Taking the Next Steps in Regenerative Rehabilitation: Establishment of a New Interdisciplinary Field

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Abstract

The growing field of Regenerative Rehabilitation has great potential to improve clinical outcomes for individuals with disabilities. However, the science to elucidate the specific biological underpinnings of Regenerative Rehabilitation-based approaches is still in its infancy and critical questions regarding clinical translation and implementation still exist. In a recent roundtable discussion from International Consortium for Regenerative Rehabilitation (ICRR) stakeholders, key challenges to progress in the field were identified. The goal of this white paper is to summarize those discussions and to initiate a broader discussion among clinicians and scientists across the fields of regenerative medicine and rehabilitation science to ultimately progress Regenerative Rehabilitation from an emerging field to an established interdisciplinary one. Strategies and case studies from Consortium institutions—including interdisciplinary research centers, formalized courses, degree programs, international symposia, and collaborative grants—are presented. We propose that these strategic directions have the potential to engage and train clinical practitioners and basic scientists, transform clinical practice and, ultimately, optimize patient outcomes.

Abbreviations

Food and Drug Administration (FDA)

International Consortium for Regenerative Rehabilitation (ICRR)

AO Research Institute (ARI)

Trauma, Regeneration and Rehabilitation (TRR)

Physical Medicine and Rehabilitation (PM&R)

Department of Defense (DoD)

Veterans Affairs (VA)

National Institutes of Health (NIH)

Military Health System (MHS)

Armed Forces Institute of Regenerative Medicine (AFIRM)

Advanced Rehabilitation Centers (ARC)

Arbeitsgemeinschaft für Osteosynthesefragen – Association for the Study of Internal Fixation (AO)

Introduction

Integration of the fields of regenerative medicine and rehabilitation sciences—known as Regenerative Rehabilitation—has the potential to transform the future of healthcare by leveraging both disciplines in order to significantly advance scientific and technological progress. Regenerative medicine as a discipline, develops therapeutics and interventions to enhance tissue repair or replace tissue that has been damaged or lost due to injury, disease, or age. This field often focusing on the endogenous and paracrine effects of stem cells or the transplantation of exogenous stem cells. Substantial progress has been made at the basic science and pre-clinical stages, offering glimpses into the promise of the field of regenerative medicine and tissue engineering; However, much of the current clinical practice for regenerative medicine technologies is based on relatively limited scientific evidence of clinical efficacy. The Food and Drug Administration (FDA) recently released clear guidelines detailing utilization of many current and forthcoming regenerative interventions; the FDA specifically emphasized the need for better scientific evidence behind this wave of regenerative therapies[1]. One key area with the potential to optimize patient outcomes is the integration of rehabilitation regimens in combination with regenerative therapies. Though the integration of these two fields is logical and has been increasingly gaining traction, the most efficient path forward for merging the areas remains unclear. Arguably, this gap has hampered effective clinical translation of regenerative therapies.

The International Consortium for Regenerative Rehabilitation (ICRR), presently comprising a total of 16 institutions from around the globe, was formed in 2014 to drive the growth of this burgeoning interdisciplinary field. During a Roundtable of stakeholders from the ICRR, which also included delegates from military and federal agencies, key challenges to progress in the field were identified. Exemplars of success in merging the two fields through the development of educational and research programs were highlighted. The goal of this white paper is to use this collated information to facilitate broad discussions and unified strategic directions among clinicians and scientists across the fields of regenerative medicine and rehabilitation science.

Current State of the Regenerative Rehabilitation Field

The worldwide regenerative medicine market has grown from an estimated ~$250 million dollars in 1995 to $28 billion in 2018[2]. This industry growth has been accompanied by over 7,000 ongoing clinical trials worldwide (registered with the keyword “stem cells” on clinicaltrials.gov)[3]. The top three disciplines applying what are categorized as “stem cell technologies” are orthopaedics, pain management and sports medicine[4]—three areas that have had a long history of benefit from rehabilitation treatments. For conditions involving these domains, rehabilitation is typically prescribed with the goal of both promoting tissue, repair as well as improving of the overall function of the surrounding tissues as the injured area heals. As the regenerative medicine field grows, the implementation of these regenerative medicine technologies and patient management after a regenerative medicine intervention is a clear area requiring better scientific evidence and cross-field collaboration.

Rehabilitation and exercise-based regimens are well-established therapeutic interventions that are among the most broadly effective therapeutic approaches across medical disciplines. Exercise, for example, can substantially reduce the risk of more than 30 chronic diseases ranging from diabetes to Alzheimer’s disease as well as numerous cancers, cardiovascular disease, osteoporosis and arthritis, and many other disorders[5]. Further, lifestyle rehabilitation modalities are commonly prescribed for these

conditions after diagnosis, suggesting that after any potential regenerative medicine intervention, rehabilitation is likely to be an integral part of the treatment continuum[6].

Rehabilitation interventions can have direct regenerative benefits, such as chemical and mechanical modulation of local stem cell micro-environments, direction of stem cell differentiation, mobilization of stem cells into circulation, and promotion of secreted regenerative factors, among numerous other actions[7,8]. These rehabilitation interventions can range from standard exercise, to directed and supervised mechanotherapies, to external stimulation (electrical stimulation, low intensity pulsed ultrasound, pulsed electromagnetic field therapy, etc.). The benefits are likely to enhance functional outcomes and biomechanics following the application of regenerative medicine interventions and, as such, is a theoretical partnership that has been increasingly recognized[8,9].

Regenerative Rehabilitation is a natural partnership that has the potential to have substantial clinical impact. Regenerative Rehabilitation has been defined as: "*The application of rehabilitation protocols and principles together with regenerative medicine therapeutics toward the goal of optimizing functional recovery through tissue regeneration, remodeling, or repair"*[8]. Although previous publications have included both Regenerative Medicine and Rehabilitation terminology as keywords in the abstracts or titles, the term "Regenerative Rehabilitation" was coined in the literature in 2010 [10]. Since that time, the number of publications that include the terms "rehabilitation" and either "tissue engineering" or "regenerative medicine," has increased substantially (Figure 1)[11].

Building an Interdisciplinary Field

The formation of a new field requires time, vision, and buy-in from key players. During an ICRR roundtable meeting in 2017, delegates from partnering institutions as well as delegates from the National Institutes of Health, the Department of Defense, and the Veterans Administration gathered to outline a communal vision for the field, identify critical challenges that will be faced in this process, and discuss key initiatives for the growth of the Regenerative Rehabilitation field. Clearly, for any field to advance, there is need for a well-defined and shared vision as to the future objectives. Panelists were in agreement that the time is right to advance Regenerative Rehabilitation research from more isolated collaborative endeavors to the formation of a distinct, interdisciplinary field.

"Multidisciplinary", defined as involving two or more disciplines or specializations in an approach to a topic or problem, has become a ubiquitous term in research as barriers between different fields have started to fade. Nearly all research now involves some aspect of multidisciplinary intervention. The advantage of multidisciplinary collaboration lies in the potential to dramatically expand the breadth of expertise and technologies implemented. However, by definition, each individual retains primary expertise in their respective area. While the idea of multidisciplinary work is largely encouraged, the trend has been towards increased specialization. The irony is that as individuals become more and more specialized, it becomes more and more difficult to effectively communicate and collaborate with other disciplines. In contrast, "interdisciplinary" research, where knowledge and approaches are integrated, is often the impetus for a new field. Under this latter model, researchers possess training and expertise that span more than one discipline, allowing them to quickly integrate fundamental principles across both fields and act as focal points to bridge collaborations. Rehabilitation medicine has a long history of interdisciplinary approaches following common conditions such as spinal injury, stroke, joint replacement, etc.. Regenerative Rehabilitation is poised to make this transition from multidisciplinary collaborations to becoming a new interdisciplinary field. The question remains as to how to most effectively and efficiently make this transition happen.

The growth of a new, interdisciplinary field often starts from foundational technological advances that have far-reaching applications. For example, biomedical engineering lies at the interface

between medicine and engineering enables technologies, like the development of computers, to facilitate collaboration between the two disciplines (e.g. computational modeling of physiologic systems and automation/control systems for laboratory assays, among many others)[12]. From this initial spark, the biomedical engineering field began to generate momentum, particularly through trainees who wanted to learn and apply these and the many subsequently developed engineering technologies to address critical challenges in biological sciences and healthcare. As the number of vested parties grew, the next critical step in harnessing the newfound interest was the institutionalization of the field – e.g. training grants (NIH and NSF), degree programs and institutes (university level), and the formation of a society (Biomedical Engineering Society)[12]. A new field is typically not created out of nothing, but, instead, forms as budding specializations from existing disciplines. Eventually, the process leads to a full-fledged new field, as was the case with biomedical engineering, when these various specializations become consolidated as groups/sub-disciplines under an umbrella field or organization (e.g., American Institute for Medical and Biological Engineering for Bioengineering). The field of Regenerative Rehabilitation parallels this example in that it started with foundational technological advances in the fields of tissue engineering and stem cell biology, which are now being integrated with rehabilitation science, to address the broader challenges in biological sciences and healthcare.

Facilitating Interdisciplinary Interactions

In an ideal setting, the merging of disciplines involves close regular interactions among scientists on all sides of the developing field. Having close proximity and daily conversations helps foster these types of developments. In the early stages, cross-pollination of ideas can occur through meetings and workshops that break down silos, providing an opportunity for researchers and clinicians across the spectrum to co-mingle. On a larger scale, multidisciplinary institutes have played a key role in the formation of many new interdisciplinary fields, including biomedical engineering and regenerative medicine. For example, many research universities now have stand-alone facilities with common space areas (coffee shops, lobbies, etc.) and even clusters and quads dedicated to these still relatively young fields. This can be more challenging when trying to bridge a clinical discipline with areas of basic science, but the transition will be a critical step in the growth of Regenerative Rehabilitation.

Case Study – AO (Arbeitsgemeinschaft für Osteosynthesefragen – Association for the Study of Internal Fixation) Foundation. Since its establishment in 1959, the AO Research Institute Davos, Switzerland (ARI) has been a key part of the AO Foundation and, together, they have revolutionized the treatment of bone fractures. ARI has three buildings on one site, all within a 2-minute walk of each other to facilitate close and easy interactions. The approach for ARI involves projects and training operating in tandem with surgeons, engineers, material scientists, biologists and veterinary medicine practitioners. AO principles for surgery are heavily influenced by controlling the mechanical environment, and the AO surgical training courses emphasize the role of mechanical stimulation on healing mechanisms, and how mechanical stimulation can be controlled to optimize outcomes. Pre-clinical projects begin with a review by an independent board of surgeons/clinicians to ensure that both the clinical problem and the patient are at the forefront of the project from day one. Clinicians are integrated into preclinical studies through clinical fellowships where they can work on basic and translational projects for up to one year. This is crucial, as the clinicians are able to immerse themselves full time into research, while the permanent ARI scientists have regular interactions with, and input from, the target users who would implement any developments that would ultimately be used in the clinic. ARI also fosters regular interactions through recurring meetings, conferences and a general tradition of academic activity and spirit—all to promote clinical translation and research relevance. From the beginning, ARI has been multidisciplinary, and more recently has involved physiotherapists in symposia to promote post-surgical care considerations.

Key Steps and Initiatives in the Formation of a New Field

In the development of a strategic plan that will establish Regenerative Rehabilitation as a burgeoning interdisciplinary field, successful models and current initiatives were identified during the 2017 ICRR roundtable. These models can serve as a template to promote growth and ultimately transformation of the field. Key steps identified include: Building an educational framework to support Regenerative Rehabilitation, increasing visibility of Regenerative Rehabilitation, establishment of seed grant and training grant programs, and adopting leading-edge technologies in Regenerative Rehabilitation.

Building an Educational Framework to Support Regenerative Rehabilitation

Developing Regenerative Rehabilitation at the Institutional Level

It is clear that the growth of an interdisciplinary field of research at the institutional level will require engagement with key pillars of academia as well as the clinicians who are actively treating patients. Regenerative Rehabilitation stakeholders, including both researchers and clinicians, must work to educate administrators and cross-disciplinary leadership, conveying the importance and potential impact of Regenerative Rehabilitation. This has been successfully accomplished by having invited speakers present on Regenerative Rehabilitation outside of their home departments to promote an understanding of the interdisciplinary nature of the field and to generate excitement about the opportunities for growth.

Case Study - Indiana University. The Indiana Center for Musculoskeletal Health (ICMH) at Indiana University in Indianapolis, Indiana has established teams of researchers and clinicians to foster interdisciplinary collaborations in research and care. The focus of one of the teams, the Trauma, Regeneration and Rehabilitation (TRR) team, is directly related to the field of Regenerative Rehabilitation. The TRR team represents a multi-center effort comprised of surgeons, basic scientists and rehabilitation specialists. The team leader receives a financial commitment from the institution and organizes monthly meetings that allow members the opportunity to present findings from their projects and discuss future needs and directions. Relationships forged through the TRR team have resulted in collaborative grant applications, presentations and publications.

Developing Regenerative Rehabilitation Curricula

The next step in the formation of a Regenerative Rehabilitation field will be the development of new curricula that integrate both the regenerative medicine and rehabilitation disciplines. Courses currently exist on either side of the spectrum (e.g. stem cell biology, cell engineering, tissue mechanics as well as kinesiology, physiology, and evidence-based practice). While these courses provide an immense value and in-depth education in established fields and disciplines, there is also a need for material that integrates the disciplines and emphasizes the relevance of these diverse topics to Regenerative Rehabilitation. Many new interdisciplinary fields develop textbooks, coursework, and educational materials that not only highlight established principles and technologies but demonstrate their applications to the new field. This enables a core set of fundamental principles and common language for the new interdisciplinary field to build upon.

Case Study – Wayne State University. Wayne State University's Physical Therapy Program has developed several components in their Doctor of Physical Therapy curriculum that focus on regenerative rehabilitation. The learning experiences help students gain foundational knowledge, as well as the

ability to integrate information and apply it to a clinical setting. An example is a Biomaterials Module in the Pathokinesiology Course. In this Module, students learn about how the components of various tissues (example: ligament, tendon, cartilage and bone) affect the mechanical properties of those tissues, and how this relates to changes through the lifespan and tissue injury, repair, and regeneration. Students attend 14 hours of classroom and lab instruction over 7 weeks and also review web-based content posted by the instructor. During each 2-hour weekly classroom and lab experience: a third of the time is spent learning foundational information on the components of the tissue being discussed; another third is spent discussing the implications of tissue biology on tissue development and aging, tissue damage, repair and regeneration; and the final third is spent performing hands-on activities, such as orthopedic special tests or exercises, and explaining the special tests or exercises from a biomaterials perspective. Testing includes: In-class quizzes, take home quizzes, and a final written exam, which follow the style of the National Physical Therapy Exam for licensure. The overall goal of this module is to help students apply their understanding of biomaterials in the clinic in order to properly assess tissue properties, minimize adverse changes, facilitate optimal repair and regeneration, and be aware of irreversible tissue limitations. Throughout the module, students work on a case study assignment, which involves describing—from a biomaterials and applied biomechanics perspective—the clinical presentation of one of their patients. The students then identify three main rehabilitation priorities for the patient and develop an evidence-based treatment plan for each rehabilitation priority. A required element is the description of a novel experimental therapy (i.e. tissue-, cell-, gene-, or rehabilitative-therapy), which might in the future change the current standard of care for the clinical condition discussed in the Case Study.

Case Study – Emory University. An interdisciplinary course, Integrating Biosensing Technology and Physical Therapy, was established in 2013 with a combination of students from physical therapy and neuroscience at Emory with engineering students from Georgia Tech. The course provides problem-based learning opportunities to students across multiple campuses and schools. Learning goals and contained topics relate to orthotic design, brain-machine interfacing, wearable sensors, tele-rehabilitation, regenerative medicine, robotics, informatics, biodesign, and processes for technology transfer, patent applications and licensing. Learning objectives are accomplished through a pedagogical framework that include lectures and demonstrations from content experts, classroom discussion, and laboratory experiences. Multidisciplinary sets of students observe and work in clinical settings with patients who had catastrophic injuries/or diseases (i.e., stroke, dystrophy, spinal cord injury, etc.) and require further rehabilitation or novel approaches to enhance their functional potential. The student teams acquire multiple skills including how to better communicate with one another, write a grant proposal based upon solving a patient problem about which all groups agreed to undertake as independent entities, how to critique one another's work and, lastly, how to do so during formal oral presentations. The course improves students' knowledge of scientific methods that identify links between biotechnologies and physical therapy application.

Establishing Training Programs in Novel Multidisciplinary Areas - Certificates, Degrees, Fellowships and Focus Areas

In many new fields, certificates and focus areas precede degrees and fellowships. New fields, such as Data Science, are showing that there are many new tools and technologies that can help with this process and have developed certificate programs from free online programs (such as Massive Online Open Courses) to formal Masters programs (i.e., in person, online and hybrid programs now exist). Practitioners and researchers within the field of Regenerative Rehabilitation would benefit from the establishment of specialized training in these areas. For basic scientists in regenerative medicine

disciplines, this could be a degree along the lines of a Masters in rehabilitative clinical research. For clinicians, this could be a fellowship in Regenerative Rehabilitation where they would receive training in the basic biology of stem cells, in mechanobiology, and in the clinical practice of regenerative interventions.

Case Study – Kyoto University. Kyoto University has introduced a comprehensive program with specialized training and research in Regenerative Rehabilitation through the Department of Human Health Sciences in the Faculty of Medicine. All undergraduate students entering the department (approximately 100 per year) receive an introduction to Regenerative Rehabilitation in their freshman year. Those interested in further specialization can engage by becoming part of a community called "Regenerative Rehabilitation for Students", which bridges numerous degree programs and allows for a cohesive multi-disciplinary community. Throughout their graduate program, students participate in project-based learning, in which they form teams and interact with mentors and supporters in a focus area called the Regenerative Rehabilitation Unit. As students progress in the program, they take classes in regenerative medicine where they learn about basic science fundamentals underlying the regenerative process, including the biology of stem cells. This course also introduces students to methods and techniques necessary for practicing regenerative medicine, including cell quality control, transplantation methods, post-transplantation care and rehabilitation, as well as concepts relating to legal and ethical questions. The students in this community later learn about specializations such as physical therapy, occupational therapy, and nursing, all specializations in which regenerative concepts can be applied. During postgraduate training, Ph.D. students can similarly receive training and perform research in Regenerative Rehabilitation working with labs in the Unit of Regenerative Rehabilitation. This unit promotes communication and engagement between clinical physicians and basic scientists by offering seminars, a regional symposium, technical assistance, and research collaborations.

Case Study - Kessler Foundation. Kessler Foundation, in partnership with New Jersey Regenerative Institute, Kessler Institute for Rehabilitation, and the Department of Physical Medicine and Rehabilitation (PM&R) at Rutgers New Jersey Medical School (NJMS), has added a Regenerative Rehabilitation Fellowship to its Rehabilitation Research Training Program. The overall purpose of the postdoctoral fellowship Training Program is to train individuals in clinical research with the goal of improving rehabilitation outcomes for individuals with neurological (e.g. spinal cord injury, traumatic brain injury, multiple sclerosis, stroke, etc.) and physical impairments. The Regenerative Rehabilitation fellowship itself focuses on integrating regenerative medicine and rehabilitation sciences principles and practices—training that will facilitate pursuit of a career in Regenerative Rehabilitation research. The fellow splits time between an active rehabilitation research program and a sports medicine clinic specializing in Regenerative and Orthobiologic treatments. One of the goals of the fellowship is to facilitate clinically based research on the effectiveness of various Regenerative and Orthobiological treatments, such as Platelet Rich Plasma (PRP), Bone Marrow, and Microfragmented Adipose Tissue (MFAT), and to establish a centralized database to record treatment outcomes from other clinics performing orthobiologic treatments. The fellow participates in resident and research fellowship didactics courses offered through the PM&R department. Training and travel funds are also budgeted in order to encourage travel to national regenerative medicine and rehabilitation medicine conferences and training programs specializing in basic science and clinical regenerative medicine techniques. The first Regenerative Rehabilitation postdoctoral fellow was added in 2018 through a grant from the Derfner Foundation and has already yielded several published abstracts, peer-reviewed publications, and additional research grants. The fellow has also served as a research mentor to many of the PM&R residents, who are required to do a research project as part of their residency training program. Given

the success of the Regenerative Rehabilitation fellowship, the goal is to expand the fellowship program with the addition of new fellows and to continue to expand the Regenerative Rehabilitation research partnership between Kessler Foundation and New Jersey Regenerative Institute, as well as other outside collaborators.

Increasing Visibility of Regenerative Rehabilitation

With the formation of any new field, advocacy and visibility are needed for the field to engage established researchers and to attract new trainees. The field will benefit from stakeholders, ICRR members, and Regenerative Rehabilitation researchers taking an active role in promoting the field's successes, engaging at both the pre-clinical and clinical levels with outreach to existing fields. In addition, the field can grow by highlighting its solutions and successes to funding partners, specifically, Department of Defense (DoD), Veterans Affairs (VA) and National Institutes of Health (NIH).

Regenerative Rehabilitation Sessions. One key method for gaining visibility and momentum for a growing field is to actively educate external and complimentary communities. Researchers and clinicians in the field of Regenerative Rehabilitation have been successfully collaborating to host sessions, workshops and symposia at a diverse range of local, national and international meetings. Sessions on Regenerative Rehabilitation have resulted in a number of new opportunities including invitations to publish and present at future meetings, which all further the visibility for this growing field. The success of these efforts highlights the importance of continuing to collaborate with colleagues to promote Regenerative Rehabilitation through this mechanism.

Case Study – Department of Defense. Extremity wounds make up the most common survivable injuries of modern military conflict and comprise the majority of initial hospital costs to the Department of Defense (DoD) Military Health System (MHS)[13]. Over the last two decades, the DoD has invested heavily to support the development the promise of regenerative medicine treatment strategies, including initiatives such as the Armed Forces Institute of Regenerative Medicine (AFIRM), among others. In concert with these regenerative medicine investments, early in the conflicts, the DoD established Advanced Rehabilitation Centers (ARC) at Walter Reed National Military Medical Center, San Antonio Military Medical Center, and Naval Medical Center San Diego who have since led the way in developing comprehensive physical rehabilitation programs, including the utilization of state-of-the-art technologies, to restore function following traumatic injuries[14]. While these current regenerative medicine therapeutics and rehabilitation programs offer proven clinical benefit, the potential synergies, and thus potential for further improved outcomes, of Regenerative Rehabilitation-based approaches are ideally suited for the DoD's MHS. To further the dialogue in this field, the DoD created, for the first time, a Regenerative Rehabilitation session at its 2018 annual research meeting, the Military Health System Research Symposium. In this inaugural session, high quality military-specific Regenerative Rehabilitation research was presented in front of an audience that exceeded the seating capacity of the room. The session had an engaged audience with vibrant dialogue and sparked numerous follow-up conversations. Moving forward, the DoD will be an ideal facilitator of the field of Regenerative Rehabilitation for years to come[15].

Case Study – Regenerative Rehabilitation Symposia. For the past seven years, the McGowan Institute for Regenerative Medicine, the School of Health & Rehabilitation Sciences, the University of Pittsburgh Medical Center Rehabilitation Institute and Stanford University/Palo Alto VA Rehabilitation Research & Development Center of Excellence have jointly organized a Symposium on Regenerative Rehabilitation. The Symposium series has grown over the years and is now an annual international meeting, with world-renowned speakers presenting on scientifically rigorous cutting-edge research and clinical management. This Symposium series represents a unique opportunity to bring together

scientists and clinicians from the fields of regenerative medicine and rehabilitation for two days with the goal of promoting interactions, the exchange of ideas, and formation of new interdisciplinary collaborations. An integral part of the meeting is mentorship of trainees and junior faculty members as a means to cultivate the next generation of Regenerative Rehabilitation researchers.

Seed Grant and Training Grant Programs

As university discretionary budgets become increasingly constrained, the availability of departmental funds to support pilot studies is expected to follow suit. However, the need for pilot studies remains high, whether they are for studies to test feasibility, to obtain preliminary data that support a novel hypothesis, or to gain experience with a research methodology. Larger scale funding mechanisms, such as NIH Research Project Grants (NIH R01 mechanism), require the submission of preliminary data, which are evaluated by reviewers as a means to predict the success of the proposed project. As such, investigators often struggle in undertaking new lines of investigation given the difficulty obtaining preliminary data outside their normal sphere of activity. An effective way to pursue novel research directions and to form new collaborative efforts is through implementation of small-scale pilot studies. These studies strengthen newly formed collaborative teams and can demonstrate productivity in bringing together investigators from different disciplines. Seed grants are, thus, a critical method to help foster new research projects. Similarly, training grants provide formal structure to enable specialization for the upcoming generation of researchers and practitioners. These funding mechanisms can be instrumental in launching new partnerships and generating preliminary data that serve as the foundation of larger research endeavors. Another potential tool for fostering work in this area is the establishment of supplemental grant awards that target the addition of a Regenerative Rehabilitation protocol onto an existing parent grant. An example would be a supplement to expand the aims of an existing stem cell interventional trial by evaluating the impact of exercise or another rehabilitation therapeutic approach. Such a mechanism has the potential to bring successful researchers doing highly relevant research into the field by decreasing barriers to launching nascent Regenerative Rehabilitation investigations.

Adopting Leading-Edge Technologies in Regenerative Rehabilitation

The rehabilitation community has often been at the forefront of implementing new regenerative technologies in the clinic. In addition to implementing new regenerative therapies, becoming early adopters of leading-edge technologies has the potential to significantly improve the translation of regenerative therapies and, ultimately, functional outcomes for patients. Personalized medicine, next generation genomics, and other omics-based approaches are changing the way medicine is practiced in terms of diagnostics and therapeutic interventions. These large data approaches can provide substantial information on the patient to tailor rehabilitation regimen to specific patients and their specific regenerative treatment. On the regenerative medicine side, there are huge efforts being led in manufacturing processes and systems for cell-based therapies that have the potential to greatly improve the consistency and potency of regenerative therapies. For these reasons, it is critical that Regenerative Rehabilitation clinicians and researchers are included in conversations with the FDA and manufacturers when translating regenerative therapeutics from bench to bedside.

Summary and Concluding Statements

The emergence and growth of the field of Regenerative Rehabilitation has great potential to improve clinical outcomes for patients with disabilities. However, this field is currently in its infancy and needs rigorous scientific inquiry to begin to elucidate the biologic underpinnings of Regenerative Rehabilitation-based approaches. A key goal in the establishment of this new field of Regenerative Rehabilitation is to cultivate a population of clinicians and scientists that have a robust training in both regenerative medicine and rehabilitation principles and approaches. Member organizations in the ICRR are beginning to implement strategies to facilitate this process—interdisciplinary research centers, formalized courses, degree programs, international symposia, and collaborative grants are just a few of the case study initiatives that have been presented. This multidirectional process has the potential to engage and train both clinical practitioners and basic scientists, transform clinical practice and, ultimately, optimize patient outcomes.

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Figure Legends

Figure 1 – N**umber of Publications by Year in the Regenerative Rehabilitation Field**. Data from Web of Science search for publications using the terms: “Regenerative medicine” AND Rehabilitation; OR “Regenerative Rehabilitation;” OR “Tissue Engineering” AND Rehabilitation (performed on 4/26/2019)[11].

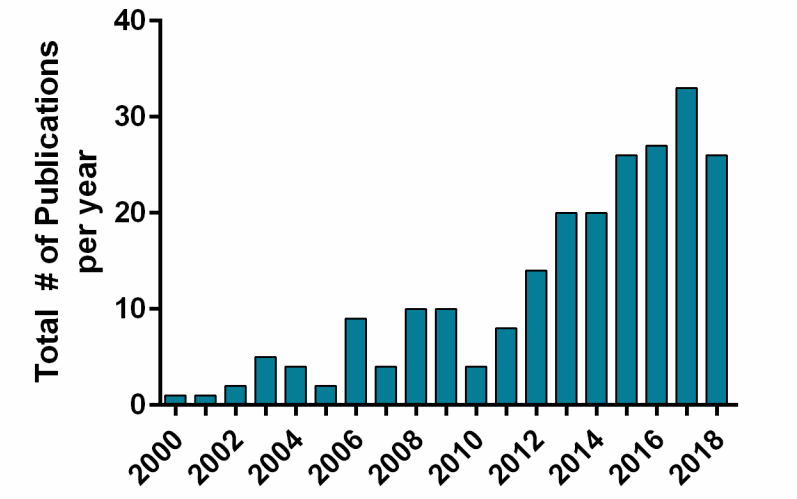

Figure 1 – N**umber of Publications by Year in the Regenerative Rehabilitation Field**. Data from Web of Science search for publications using the terms: "Regenerative medicine" AND Rehabilitation; OR "Regenerative Rehabilitation;" OR "Tissue Engineering" AND Rehabilitation (performed on 4/26/2019).