Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

Canada

IMHA Reports

The seeding of new research projects with IMHA's *Catalyst Grant: Muscle and Musculoskeletal Rehabilitation* program

IMHA Analysis & Evaluation Unit
University of Toronto
Marc R. Milot & Phillip Gardiner

September 2012

Prepared for the Institute of Musculoskeletal Health and Arthritis at the Canadian Institutes of Health Research

CIHR - Institute of Musculoskeletal Health and Arthritis
University of Toronto, Faculty of Medicine
The Banting Institute, Room 207B
100 College St., Toronto, ON M5G 1L5

Canadian Institutes of Health Research
160 Elgin Street, 9th Floor
Address locator: 4809A
Ottawa, ON K1A 0W9

Cat. No.: MR4-16/2012E-PDF
ISBN: 978-1-100-21296-8
http://www.cihr-irsc.gc.ca/e/13217.html

EXECUTIVE SUMMARY

- IMHA's Catalyst Grant: Muscle and Musculoskeletal Rehabilitation program provided an average of $79,233 for one year to five new research projects.
- The research findings of the funded projects were reported in many peer-reviewed publications disseminated at numerous conferences through presentations and posters. Many trainees and post-doctorates worked on and were financially supported through these catalyst grants.
- The research projects/findings included:

i. The development of a model and treatment of a painful disorder of the jaw muscle for preclinical and clinical testing, with the potential to lead to the identification of biomarkers for this chronic pain syndrome in human patients.

ii. An investigation of the impact of conventional and unconventional exercise training on bone health and strength, with a particular training type found superior for increasing muscle mass in the elderly; findings which could eventually have an impact on exercise prescriptions for older individuals for the prevention of age-related muscle mass decline.

iii. The imaging of brain activity during movement, with results showing that accurate measurement of brain activity during physical motion is possible; findings which will facilitate the study of the impacts of musculoskeletal rehabilitation interventions on brain plasticity and recovery.

iv. The study of muscle repair following exercise-induced damage, leading to a greater understanding of the factors that contribute to dysfunction in muscle repair in elderly; findings which could potentially inform the development of drugs to reduce loss of muscle in advanced age.

v. The study of muscle restoration in muscular dystrophies, with findings that may help address the overarching goal of improving therapeutic approaches for their treatment.

- IMHA's catalyst program met its primary goal to serve as a catalyst for the generation of preliminary findings as a first step towards the pursuit of more comprehensive funding opportunities, with many of the funded researchers reporting success in acquiring subsequent funding to follow-up on initial findings, and the others with grant applications in progress.
- The overall findings of this report indicate that substantial progress has been made by the projects seeded by the program, with outcomes expected to contribute to informing future developments and advancements in muscle and musculoskeletal rehabilitation research.

I. PREFACE

This report describes the outcomes of research projects supported by the Catalyst Grant: Muscle and Musculoskeletal Rehabilitation (MMR) program launched in July 2007 and funded by the institute's Strategic Initiatives budget in 2008.

IMHA is the primary source of funding for Canadian health research across six research foci: arthritis, musculoskeletal (MSK) rehabilitation, bone, skeletal muscle, skin and oral health. Each of these areas is equally important and offers significant opportunities for advancement of research and knowledge translation. IMHA's vision is to sustain health and enhance quality of life by eradicating the pain, suffering, and disability caused by arthritis and other MSK, oral and skin conditions. Advances in understanding, preventing and treating diseases and conditions across all six research foci provide a formidable means of achieving this vision. IMHA's mission reflects that of the Canadian Institutes of Health Research (CIHR) - to excel, according to internationally accepted standards of scientific excellence, in the creation of new knowledge in all relevant areas, and to translate that new knowledge into improved health for Canadians, more effective health services and products, and a strengthened Canadian health care system[1].

The Analysis & Evaluation Unit aims to help IMHA understand the impact of its targeted funding and programs, and to assist the Institute Advisory Board (IAB) in decision-making and the development of strategic initiatives using an evidence-based approach. IMHA has systematically collected data on funding trends within its mandate, and surveyed researchers funded by its programs. Both funding trends and research outcomes data are analyzed and used to inform strategic directions and activities. Recognizing the potential value of such data to others, in 2012, IMHA initiated a knowledge translation activity that involved a comprehensive approach to data collection, analyses, and evaluation. This activity generated reports on the outcomes of IMHA's funded programs and initiatives.

IMHA Reports are disseminated to IMHA's IAB as well as to a variety of interested stakeholders including senior management and staff at IMHA and CIHR, researchers, organizations, policymakers and others interested in knowledge translation and/or outcomes of projects funded in relevant health research areas.

II. INTRODUCTION

Skeletal muscle is the most abundant tissue in the human body. It is crucial for everyday movements and activities, and while exercise and motion can increase muscle size and strength, inactivity has the opposite effects. In addition to strains, sprains and outright trauma, there are many different diseases that also affect skeletal muscle, including chronic pain syndromes, inflammatory arthritis, muscular dystrophies, and various types of paralysis and conditions

[1] http://www.cihr-irsc.gc.ca/e/40490.html

that cause muscles to weaken and waste away. In the presence of skeletal muscle damage or wasting (which can also be the result of aging), there can be disability such as mobility impairments and reductions in agility and dexterity which severely reduce quality of life. Consequently a need for preventive measures, treatments, and rehabilitation therapies for muscle diseases and MSK injury exists. This article describes the background and objectives of an IMHA muscle research program and the research projects that received funding.

A. IMHA's Catalyst Grant: Muscle and Musculoskeletal Rehabilitation – Background

In June 2006, 65 delegates from the muscle and MSK rehabilitation communities convened for a direction-setting workshop entitled Muscles: From Molecules to Mobility organized by IMHA in partnership with the Institute of Aging. The purpose of the workshop was to identify and set common research objectives and directions in the area of muscle and MSK rehabilitation research. Participants at the workshop included patients, representatives from government, non-governmental and voluntary organizations, and researchers from such diverse backgrounds as physical therapy, mechanical engineering, rehabilitation sciences, biochemistry, physiology, occupational therapy, molecular biology, and kinesiology. This was the first time that such a diverse group of stakeholders had an opportunity to meet and discuss these topics. The meeting resulted in the creation of a list of defined research priorities which informed the basis of the MMR program.

B. Objectives

The purpose of catalyst grant programs is to provide seed money, on a short-term basis, to support health research activities in new areas which represent a first step towards the pursuit of more comprehensive funding opportunities (e.g. operating grants, team grants). Other objectives of the MMR program included:

- Generation of preliminary data, observations, or knowledge.
- Development of research agendas and/or action plans to advance research in specific priority areas.

C. Relevant Research Areas

Applicants were encouraged to address research areas within the context of any one of IMHA's following priorities:

- Tissue injury, repair, replacement (TIRR)
- Physical activity, mobility, and health (PAMH)
- Pain, disability, and chronic diseases (PDCD)

More specifically, the investigation had to include one or more of the following areas/types of research:

- Muscle atrophy
- Muscle function and dysfunction
- Movement, exercise and rehabilitation
- Animal models for therapy and rehabilitation research
- Muscle response to non neuromuscular diseases/conditions
- Modern imaging technology related to muscle/neuromuscular research
- Translational research

D. Funded Research Projects

CIHR's peer-review process identified the top six projects that were approved for funding from a total of nine applications. One applicant declined the grant because they received funding from another source, leaving five Nominated Principal Investigators (NPIs) as recipients of funding (see below table). The total amount provided by CIHR/IMHA for this funding opportunity in 2008 was $396,168. The average amount awarded for a single grant was $79,233.

Table 1. Details of the funded research projects

Research Institution	Nominated Principal Investigator	Project Title
University of British Columbia	*Brian E. Cairns, PhD*	Intramuscular injection of nerve growth factor to model non-inflammatory myofascial pain disorders.
University of Saskatchewan	*Philip D. Chilibeck, PhD*	Eccentric versus concentric training for improving predictors of bone and muscle strength.
University of British Columbia	*Janice J. Eng, PhD*	Brain activation: From mechanisms to mobility.
McMaster University	*Gianni Parise, PhD*	The response of signaling factors, in blood and muscle, for the mobilization of muscle stem cells following exercise-induced muscle damage and repair in old and young adults.
University of Manitoba	*Joerg Stetefeld, PhD*	Mini-Agrin: molecular studies on a designed miniaturized agrin used as therapeutic tool.

III. METHODOLOGY

A. Micro Impact Survey

The MIS was developed to gather information pertaining to broad outcomes of any type of research grants. It is a web-based survey instrument designated for the Nominated Principal Investigators (NPIs) of the research project. The MIS was constructed and conducted online using kwiksurveys.com, a cost-effective and flexible survey creation website allowing responses to be collected and data to be exported in Excel format. The survey was designed to allow for both quantitative and qualitative input. Pilot testing confirmed the survey was suitable for assessing outcomes of research projects from all of CIHR's research themes, i.e., biomedical (Theme I), clinical (II), health services/systems

(III), and social-cultural-environmental/population health (IV) research areas. The survey takes on average only 5-10 minutes to complete.

The survey has 19 and 5 questions, requiring quantitative and qualitative input respectively, under the impact categories of:

- Advancing knowledge (e.g., publications)
- Capacity building (e.g., training, collaborations, team building)
- Knowledge exchange, synthesis and dissemination
- Health systems impact (e.g., health policy documentation, clinical guidelines)
- Economic impact (e.g., employment, patents, commercialization)

The MIS has two types of questions: those inquiring about number of contributions or "planned contributions", and others inquiring about outcomes answerable by "Yes" or "No" or "No but likely in future". NPIs therefore had the opportunity to report both "to date" and planned outcomes. The data summarized in this report are the combination of "to date" and planned outcomes of selected questions. Previous analyses by this author have shown that NPIs of more recent and ongoing research projects do not overestimate planned outcomes. Thus, the total outcomes of ongoing research projects as measured by the MIS are likely a good estimate of eventual/actual outcomes. For more details on the data analysis and methodology and for the actual survey questions, please consult previous reports[2].

B. Procedure and timeline

The first MIS e-mail survey invitations were deployed to the five MMR-supported NPIs in February 2010. Up to two additional reminder e-mails were sent to non-respondents, and the survey was closed April 2010. All five funded NPIs responded to the survey. In December 2011, e-mails were sent to the five NPIs requesting further details related to outcomes of their research projects; some of the NPIs were contacted via telephone. In April 2012, the NPIs reviewed a draft of the text related to their grant outcomes and provided feedback to ensure accuracy and up-to-datedness.

IV. SURVEY FINDINGS

This section outlines the outcomes of research projects funded by the MMR program, as determined and summarized by surveys results and other researcher feedback.

A. Knowledge creation and dissemination

The dissemination of scientific research results is crucial for the advancement of health research. It can be achieved through peer-reviewed publications, technical reports, book contributions, and conferences - where different knowledge users ranging from (and not limited to) researchers, health professionals, government officials, and the public can be reached. The survey asked for the number of contributions, and dissemination targets – both actual and planned – of the research findings.

In total, 40 contributions to knowledge were reported, with an average of 8 items per grant as a result of the research projects supported by the MMR program. Most frequently reported were conference disseminations, followed by peer-reviewed articles and technical reports.

Aggregate Outcomes:

Total contributions: **40**	Per grant average: **8**

The Specifics:

Grant	Peer-reviewed articles/report	Book contributions	Conference posters and oral presentations
1	2	1	9
2	2	n/a	4
3	4	n/a	4
4	3	n/a	4
5	1	n/a	6

Fig. 1. Details on the number and type of contributions to new scientific knowledge.

The survey also inquired about the dissemination of research findings to specific knowledge users. The most frequently reported targets/knowledge users of the research findings were health professionals, followed by the public, patients, policymakers, and news media.

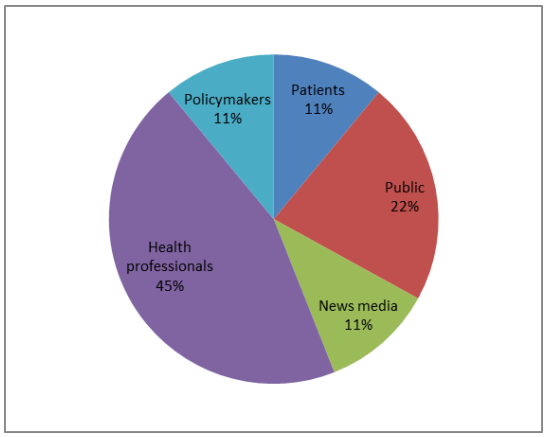

Fig. 2. The frequency of dissemination to specific knowledge users

Summary

The numerous articles, book contributions, conference posters, and oral presentations resulting from the MMR-supported research projects have increased the dissemination of new research knowledge related to muscle and MSK rehabilitation to a variety of knowledge users, and will continue to do so. These outcomes are expected to contribute to informing future developments and advancements in this area.

[2] http://www.cihr-irsc.gc.ca/e/44018.html

B. Training, Support and Employment

Training and employment is central to many research programs, with NPIs relying heavily on trainees (undergraduate and graduate students), post-doctoral fellows, and trained professionals (technicians and research associates) to conduct research. The survey questions inquired on the number of such individuals trained or working on the MMR-supported research projects, and the degree of financial support received. In total, 17 individuals were reported as working on the research projects, with the majority supported financially (82%) by the grant funds.

Summary

The survey findings showed that many undergraduate and graduate students were involved in the research projects, and that the majority were financially supported. The training and support of students, post-doctoral fellows, and technicians/associates may promote continued employment and/or increased researcher capacity in the muscle and MSK rehabilitation research field.

Aggregate Outcomes:

Total: **17**

Per grant average: **3.4**

The Specifics

Grant	Undergraduates	Graduates and post-doctorates	Technicians and associates
1	1 / 0	1 / 1	1 / 0
2	1 / 0	2 / 0	2 / 0
3	0 / 0	2 / 0	0 / 0
4	0 / 2	2 / 0	0 / 0
5	0 / 0	2 / 0	0 / 0

Fig. 3. Details on the number of trainees, post-doctoral fellows, and technicians/associates working on the MMR-funded research projects (supported financially by grant / other sources)

C. New Collaborations and Researcher Interactions

New collaborations and researcher interactions are often the result of new research projects. The survey inquired on the number of new and lasting collaborations (actual or planned) with other researchers (beyond those listed as co-applicant or other-PI on the MMR application) resulting from research activities supported by the catalyst program. It also inquired about the nature of these interactions, including those within an industrial or non-industrial context, with researchers in a different discipline, and with health care providers/policy makers or other health care experts. In total, 16 new research collaborations were reported as a result of research activities associated with the projects, with an average of 3.2 collaborations per grant, as well as numerous types of interactions.

Summary

The survey showed that a number of new collaborations resulted from the MMR-funded research activities, and that networking extended beyond the initial grant application

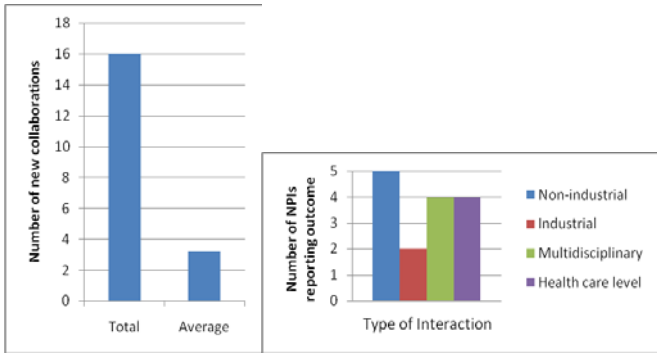

Figure 4. The number of new collaborations resulting from MMR-supported research activities (left panel), and the type of interactions (right panel)

Practically all researchers reported that interactions with other researchers and/or health professionals were non-industrial, multidisciplinary, and at a health care level. Such collaborations and interactions may improve and/or extend the development of the MMR-supported research projects.

V. GRANT OUTCOMES

In this section, we report specific research goals, activities, and outcomes of the five MMR-supported projects (in alphabetical order of awardees) based on both the online survey (February 2010) and follow-up e-mails and/or phone conversations (updated to April 2012).

A. Grant 1: Development of a model and treatment of a painful disorder of the jaw muscle

- The aim of this research project was to develop a preclinical model of a painful disorder of the jaw muscle: myofascial temporomandibular disorder.

- Myofascial pain disorders (MPD) are characterized by chronic pain in muscular areas of the body. The pain can range from mild to excruciating, knots can occur, and any muscle or muscle group can be affected.

- This research investigated a protein called nerve growth factor (NGF), which helps keep nerve fibers functional. If injected directly into the jaw muscle of humans, this protein can produce muscle sensitivity and pain similar to that observed in myofascial temporomandibular disorders.

- Important insights in the development of muscle pain in patients might be attained by studying the functioning of the NGF protein.

Outcomes to date

- *Development of a model of jaw muscle pain for preclinical and clinical testing.* The long-term goal of the research is the development of a well characterized model of jaw muscle pain that can be used to test novel analgesic compounds both preclinically and clinically. Dr. Cairns is confident his work could lead to the identification of biomarkers for this chronic pain syndrome in human patients.

- *Commercial research opportunities.* Based on the existing findings of the research, preliminary discussions are already underway with a Canadian pharmaceutical firm about the potential to use the NGF muscle pain model for commercial research, towards a potential clinical treatment.

- *Wide dissemination of findings.* According to Dr. Cairns, there is a great deal of interest in modulating NGF levels to treat human chronic pain. As a result, his research findings have already been broadly disseminated to a variety of researchers and stakeholders. For example, he gave a plenary lecture on his research at the 2008 Annual Thai Association for the Study of Pain meeting (Thailand). In 2011 he also organized a workshop with Dr. Andre Dray from Astra-Zeneca at the Canadian Pain Society meeting (Niagara, Ontario) on the topic of NGF and the potential for modification of its action to treat various forms of pain.

- *Training.* The MMR grant permitted the training of a Master's student who subsequently worked as a technician in Dr. Cairn's laboratory. Further, a senior scientist from Denmark visited the laboratory to learn about the specialized techniques of the research, further expanding the use of the NGF muscle pain model.

- *Follow-up application to CIHR.* The research team has since applied for a CIHR operating grant to follow-up on the initial findings seeded by the MMR program.

B. Grant 2: Investigating the impact of conventional and unconventional exercise training on bone health and strength

- This research project investigated different types of exercise training on bone structure and strength in a sample of elderly individuals. The thinning of bone tissue and loss of bone density over time, known as osteoporosis, is one of the most common causes of chronic pain, disability and death in the elderly population.

- Although conventional exercise training might improve bone health, little is known about the impact of different types of training. In this study, conventional (concentric) training, where muscle shortens while lifting a weight, was compared to unconventional (eccentric) training, where muscle lengthens while resisting weight.

- Changes in bone mass were assessed with conventional (dual energy X-ray absorptiometry) and novel (ultrasound and peripheral quantitative computed tomography) techniques to provide new and unique information about changes in bone structure and strength.

- The findings of this research project could therefore prove useful for the development of preventive exercise strategies against osteoporotic fractures.

Outcomes to date:

- *Informing development of home-based preventive strategies against osteoporotic fractures.* Dr. Chilibeck's research showed that a specific type of unconventional training (with eccentric overload) was superior for increasing muscle mass in the elderly. He hopes that these findings will have an effect on exercise prescriptions for older individuals for the prevention of age-related loss of muscle mass.

- *Device development with potential commercial applications.* In a follow-up study the research team plans to develop a hand-held exercise device to simulate the type of training experienced by their research participants. This could lead to the development of a cost-effective home-based exercise device for older individuals that might be effective at improving bone health and overall MSK health, with the potential to prevent osteoporotic fractures and other injuries.

- *Wide dissemination of findings.* The findings of this research project have been presented at the Canadian Society for Exercise Physiology meeting (Vancouver, 2009), the American College of Sports Medicine meeting (Baltimore, 2010), and at the American Society for Bone Mineral Research meeting (Toronto, 2010). The research team is currently in the process of preparing a manuscript based on findings from the study comparing eccentric versus concentric exercise training in old adults.

- *Improved capacity for research.* Dr. Chilibeck reported that the research allowed him to increase and improve collaborations with other researchers in the areas of bone and muscle imaging, an outcome which has helped improve his capacity for future research.

- *Training.* Three Master's students and one undergraduate summer research student were trained during this study. One of the Master's students is now working towards a PhD, one is completing a degree in physical therapy, and the third is in the process of completing their degree. The undergraduate student has continued studies in dentistry.

- *Follow-up application to CIHR.* The research team plans to submit a follow-up application to CIHR.

C. Grant 3: The imaging of brain activity during movement

- This research project involved the development of a protocol for assessing brain activation from functional magnetic resonance imaging (fMRI) during a task which challenges coordination and motor control in older adults with a history of falling/balance problems.

- Human mobility requires coordinated muscle activity across multiple muscles and joints. One of the distinguishing

features of human mobility is the ability to coordinate movements, a characteristic thought to involve substantial input from higher brain structures.

- The study of brain activation during motion has traditionally not been possible, but recent innovation has allowed for the mapping of changes in brain activity during movement.

- In this study, subjects were on their back with their head fixed in the imaging machine and their feet on a platform which could assess coordinated limb movements. The brain activity of 10 older adults was monitored during the coordination task.

- This research project tested the feasibility of studying the brain during the motion task, and results could expand the application of neuroimaging tools to a wide array of mobility-related activities relevant to balance and falls.

Outcomes to date:

- *Successful imaging of the brain during movement task.* The findings of this research supported the recent discovery that accurate measurement of brain activity during physical motion is possible, despite previous limitations.

- *Informing rehabilitation intervention studies.* Although Dr. Eng reported that the research is "mechanistic", she now hopes to move her research focus on the measurement of brain neuroplasticity in the context of rehabilitation. Specifically, while the current research dealt with normal/healthy young and older adults, the research team aims to now transition to older adults with neurological conditions to understand the effect of MSK rehabilitation interventions on brain plasticity and recovery.

- *Michael smith foundation for health research senior scholar award.* Dr. Eng was awarded a Michael Smith Foundation for Health Research Senior Scholar Award ($500,000), and the fMRI imaging data resulting from research supported by the MMR program was considered an important component of the application.

- *Wide dissemination of findings.* Results of the fMRI study were published in the journal *Experimental Gerontology*, and presented at the Society for Neuroscience conference (Washington, 2011), the world's largest symposium in brain research. An article on the research was also featured in Reuters News, and two additional research papers are in preparation.

- *Expanded inter-discipline collaborations.* It was reported that numerous collaborations resulting from the research funded by the MMR program were developed, including those with physical therapists and engineers. These collaborations were reported as long-lasting and the researchers continue to collaborate with each other on various projects.

- *Follow-up applications for funding.* Dr. Eng holds the catalyst grant programs in high regard, and feels that "this type of funding mechanism is very useful for getting high risk pilot projects up and running". Her research team is currently preparing a Canadian Foundation of Innovation Grant for additional imaging equipment, and experience gained from the catalyst grant was considered important for the application.

D. Grant 4: Muscle repair following exercise-induced muscle damage

- This research investigated factors that are involved in the efficient repair/building of muscle following exercise in old and young adults.

- Aging is associated with a progressive loss of muscle mass (sarcopenia). Identifying the underlying causes of this loss is important for the development of effective strategies to maintain mobility and quality of life in older adults.

- Skeletal muscle is associated with a unique population of stem cells that have a remarkable ability to induce muscle regeneration and growth. In fact, muscles are built following exercise largely due to regeneration and repair of damaged muscle tissue, a process relying on stem cells.

- The research goals were to examine the factors in blood and muscle that may be involved in the efficient activation, proliferation, and differentiation of muscle stem cells following a damaging bout of exercise. These factors included hepatocyte growth factor, interleukin-6, insulin-like growth factor-1, and myostatin.

- The experiments were designed to determine whether and how aging impacts the functioning of muscle repair, to help inform the development of effective strategies to maintain mobility and quality of life in older adults.

Outcomes to date:

- *Greater understanding of mechanisms of muscle repair in the elderly.* The research from this grant has led to a greater understanding of the factors that govern muscle repair following damage, and explored potential factors that contribute to dysfunction of repair and growth in the elderly**.** Dr. Parise noted that one of the biggest problems facing aging populations is the maintenance of muscle mass and strength. Central to this problem is the appropriate function of muscle stem cells. The research team continues to make progress in understanding how muscle stem cells function in their native environment.

- *Informing development of pharmaceutial targets for muscle repair dysfunction*. Dr. Parise hopes his work will provide potential pharmaceutical targets for the development of drugs to reduce the loss of muscle in advanced age. They will focus their efforts on key factors and their manipulation to determine the most promising candidates for treatment of muscle stem cell dysfunction.

- *Wide dissemination of findings.* Two articles related to the funded project have been published, one in the journal *PLoS One*, the other in the *Journal of Physiology*. These articles report on specific signaling cascades associated with repair following exercise-induced muscle damage. Further, all research outcomes associated with the project were presented at international conferences, including the Experimental Biology (Anaheim, 2010) and American College of Sports Medicine (Seattle, 2010) meetings.

- *International collaborations.* Dr. Parise was invited to the Netherlands to advise two international collaborations, one originating in Ireland and one in the Netherlands. Both of these projects are joint private/public ventures and have resulted in numerous other smaller scale collaborations.

- *Extensive training*. The research program supported an undergraduate student who has since enrolled in graduate studies, one Master's student, and one PhD student who will be pursuing a medical degree. There were several other graduate students who were co-authors on research publications related to the funded research.

- *Follow-up funding from CIHR.* Dr. Parise and his team are recent recipients of an aging pilot grant at CIHR that will allow the team to follow-up on the initial findings of the MMR-supported project. They expect that the funding and experience gained from both the grants will contribute to the development of successful operating grant applications in 2012.

E. Grant 5: Muscle restoration in muscular dystrophies

- The research program objectives were to elucidate the mechanisms through which a molecule (mini-agrin) important in the organization and functioning of skeletal muscle cells can restore muscle function in muscular dystrophies.

- Muscular dystrophies are characterized by a generalized and progressive loss of muscle mass. The wasting of muscle has a big impact on the quality of life of patients because it often leads to the inability to walk, and in some severe cases respiratory failure.

- All of these genetic diseases are rare and are caused by mutations, most of which affect the function of molecules that belong to the dystrophin-glycoprotein complex (DGC), a protein found at the inner surface of muscle fibers.

- Despite tremendous progress made to date, muscular dystrophies are still understudied and currently no curative treatments are available.

- The overarching goal of the research was the design of structural booster genes based on mini-agrin for improved muscular dystrophy treatments.

Outcomes to date:

- *Informing development of therapeutic approaches.* In the long-term perspective Dr. Stetefeld hopes his research will contribute significant data to the field of muscular dystrophy research by addressing the overarching goal of improving therapeutic approaches for the treatment of the group of disorders. The MMR-supported research has helped better position Dr. Stetefeld's research team for the development of essential information leading to structure-booster gene therapies with mini-agrin. He considers basic research, like his own, as the foundation for the application-driven specialist.

- *Greater understanding of the role of mini-agrin in muscle restoration.* The findings of this research project continue to increase the understanding of the role of mini-agrin in the rescue of muscular pathology. The research teams expect to publish the findings of this project in the coming year.

- *Collaborations.* The catalyst grant was reported to be "a perfect seed to establish a lasting collaboration with two partners" in the University medical school.

- *Training.* A Master's and PhD student were trained during this grant.

- *Follow-up CIHR funding.* The research team submitted a CIHR operating grant application related to agrin, and received funding to follow-up on the initial MMR-supported findings.

VI. DISCUSSION

A. Catalysis of new research programs and funding opportunities

Catalyst-funded research projects are unique in that they strongly emphasize the exploration of novel research ideas and directions. A central objective of catalyst and seed grant programs is to provide new research projects with the initial funding and momentum necessary to achieve success in subsequent funding opportunities. It is therefore important to note the success of the MMR program in these respects: all the funded NPIs reported subsequent or planned applications to CIHR (or other agencies) to follow-up on their initial

findings, with two teams (at the time of writing) already successful in acquiring funding. Specifically, one research team received funding from a CIHR pilot grant program to continue building on the research supported by the MMR program; they hope this will contribute to the acquisition of an operating grant of greater duration and funding. The other team has already been successful at acquiring a CIHR operating grant to follow-up on the initial MMR-supported research findings. In this context, IMHA's MMR program seems to have indeed served as a catalyst for the development of new research projects generating enough preliminary findings and momentum, in a relatively short-time period, to allow for subsequent applications to follow-up funding opportunities. Indeed, many of the NPIs funded by this program remarked that this funding tool was indispensable for the initial funding of pilot and/or high risk ventures and were thankful for the opportunity to apply.

B. Collaboration and training

The MMR program was also successful at mobilizing research communities. Many trainees were involved in the research projects, and NPIs reported a significant number of new collaborations resulting from the research activities. The training and support of undergraduate/graduate students, post-doctoral fellows and technicians/associates, and the resulting high number of collaborations may have the long-term impact of increasing researcher capacity and employment in muscle and MSK rehabilitation areas. Although it is difficult to measure the long-term impact of training on future research capacity and employment, results (unpublished) from a previous IMHA survey of undergraduate students receiving a stipend (summer award) do indicate that the majority of these students continue on to graduate studies in a similar domain.

C. The gap between short and long-term outcomes

While the short-term outcomes presented in this report are important and noteworthy, from an evaluation perspective whether (and how many of) the seeded projects will eventually develop enough to reach their stated long-term goals and/or impacts remains to be determined. These long-term goals and/or impacts include the use of a jaw pain model at a clinical level, the use of exercise prescriptions for the prevention of muscle mass loss in the elderly, the development of drugs to treat the loss of muscle or muscular dystrophies, and the use of new imaging techniques in MSK rehabilitation intervention. Some of the potential long-term impacts were at the patient level (e.g., therapeutics, treatments), and because passive dissemination of research findings is generally ineffective at impacting clinical practice (Bero et al., 1998), future evaluation and follow-up would be necessary to determine whether the MMR-funded projects had such longer-term impacts beyond those outcomes already reached. It may be that the findings of research teams engaged in interactions and research at the health systems/services level (four of the five teams reported such interactions) will eventually contribute more directly towards the improvement of Canadian muscle and MSK health, although there is evidence suggesting that health research is more influential in the presence of interactions with policy-makers (Davis and Howden-Chapman, 1996), an outcome which was not reported by the majority of the MRR-funded researchers. However, the translation of research findings to a patient-oriented level is a complex process, and was not a distinct component of the catalyst program. Despite this, longer-term evaluation, not just of catalyst/seed grants, but of any research grants is needed to better determine the factors contributing to patient-oriented knowledge translation and the barriers faced by researchers (and other stakeholders) in their attempts at such translation.

D. Summary

The overall findings of this report suggest that substantial progress has been made by the five MMR-funded research teams and that program objectives have largely been met. The NPIs each received on average $79,233 for a period of one year. Compared to research projects funded by CIHR's open operating grants program (2010-2011) which received funding for 5 years or more, with the average value of all grants approved for funding in that fiscal year being approximately half a million dollars, the MMR funding values and durations are greatly dwarfed. In this context, it might be said that progress achieved to date (e.g., number of publications, training, collaborations, other outcomes) has been significant considering the limited amount and duration of funding.

Limitations

There are numerous limitations to take into account when considering the findings presented in this report. Primarily, survey research is based on self-reported information and it cannot be determined whether measured outcomes match those occurring in the real world. Further, while the Micro Impact Survey (MIS) is low burden and takes on average only 5-10 minutes to complete, the brevity also means that the reportable outcomes are not as comprehensive or detailed as might be achieved with a longer and more extensive survey. Additionally, some of the terms used in the survey may have been interpreted in different ways depending on the experience and knowledge of the respondent (for example, the term "health professionals" can be interpreted in a number of ways). Finally, outcomes measured by the MIS can be those associated with research projects receiving funding from other grants or financial sources, and thus not necessarily reflecting outcomes related solely to CIHR/IMHA funding opportunities (see Methodology section for more details on the MIS). However, in this case none of the five MMR NPIs reported that funding from another organization enabled the reported research findings.

ACKNOWLEDGEMENTS

Marc Milot developed the Micro Impact Survey tool, carried out the survey, data analysis and wrote this report in collaboration with Phillip Gardiner, and with feedback from IMHA staff: Liz Stirling, Elizabeth Robson, Tanya Gallant, Julie de Courval, and Emily Neff. Also acknowledged is the feedback from IMHA's Performance Evaluation Committee, the Institute Advisory Board, as well as from the IMHA-funded researchers who responded to the survey and to other evaluation-related requests.

REFERENCES

Bero, L. A., Grilli, R., Grimshaw, J. M., Harvey, E., Oxman, A. D., Thomson, M. A. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. British Medical Journal 1998; 317(7156): 465-468

Davis, P., Howden-Chapman, P. Translating Research Findings into Health Policy. Social Science and Medicine 1996; 43(5): 865-872