific inquiry. We are ideally positioned to foster the necessary interdisciplinary training at both pre- and postdoctoral levels via the proposed *Interdisciplinary Training in Pathobiology and Rehabilitation Medicine Program (P&RMP)*. The rationale for P&RMP, and its exciting opportunities for scientific discovery and research training, are summarized in **Figure 1**.

The **overarching goal** of the mixed predoctoral and postdoctoral P&RMP is to develop burgeoning scientists into future leaders in translational rehabilitation research who are specifically equipped to test and disseminate novel rehabilitative strategies that will alleviate functional impairment and overall compromised HRQoL in the face of chronic disease management. The program goals will be met by taking advantage of an exceptionally rich institutional environment that offers myriad resources and a complementary and collaborative team of 31 basic, clinical, and translational research mentors committed to training and career development (**Data Table 2**). Because exercise training in its many forms is perhaps the most pluripotent treatment modality available in all of rehabilitation and preventive medicine—inducing structural, physiologic, and metabolic adaptations in virtually every tissue and organ system—exercise biology and medicine will be a common thread coursing through P&RMP. P&RMP provides clear avenues for bidirectional research: trainees will be prepared to take bench discoveries to clinical application and, of equal importance, to understand the mechanistic underpinnings of clinical findings. Both predoctoral and postdoctoral trainees will benefit from two years of a unique, interdisciplinary training experience that carefully melds three core levels of scientific inquiry: (i) cellular and molecular pathobiology of disease; (ii) rehabilitation science and exercise physiology; and (iii) rehabilitation medicine (i.e. clinical trials). Training will occur in one of two areas of concentrated strength: 1) Neuromusculoskeletal Disorders; or 2) Cardiometabolic Diseases. Cross-cutting themes with research training opportunities include cancer and aging.

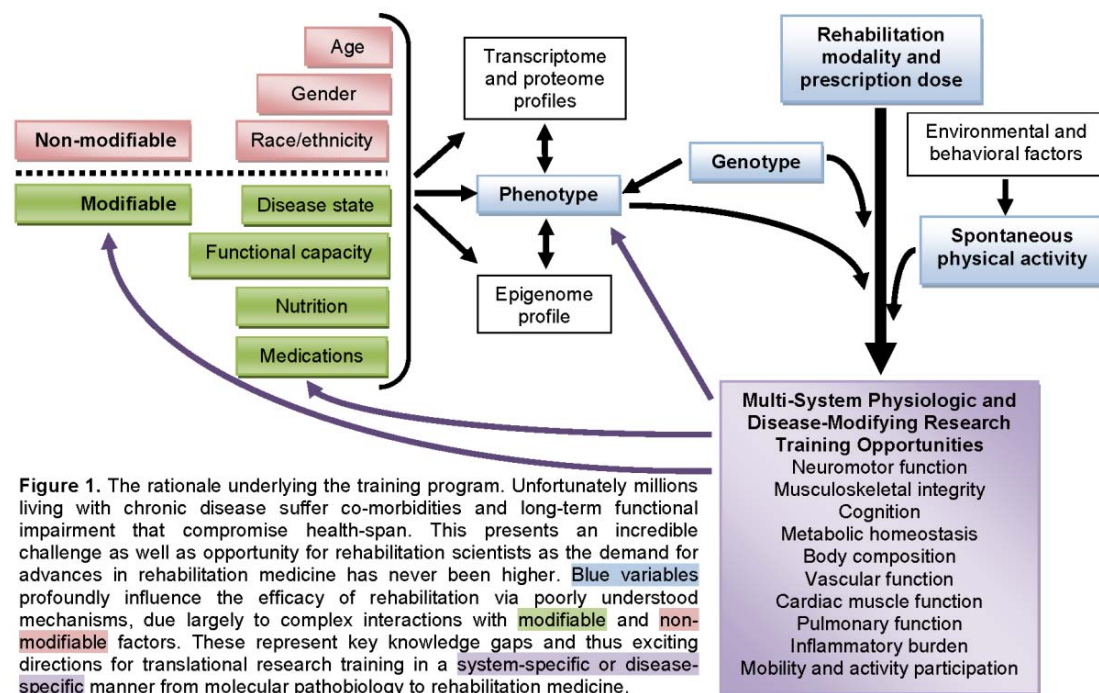
Like any other form of treatment, efficacy of a rehabilitative strategy or exercise prescription is highly dependent on the type and dose of the prescription as well as genetic variation, with substantial gaps in knowledge remaining⁹. This dose-dependency has become even more apparent today with recent scientific advances in genomics, proteomics, metabolomics, stem cell biology, tools for assessing physical activity and metabolism, and imaging technologies. While well-controlled rehabilitation trials involving dose titration^{10, 11} and exercise-drug interactions¹² are only emerging, these tools present rich opportunities for innovative and translational research and training that will dramatically advance the field and prepare tomorrow's leaders in the field (**Figure 1**). Such research and training is clearly needed before the most efficacious rehabilitation approaches are defined in a disease-specific manner, and this has in fact become a major point of emphasis among both scientists and healthcare professionals^{13, 14}.

A truly translational research and training program in rehabilitation medicine is only possible at an academic health center poised to meet the challenges of integrating basic biological sciences with clinical applications. As a top 25 NIH-funded academic health center with over 80 state-of-the-art scientific core facilities and 28 University-Wide, Interdisciplinary Research Centers (UWIRCs), the University of Alabama at Birmingham (UAB) is remarkably well-positioned to cultivate translational scientists equipped to drive the field of rehabilitation medicine with cutting edge research.

The 31 primary mentors, many of whom are united by long-standing research and mentoring collaborations, span 13 departments and divisions across the UAB Schools of Medicine (cell and integrative biology, physical medicine and rehabilitation, medicine, neurology, pathology, genetics, cardiology, geriatrics), Health Professions (physical therapy, occupational therapy, nutrition sciences), Public Health (epidemiology), and Arts and Sciences (psychology) (**Data Table 1**). Mentors direct research relevant to the two areas of concentrated strength (Neuromusculoskeletal Disorders or Cardiometabolic Diseases) and, within these two concentrations, some mentors study one or both of the cross-cutting themes (cancer and aging) (**Data Table 2**). Mentors were selected based largely on research synergy within the program focus areas, but also to provide a balanced distribution of senior and junior faculty. The mentoring team is comprised of 20 senior faculty at the full Professor rank (many of whom serve as leaders of various departments and centers), seven mid-level Associate Professors, and four Assistant Professors. The four promising junior faculty were identified as ideal candidates to participate in the *Mentoring on Mentoring Program* built into the overall training plan.

How the Program Relates to Current Training Activities at UAB

UAB has a long-standing history of research training and national/international recruitment of outstanding pre- and postdoctoral trainees. This successful recruitment results in part from the institution's reputation as a leading biomedical research university—known for its consistent level of excellence in research innovation and



clinical application. Equally important is UAB's commitment to outstanding research training. In addition to recruitment efforts nationally for the proposed postdoctoral training program, UAB boasts a nationally and internationally recruited pool of predoctoral trainees.

At UAB there are numerous institutional T32 NRSA training programs, along with other training grants, that support pre- and/or postdoctoral trainees in a variety of disciplines, and many of the 31

primary mentors in the proposed program are affiliated with 22 of these programs (**Data Table 3**). We carefully considered the existence of the other training grants and whether they would overlap with P&RMP. Because of the cross-cutting nature of rehabilitation and exercise medicine, one could argue overlap with most any training program in biology or medicine; however, none of the current training programs at UAB describe rehabilitation or exercise medicine as an area of focus. Further, despite the fact that our program's 31 faculty have mentored 192 predoctoral trainees and 149 postdoctoral trainees over the past 10 years (**Data Tables 5a and 5b**)—many of whom would have been appropriate candidates for the proposed program—only a small minority of these trainees received institutional NRSA training grant support. Clearly there is a great need to expand the number of institutional NRSA training opportunities for the ever-expanding pool of talented trainees at UAB and, as we are faced with enormous challenges born by the growing number of functionally compromised individuals living with chronic disease and disability⁷, the timing is critical to offer comprehensive and translational research training in this focus area. P&RMP trainees will be the next generation of scientists establishing laboratories to advance rehabilitation medicine and exercise biology.

Graduate Biomedical Sciences (GBS) Predoctoral Program. Predoctoral trainees in P&RMP will be selected from a highly competitive and diverse national pool of students admitted to either the Graduate Biomedical Sciences (GBS) program or Rehabilitation Science program, and will complete a didactic curriculum that combines aspects of both existing programs (**Table C**). During 2008-2009, the School of Medicine and Joint Health Science departments revamped graduate (predoctoral) education in the biomedical

sciences, combining all of the major departmental graduate programs into a centralized, thematically based program (i.e. GBS). Students in GBS study in one of eight themes: Biochemistry & Structural Biology; Cancer Biology; Cell, Molecular, & Developmental Biology; Genetics & Genomic Sciences; Immunology; Microbiology; Neuroscience; or Pathobiology & Molecular Medicine. Most of the mentors associated with the proposed training program participate in one or more of these themes; 13 are in Pathobiology and Molecular Medicine, 10 are affiliated with Cell, Molecular, and Developmental Biology, and Cancer Biology, Genetics & Genomic Sciences, and Neuroscience each have four faculty serving as mentors in this program (**Data Table 1**). Recruitment into GBS began in 2010 and was a resounding success (**Figure 2**). GBS attracted a highly competitive national and international pool of 711 applicants and admitted 73 students into this inaugural class. Of the 73 admitted, 57 were domestic and seven were underrepresented minorities. GBS continues to be a highly competitive program, with 736 applicants in 2011 and 797 in 2012 and an admission rate of only 7-10%. The percentages of those admitted who are domestic (87%) or from underrepresented minorities (12%) are on the rise. Over these first three recruitment years, the mean GRE of domestic applicants has been above 1230, with a mean GPA of 3.6. The GBS curriculum includes rigorous courses in biological chemistry, genetics, and cellular and molecular biology. Advanced courses in cellular and integrative physiology, pathobiology, and pharmacology are organ system-based and in some cases disease-specific as defined by the individual themes. Three research rotations are performed during the first year. Faculty members throughout the University participate in the teaching of courses, sponsor predoctoral students for rotations, and serve as mentors. Faculty members in clinical departments with secondary appointments in basic science departments also actively participate in teaching and serve as mentors. The UAB Center for Exercise Medicine journal club, which is focused on disease-specific rehabilitation and preventive medicine, is offered each semester and has been popular among students from multiple GBS themes (e.g., Cancer Biology; Genetics & Genomic Sciences; Neuroscience; and Pathobiology & Molecular Medicine).

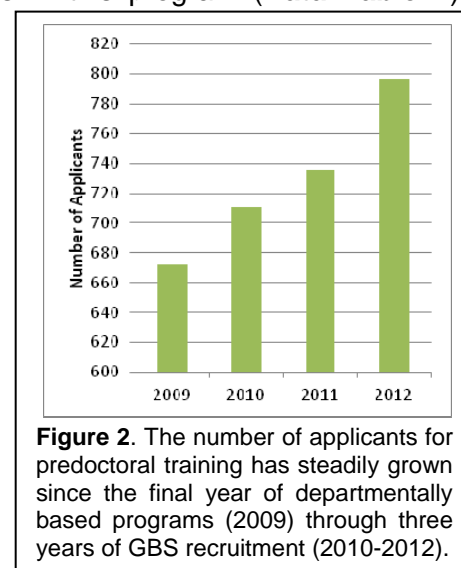


Figure 2. The number of applicants for predoctoral training has steadily grown since the final year of departmentally based programs (2009) through three years of GBS recruitment (2010-2012).

Rehabilitation Science Predoctoral Program. The Rehabilitation Science program is the partnering predoctoral program closely integrated into this training program. The School of Health Professions obtained approval for this exciting new program in February 2011. Currently 21 of 31 mentors in the proposed T32 training program are members of the Rehabilitation Science program (**Data Table 1**). Dr. David Brown was recruited in 2011 from Northwestern University to serve as Director of the Rehabilitation Science program. In its first year under his leadership, the program attracted 12 talented applicants from diverse backgrounds and accepted four for entry in August 2012. The incoming trainees have strong backgrounds in physical therapy and neuromotor control, exercise physiology, health education, and experimental psychology. All four bring research experience and 3 of 4 earned masters degrees elsewhere. Like GBS, the Rehabilitation Science program is not departmentally based, but is affiliated most closely with the Departments of Physical Therapy and Occupational Therapy. The program offers research training in numerous aspects of rehabilitation and exercise science/medicine. This program is distinct from, but complementary to, the clinical track leading to the Doctor of Physical Therapy degree. We think the innovative merger of GBS and Rehabilitation Science predoctoral programs creates a unique and exciting environment for translational research training in rehabilitation medicine. Additionally, we are confident that the integrative predoctoral program will enhance recruitment to our postdoctoral training program.

Departmentally-Based Predoctoral Programs. Seven of the 31 faculty mentors in this training program also participate in departmentally-based programs in Nutrition Sciences (5), Epidemiology (1), and Psychology (1) (**Data Table 1**). All departmental graduate programs have requirements for advanced courses, journal clubs, qualifying examinations, seminar presentations, publications and thesis research. Exceptional TGE graduates of these departmental programs (along with GBS and Rehabilitation Science graduates) with pertinent research training interests may be recruited to postdoctoral positions in this training program.

Medical Scientist Training Program (MSTP). The MSTP has close ties to the GBS program since the two programs share many faculty members. Of the 31 mentors, 12 are members of the MSTP (**Data Table 1**). Dr. Bamman served on the MSTP Steering Committee and mentored seven MSTP trainees, serving as primary research mentor for one. The general structure of the MSTP is similar to that of most MD/PhD programs. One unique and especially strong feature of the UAB MSTP is that it is truly a joint undertaking between the Medical

and Graduate Schools. Rather than taking only the Medical School curriculum, our MSTP students also complete GBS courses, providing solid training in basic and clinical sciences. The presence of MSTP students in the same classes and laboratories as PhD students fosters communication and collaboration between laboratories and promotes interdisciplinary, translational research. The T32-funded MSTP program enrolls 8-10 new students each year. Because of the quality and breadth of training opportunities in clinical specialties at UAB, many MSTP graduates match at UAB for residency. These are obviously research-oriented trainees; thus some in this talented cohort may be ideally suited for advanced postdoctoral research training in this program after residency.

Howard Hughes Medical Institute Med-to-Grad Program (HMG). UAB received a prestigious \$650,000 award as part of a \$16 million effort by the Howard Hughes Medical Institute (HHMI) to change how graduate schools train students and quicken the translation of basic science discoveries into new medical treatments. UAB was one of the originally (from 13) funded HMG programs in 2006, which was successfully renewed in 2010. Currently, there are 23 such HHMI funded programs until 2014. With this award, a new pathway of graduate education was created at UAB to provide targeted exposure of PhD students to the pathobiology of human disease. The HMG program works with all departmental and theme-based graduate programs and facilitates pairing of students with mentors conducting cutting-edge, disease-based research who will guide their training. The overarching goal is to prepare graduate leaders who enter the workforce with the experience in translational research to move discoveries effectively from bench to bedside. This is complemented by a customized curriculum providing exposure to patient-oriented, case-based topics; drug development and research; valid experimental design and statistics and vocabulary in clinical research. We anticipate that this program (through 2014) will broaden the base of highly-qualified potential postdoctoral trainees.

UAB Office of Postdoctoral Education (OPE). Based largely on the wide array of carefully planned programs and career development services provided by the OPE, **UAB ranks #1 among public universities nationwide in “Best Places to Work for Postdocs”**, according to the 2012 rankings published in *The Scientist*, April 2012. The OPE was established in 1999 and was one of the first Postdoctoral offices in the country. Since its inception, the OPE has been instrumental in establishing and maintaining competitive terms, benefits, and training programs for all postdoctoral fellows. At UAB, approximately 250 postdoctoral fellows are training currently in a variety of disciplines, including biomedical sciences, dentistry, engineering, health professions, clinical medicine, natural sciences, mathematics, public health, optometry, and social and behavioral sciences. Our postdoctoral community is 55% US citizen or permanent resident, 55% female, and 17% are from underrepresented minorities. In addition to assuring proper instruction in the responsible conduct of research, the OPE offers an **extensive curriculum in professional skills development**, providing postdoctoral scholars with training in new skills that differ from and/or complement those that they learned as graduate students. A variety of workshops, seminars, and opportunities are offered. Past and on-going opportunities include *Transition to Independence Seminar Series* and *Job Fair*; each presents information regarding career opportunities and job skills for the biomedical field. The OPE also offers the *How do you Manage* workshop, which provides self-assessment tools for the improvement of management and leadership skills. In addition, the OPE provides several interactive and didactic courses (e.g., *Grant Writing Course*, *Laboratory Management Course*, *Translational Science Course*, and *Job Skills Course*), and the *Mentored Experiences in Research, Instruction, and Teaching (MERIT) Program*. Each of these, along with several **incentives and training enhancement awards** sponsored by the OPE, are described in latter sections of this application. **OPE recruitment process.** Postdoctoral scholars are recruited to apply through a multi-pronged approach that includes advertisements in scientific journals, web postings, and attendance at recruitment fairs. Specifically, advertisements are listed in scientific journals, including *The Scientist*, *Science*, and *Nature*. Web postings are targeted toward academic career-related websites, including *Science Careers* and *FASEB Minority Access to Research Careers*. To enhance recruitment of minorities, OPE representatives attend postdoctoral recruitment fairs, such as the *Annual Biomedical Research Conference for Minority Students* and the *National Conference of the Society for Advancement of Chicanos and Native Americans in Science*, to increase awareness of UAB's postdoctoral training programs. In addition, UAB will host its inaugural *Postdoctoral Recruitment Conference* for outstanding senior graduate students nation-wide this fall.

Center for Clinical and Translational Science (CCTS). The Center for Clinical and Translational Science (CCTS) is a designated UAB University-Wide Interdisciplinary Research Center (UWIRC). The CCTS was developed in response to the NIH request for applications for Clinical and Translational Science Awards (CTSAs). The Center was officially approved by the University of Alabama's Board of Trustees on February 3, 2006 and funded by the NIH on May 19, 2008 (5UL1 RR025777). Robert P. Kimberly, MD, directs the Center. UAB is one of 60 academic health centers nationwide that are member institutions of the CTSA Consortium.

The mission of the CCTS is to enhance human health by driving scientific discovery and dialogue across the bench, bedside, and community continuum. The vision of the CCTS is to speed the translation of research into improved human health. The Center is comprised of nine Components [Biomedical Informatics; Pilots; Drug Discovery; Research Ethics, Regulatory Knowledge and Support; Research Education and Training; Biostatistics, Epidemiology and Research Design (BERD); the Clinical Research Unit (CRU); One Great Community; and Cores] and the Research Commons. The **Research Education and Training Component** is helping UAB produce intellectually innovative and methodologically rigorous clinical and translational researchers. Several valuable CCTS-sponsored courses and training activities for predoctoral and postdoctoral trainees are incorporated into the training plan described later in this application.

Professional Development Program. UAB's Professional Development Program was established to foster the development of graduate students, postdoctoral fellows, and visiting scholars to promote their success in an increasingly competitive world for scientists and academicians. The program targets the enhancement of skills in the areas of professional presentations, university teaching, publishing, interdisciplinary collaboration, and fellowship and grant writing. Indeed, many leading institutions view these communication abilities as prerequisites for career advancement. Numerous trainees and visiting scholars take advantage of the program's resources and offerings to enhance their skills. Under the direction of Dr. Julia Austin, the program offers semester-long credit courses as well as day-long workshops in a variety of areas such as: (i) Career Support & Advancement; (ii) Academic & Grant Writing; (iii) Teaching at the College Level; (iv) Presentation & Discussion Skills; and, for international scholars, (v) Academic English for Internationals and (vi) Pronunciation & Accent Improvement.