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Faculteit Geneeskunde en Levenswetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effect of exercise training on satellite cell response within skeletal muscles

Lize Daems
Gilles Nyns

Eerste deel van het scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

PROMOTOR :
Prof. dr. Frank VANDENABEELE

COPROMOTOR :
dr. Anouk AGTEN

BEGELEIDER :
De heer Sjoerd STEVENS

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THE EFFECT OF EXERCISE TRAINING ON SATELLITE CELL RESPONSE WITHIN SKELETAL MUSCLES

Outline

Muscle satellite cells are a population of precursor cells between the plasma membrane of the muscle fiber and the basement membrane with a unique role in muscle repair, maintenance and remodeling in humans and animals. The regeneration and adaptation processes of skeletal muscles when performing exercise training are facilitated by satellite cells. With this review an overview of training interventions and the accompanying satellite cell response is listed.

The most important findings of this literature are the following:

- Satellite cell number and activity increased when performing resistance training. Eccentric strength training is the most common training modality to induce structural damage to investigate the role of satellite cells in skeletal muscle fiber repair. Satellite cells also play an important role in non-hypertrophic stimuli via endurance training.
- When performing strength training, studies show that satellite cell markers Pax7, CD56, NCAM, myogenin and Myf5 cells are up-regulated. Mixed evidence is found about the increase of MyoD.
- When performing endurance training, a highly significant positive correlation was found between the number of Pax7 cells and VO_2max. No or a small change is found in MyoD and mixed evidence is found about myogenin.
- Myofiber type-related differences are found in the satellite cell response to exercise in type I, type II and mixed muscles.

Gilles Nyns

Lize Daems

Promotor: Prof. dr. Frank Vandenabeele, MD, PhD

Copromotor: dr. Anouk Agten, PhD, Mr. Sjoerd Stevens

Context of the master thesis

This master thesis fits in the research domain of the micro-biological component of exercise physiology integrated into physical therapy. The subject of this thesis is 'the satellite cell' also called 'muscle stem cell' and the influence of training interventions on these cells are investigated. Satellite cells play a vital role in muscle fiber regeneration. This research field is directed to a diverse population: healthy adults, children, elderly and in pathological conditions such as Multiple Sclerosis, Duchenne muscular dystrophy, etc. Satellite cell response in a healthy population is described in this review. Satellite cells are studied by sampling muscle biopsies. Biopsies are then immuno-stained with markers under immunofluorescence microscopy. The main protein markers considered to play a role in the process of satellite cell activation, proliferation, and/or differentiation are investigated in this literature study.

The literature search was based on the following research question: "What is the effect of training on the satellite cell response within skeletal muscles?". This research question was further specified to: "What is the effect of resistance training in comparison to no - or other training interventions on the activation, proliferation and differentiation (early and late phase) of satellite cells within skeletal muscle fibers (fast - and slow twitch) in healthy individuals?".

Part 1 of the master thesis is a literature study, that runs during the course of the first master year, performed at the University of Hasselt under the supervision of PhD Frank Vandenabeele, Dr. Anouk Agten and Mr. Sjoerd Stevens, at the Rehabilitation Research Center REVAL of UHasselt in Diepenbeek.
For this literature review, the final research question and literature search strategy were developed in co-operation with PhD Frank Vandenabeele, Dr. Anouk Agten and Mr. Sjoerd Stevens.
This master thesis is part of a broader research project, a doctoral study led by Mr. Sjoerd Stevens.

For this thesis the central format was applied.

This thesis was a dual master thesis.

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PART 1: OVERVIEW OF THE LITERATURE

1. Abstract

Background: Adult skeletal muscle has an enormous capacity to regenerate after injury. This capacity is accomplished by muscle satellite cells which were discovered 57 years ago. Satellite cells are in a quiescent state and upon stimuli they become activated and begin to proliferate and fuse to myoblasts and myocytes to form or repair myofibers. In addition, they are able to self-renew and replenish the stem cell pool. Every phase of satellite cell activity is orchestrated by many molecules and signalling pathways. This review gives an overview of the crucial points that could be modulated to extract the optimal response from these satellite cells in exercise training.

Method: Literature review, used databases: Web of Science and PubMed.

- Web of Science: (TI="satellite cell*" OR TI="Stem cell*" OR TI="muscle stem cell*") AND (TI="training" OR TI="resistance training" OR TI="exercise training" OR TI="power training*" OR TI="exercise") NOT (TI="animal*" OR TI="mice*" OR TI="mouse*"). The search resulted in 302 hits.
- PubMed: 3 main categories were put together, first 'satellite cells and derivatives', secondly 'resistance training and derivatives' and thirdly 'skeletal muscles and derivatives'. The AND-Boolean operator combined these categories. After activated filter 'humans', the search resulted in 195 hits.

Results: Further analysis of these articles resulted in 18 studies, 12 articles describe resistance training and 6 endurance exercise. Satellite cell number and activity increased significantly from pre- to post exercise intervention after 24 hours. When performing strength training, Pax7, CD56, NCAM, myogenin and Myf5 cells are up-regulated. Inconclusive evidence for an increase of MyoD. When performing endurance training, a highly significant positive correlation was found between the number of Pax7 cells and VO2max. No or a small change is found in MyoD and mixed evidence is found about myogenin.

Discussion and conclusion: After both endurance and resistance training the satellite cell response was significantly increased. When expressed in a fiber-type specific manner: resistance training increased the number of satellite cells per type II muscle fibers significantly after 24 hours recovery. Endurance training had a greater effect on type I muscle fibers. In the future more research is needed on different pathologies and the effect of different training modalities on the satellite cell response within these pathologies to make a possible link for clinical application.

Aim of the research: To describe the satellite cell response in particular the number of satellite cells after exercise in a healthy adult population.

Operationalization research question: This master thesis is part of a doctoral program at the rehabilitation research centre REVAL of UHasselt in Diepenbeek. This study is under supervision of Prof. dr. Frank Vandenabeele, MD, PhD as promotor and dr. Anouk Agten, PhD, Mr. Sjoerd Stevens as copromotors.

Keywords: Satellite cells, muscle stem cells, skeletal muscle, resistance training, endurance training, exercise therapy, types I/IIa/IIx muscle fibers

2. Introduction

Satellite cells are the stem cells in skeletal muscles and were first described by Alexander Mauro in 1961 in frog and rat muscles. The skeletal muscle satellite cell was named after its anatomical location between the plasma membrane of the muscle fiber and the basement membrane (Mauro, 1961). Satellite cells play an important role in muscle fiber repair and regeneration under normal physiological (Parise, McKinnell, & Rudnicki, 2008) and pathological conditions (Murphy, Lawson, Mathew, Hutcheson, & Kardon, 2011). Both conditions can give stimuli that cause the activation, proliferation, early differentiation of the satellite cells to myoblasts, then to myocytes and in the late differentiation to myofibers (Almeida, Fernandes, Ribeiro Junior, Keith Okamoto, & Vainzof, 2016). By this mechanism muscle satellite cells can either donate their nuclei to already existing muscle fibers or congregate to repair or form new myofibers (Yin, Price, & Rudnicki, 2013). This process is triggered by an inflammatory response secondary to myofiber damage. Even though satellite cells donate their nuclei or congregate to form new fibers, the total number of satellite cells remains equal through multiple rounds of regeneration (Wang & Rudnicki, 2011). This equilibrium is maintained due to the ability of satellite cells to renew themselves, giving progeny for differentiation while retaining uncommitted mother cells (Collins et al., 2005). Satellite cells are located in a specialized local environment called the muscle satellite cell niche. Self-renewal, activation, proliferation and differentiation are regulated by extrinsic factors in this niche. The processes mentioned above involves a complex interplay between growth factors, cytokines, adhesion molecules and extracellular matrix (ECM) (Bentzinger, Wang, Dumont, & Rudnicki, 2013; Cermak et al., 2013; Wernbom et al., 2013).

Satellite cells can be identified by markers which can be seen using immunofluorescent microscopy (Petrella, Kim, Mayhew, Cross, & Bamman, 2008). A characteristic of human satellite cells is their expression of the Pax7 gene (Bellamy et al., 2014; Cermak et al., 2013; Farup, Rahbek, Knudsen, et al., 2014; Farup, Rahbek, Riis, et al., 2014; Fry et al., 2014; Joanisse et al., 2013; Mackey, 2013; Mackey, Andersen, Frandsen, & Sjogaard, 2011; Mackey, Esmarck, et al., 2007; Mackey, Holm, et al., 2011; Mackey et al., 2014; Mackey et al., 2009; McKay, O'Reilly, Phillips, Tarnopolsky, & Parise, 2008; McKay et al., 2013; McKay, Ogborn, Bellamy, Tarnopolsky, & Parise, 2012; Menon et al., 2012; Nielsen et al., 2012; Snijders et al., 2014; Toth et al., 2011; Walker et al., 2012). This gene is mostly used to identify muscle satellite cells, although others exist such as NCAM and CD56 (Charifi, Kadi, Feasson, & Denis, 2003; Crameri et al., 2007; Crameri et al., 2004; Dreyer, Blanco, Sattler, Schroeder, & Wiswell, 2006; Kadi, Eriksson, Holmner, & Thornell, 1999; Kadi, Johansson, Johansson, Sjostrom, & Henriksson, 2004; Kadi, Schjerling, et al., 2004; Kadi & Thornell, 2000; Lindstrom, Pedrosa-Domellof, & Thornell, 2010; Mackey, Andersen, et al., 2011; Mackey, Esmarck, et al., 2007; Mackey et al., 2014; Mackey et al., 2009; Mackey, Kjaer, et al., 2007; O'Reilly, McKay, Phillips, Tarnopolsky, & Parise, 2008; Petrella, Kim, Cross, Kosek, & Bamman, 2006; Snijders et al., 2014; Verdijk et al., 2014; Verdijk, Snijders, Holloway, J, & LJ, 2016; Verney et al., 2008). Other proteins called myogenic regulatory factors orchestrate the process of satellite cell activation to fusion or congregation. The most important regulatory factors are MyoD, Myf5 and Myogenin. These factors together with Pax7 can be used to determine the phase of myoblast formation.

Research indicates that muscle fiber hypertrophy is associated with a larger amount of satellite cell nuclei in human skeletal muscles (Kadi et al., 2005; Phillips, 2014). The largest increase in the number of satellite cells is possible with high intensity resistance exercise that causes disturbances of proteins in the myofiber (Crameri et al., 2004). Evidence is showing that resistance exercises is not the only training tool to trigger satellite cell expansion. Aerobic training also resulted in an increased satellite cell content (Fry et al., 2014). Exercise-induced expansion of satellite cell pool creates a new vision that is non-pharmacological. This should be considered in therapeutic and rehabilitative strategies aiming to improve skeletal muscle function (Kadi & Ponsot, 2010).

There is not much evidence about the long-term influence of training in satellite cells. There is also mixed evidence if there is a difference in satellite cell pool in types I, IIa and IIx muscle fibers (Babcock et al., 2012; Cermak et al., 2013; Herman-Montemayor, Hikida, & Staron, 2015; Joanisse et al., 2015; Murach et al., 2016; Snijders et al., 2012). Most research is done on mice and there is little evidence of whether the results found on mice are representative for humans. For the time being it is difficult to integrate the satellite cells in a rehabilitation context as a physical therapist. In this literature study we are interested in the satellite cell response to training in healthy adult humans between 18 and 65 years old.

The main objective of this study is to obtain insights on the effect of training on the satellite cell response. To indicate which type of exercise modality has the most effects on satellite cell activation, proliferation, differentiation and the time course of these caused effects. This to optimize rehabilitation in function of muscle hypertrophy and recovery after exercise.

3. Methods

3.1. Research question

This literature study aims to find an answer to the research question: “What is the effect of resistance training in comparison with no - or other training interventions on the activation, proliferation and differentiation (early and late phase) of satellite cells within skeletal muscle fibers (fast - and slow twitch) in healthy individuals?”

In this review the focus was primarily on the acute and chronic effects of resistance training in healthy individuals, between 18-65 years of age. The main outcome is the number of satellite cells, furthermore the effect of training on activation, proliferation and differentiation (early and late phase) of satellite cells is investigated, measured from several hours till days after the intervention. Our second aim is to make the comparison between different types of intervention, so in the future physical therapists can optimize therapeutic intervention to increase the satellite cell response.

PICO:

- P: healthy individuals between 18-65 years old
- I: resistance training
- C: no - or other training interventions (HIT or endurance training)
- O: number, activation, proliferation and differentiation of satellite cells

3.2. Literature search

Search engines PubMed and Web of Science (Web of Knowledge) were consulted for this literature study. To put together the literature search, the research question was split in 3 main categories of the different divisions/branches of this research domain. Each main category was composed of a wide range combination of different keywords and search terms, combined with the OR-Boolean operator. Afterwards the AND-Boolean operator combined the 3 main categories. The initial search contained different options and combinations of synonyms for the main categories. The most suitable and comprehensive search strategy was selected based on the number of hits and the conformity of the content of the articles found. The resulting articles were filtered on humans and animal studies were excluded with the use of a NOT-Boolean operator. This review is based on the search strategy of December 2017.

The following search strategy was applied to the PubMed database:

3.2.1. PubMed

The PubMed search builder was built up from the 3 main categories, first 'satellite cells and derivatives', secondly 'resistance training and derivatives' and thirdly 'skeletal muscles and derivatives'. The AND-Boolean operator combined these categories. An overview of the different search strategies and the exact keywords used for the search builder, can be found in the appendix table 1.

1st category: satellite cells and derivatives

satellite cells, skeletal muscle[MeSH Terms] OR satellite cells[Title/Abstract] OR muscle stem cells[Title/Abstract] OR stem cells[MeSH Terms] OR stem cells[Title/Abstract]

2nd category: resistance training and derivatives

resistance training[MeSH Terms] OR resistance training[Title/Abstract] OR exercise therapy[MeSH Terms] OR exercise therapy[Title/Abstract] OR power training[Title/Abstract] OR exercise training[Title/Abstract] OR exercise[MeSH Terms]) OR training[Title/Abstract]

3rd category: skeletal muscles and derivatives

skeletal muscles[MeSH Terms]) OR fast twitch muscle fiber[MeSH Terms]) OR slow twitch muscle fiber[MeSH Terms]) OR muscle fiber[Title/Abstract]) OR muscle fibre[Title/Abstract]) OR skeletal muscles[Title/Abstract]) OR fast twitch muscle fiber[Title/Abstract]) OR slow twitch muscle fiber[Title/Abstract]) OR fast twitch muscle fibre[Title/Abstract]) OR slow twitch muscle fibre[Title/Abstract]

Combined search builder PubMed:

(((((((satellite cells, skeletal muscle[MeSH Terms]) OR satellite cells[Title/Abstract]) OR muscle stem cells[Title/Abstract]) OR stem cells[MeSH Terms]) OR stem cells[Title/Abstract])) AND (((((((((resistance training[MeSH Terms]) OR resistance training[Title/Abstract]) OR exercise therapy[MeSH Terms]) OR exercise therapy[Title/Abstract]) OR power training[Title/Abstract]) OR exercise training[Title/Abstract]) OR exercise[MeSH Terms]) OR training[Title/Abstract])) AND ((((((((((skeletal muscles[MeSH Terms]) OR fast twitch muscle fiber[MeSH Terms]) OR slow twitch muscle fiber[MeSH Terms]) OR muscle

fiber[Title/Abstract]) OR muscle fibre[Title/Abstract]) OR skeletal muscles[Title/Abstract]) OR fast twitch muscle fiber[Title/Abstract]) OR slow twitch muscle fiber[Title/Abstract]) OR fast twitch muscle fibre[Title/Abstract]) OR slow twitch muscle fibre[Title/Abstract]))

The merger of the three categories resulted in 285 articles on December 2017 and 293 on May 2018, after activated filter 'humans', 195 hits remained on December 2017 and 203 hits on May 2018. No filter used on publication dates, article types or full text availability.

3.2.2. Web of Science

The same research method was applied for the 'Web of Science Core Collection Database' search builder. The first main category 'satellite cells and derivatives' and second main category 'resistance training and derivatives' were combined with the AND-Boolean operator resulting in 321 hits on December 2017 and 331 hits on May 2018. The field tag 'title' was used. A third category 'skeletal muscles and derivatives' was not used since this narrowed the results too strong. Web of Science doesn't have the usage of the filter 'humans'. To substitute for the filter 'humans', animal studies were excluded by composing a new category. This new category combined title field tag search terms (TI="animal*" OR TI="mice*" OR TI="mouse*").

1st category: satellite cells and derivatives

TI="satellite cell*" OR TI="Stem cell*" OR TI="muscle stem cell*"

2nd category: resistance training and derivatives

TI="training" OR TI="resistance training" OR TI="exercise training" OR TI="power training*" OR TI="exercise"

Web of Science advanced search: (Web of Science Core Collection Database)

#10= combined search builder Web of Science:

(TI="satellite cell*" OR TI="Stem cell*" OR TI="muscle stem cell*") *AND* (TI="training" OR TI="resistance training" OR TI="exercise training" OR TI="power training*" OR TI="exercise") *NOT* (TI="animal*" OR TI="mice*" OR TI="mouse*")

After using the NOT-Boolean operator for this category, 302 articles remained on December 2017 and 320 articles on May 2018. The results were not further refined by publication years, Web of Science categories or document types. An overview of the different search strategies and the search builder, can be found in the appendix table 1A and 1B.

3.3. Selection criteria

Articles went through a selection process and were included if the following criteria were met:

- Human population
- Age study participants between 18-65 years old
- Healthy individuals (no pathology and a BMI between 20-25)
- Resistance training or other training interventions (endurance, aerobic, anaerobic and HIT)
- Vastus lateralis skeletal muscle biopsy

- The results section describes at least Pax7 (or CD56/NCAM) or one of the following outcomes: MyoD, Myf5, Myogenin, Myosin heavy chain isoforms I, IIa, IIx and myofiber size/type distribution.

Articles were excluded from further screening if they were found positive for one or more of the following exclusion criteria:

- (Systematic) reviews
- Qualitative research
- Interventions other than resistance, endurance, aerobic, anaerobic and HIT training
- Any form of additional therapy such as medication or supplementation that influences muscle physiology and trophy
- Impaired vascularization (in and around the investigated muscle)
- Muscle pathology or traumatic lesions (other than exercise induced)

3.4. Quality Assessment

To assess the quality of the articles, 'the Dutch Cochrane Centre checklist for a Randomized Controlled Trial (RCT)' or 'The Joanna Briggs Institute checklist for Quasi-Experimental Studies' were used based on the design of the included studies.

3.5. Data-extraction

The main outcome is satellite cell number or satellite cell content, the latter is usually expressed in number satellite cells per fiber or per 100 fibers. Data that contributes to a possible finding about the activation, proliferation and differentiation (early and late phase) of satellite cells, when performing resistance training or other training interventions, is also extracted. Pax7 (or CD56, NCAM), MyoD, Myf5, Myogenin, Myosin heavy chain isoforms I, IIa, IIx and myofiber size/type distribution are included outcomes.

4. Results

4.1. Results study selection

The records identified from the PubMed and Web of Science database, 195 and 302 articles respectively went through a first screening on title and abstract. If the title of the article in question showed that the study could be excluded based on the predetermined criteria or when the content did not match with the topic of this literature study on satellite cell response, the abstract was not further consulted. This was the case when clear statements in the title such as 'protein supplementation', 'stem cell transplantation', 'animal study', 'review', 'obesity' or 'electrical stimulation' were mentioned. Exclusion on title was applied when this was evident.

The abstract was consulted for the majority of the articles. Abstracts of the studies were read and checked by the two authors of this literature study. When the content of the abstract met the inclusion criteria and there was no reason for exclusion, the full text article was assessed for eligibility. The

abstract provided enough information in almost all records. When no abstract was available or when the abstract did not offer sufficient information, the full text was consulted. The article was excluded when no full text was available, this after consulting external search engines and after sending a request for the full-text directly to the author via ResearchGate.

The exclusion criteria and the number of studies that were excluded can be found in table 2A in the appendix. All the articles, with accompanying source, included or excluded plus reason are listed in table 2B in the appendix. The flowchart can be consulted in figure 1.

The articles included in the qualitative synthesis had to meet the following criteria:

- Are the subjects from the study 'healthy humans between 18-65 years old'?

This first question is important since the satellite cell response is a relatively recent research domain and most research has been done on animals. Despite the fact that the search strategy aims to target just humans, the fourth most common reason for exclusion was 'animal study' (n = 64). This literature study focusses only on the satellite cell response in healthy adults (18+) with an upper limit of 65 years. The term 'healthy', excludes roughly all pathologies and focusses on individuals with a normal BMI between 20-25. The aim of only incorporating healthy adults is to ensure that the natural satellite cell response is not disturbed by any pathology or disruption in the metabolic processes. Studies with patient characteristics such as obesity, diabetes, aged, sarcopenia, neurological pathologies, among others were frequently excluded. 'Non-healthy participants' was the fifth most common reason for exclusion (n = 56) followed by 'age participants <18 or >65 years old' (n = 39).

- Does the study investigate the effect of a physical intervention on the satellite cell response in skeletal muscles?

The intention is twofold: first to include only studies with interventions of a physical/bodily nature such as endurance training, (an)aerobic training, HIT training, and strength training, especially the latter is the focus of this literature study. Secondly to exclude other interventions such as medical interventions, medication and/or supplementation that influences muscle physiology and trophy. In many studies the dietary intake is described. However, if one speaks of specific supplementation, additional meals or shakes that exceed the daily protein limits, these studies have been withheld from admission. Another less frequent example is erythropoietin, also known as EPO, and is a performance-enhancing drug. Since this may have a supplementary effect on the natural response and physiology of the muscle or the delivered performance, this is a reason for exclusion. This can be summarized in one denominator 'additional therapy' and this is the number one most common exclusion criteria (n = 125), with 'stem cell therapy' as a very common example.

- Is the satellite cell response (activation, proliferation and early-late phase differentiation) within skeletal muscle fibers (I, IIa, IIx) measured or analysed?

One of the biggest challenges is to get a clear and unambiguous picture of the satellite cell response. It is not possible and simply too confusing to visualize all the markers. The most important outcomes can

also map the different stages, these outcomes are: Pax7 (or CD56, NCAM); MyoD; Myf5; Myogenin; Myosin heavy chain isoforms I, IIa, IIx and/or myofiber size/type distribution. If none of the above outcomes are described, the article is excluded. This makes that 'SC outcome not described' was the third most common exclusion criteria (n = 70). We must note that articles with a content that did not match with the topic of this literature study on satellite cell response likewise fell under this exclusion criteria. Another reason for incorporation under this heading is if the satellite cell response was not directly investigated but indirectly a statement about the response was made based on other outcomes for example growth hormones.

Reviews or systematic reviews were incorporated into a single exclusion criterion '(Sys.) Reviews' and this makes up the second largest exclusion criterion (n = 74). Other less used reasons for exclusion in order of occurrence were: 'Article type' (n = 15) this when no abstract/full text was available or when the article was a commentary or symposium; 'Vascularization impaired' (n = 5) natural or administered; 'Muscle pathology' (n = 2) and 'No vastus lateralis skeletal muscle biopsies' (n = 2), the latter was to facilitate an optimal comparison between the studies.

To summarize briefly, after removing the duplicates from the 195 PubMed and 302 WoS articles, 476 articles remained for screening on title/abstract, 442" articles were excluded, resulting in 34 full-text articles. After assessment for eligibility, 16 more articles were excluded. This literature study is based on the remaining 18 articles.

4.2. Results quality assessment

A detailed overview of the critical appraisal based on the 'Dutch Cochrane Centre checklist for a Randomized Controlled Trial (RCT)' or 'The Joanna Briggs Institute checklist for Quasi-Experimental Studies' can be found respectively in table 3A and 3B in appendix.

Each of the 18 included studies was read by both researchers from this literature study and the checklist was completed after consultation to optimize standardization. To indicate the scoring: if a statement of the accompanying checklist was met, a 1-point score was attributed; if a criterion was not met, or explicitly described or could not be derived from the article, a 0-point value was given. If a statement did not apply, it was removed from the checklist for that given study. In order to make a general report, the scoring points were expressed in percentages. Each included study achieved a percentage of 50 or more.

The overall quality of the included studies is rather low. This is partly due to a low sample size (on average 8 participants). Mainly male students were recruited, hence the age of the subjects was between 20 and 31 years. The examined patient population is young and not representative for an adult population between 18 and 65 years old. This has an influence on the generalizability of the results. One study shows middle aged subjects around 56 years (Murach et al., 2016). From the 18 included

full-text articles, 3 studies are randomized controlled trials (RCT's) and 15 studies have a quasi-experimental design, with-or without a control group with pre- and post-test.

The quasi-experimental studies are discussed first. Five out of the 15 quasi-experimental studies contained a control group (either an external no-intervention control group or a within-participant contralateral no-intervention leg). This is important for a more accurate interpretation of the used intervention and the accompanying satellite cell response.
Follow-up or loss to follow-up was not explicitly mentioned in most studies, almost no article contained a flow chart, but the number of patients examined could often be recovered in the results, therefore it could be concluded if follow-up was completed or not. In seven studies follow-up or loss to follow-up was not mentioned and could not be distracted from either methods, results or discussion. In all 15 studies there was no mentioning about the reliability of the measurements including inter-rater and intra-rater reliability. Appropriate statistical analysis was used in all included articles.

Next are the randomized controlled trials. In all three RCT's allocation was randomized. Randomization methods were not mentioned. There was little to no information in the studies to determine whether the subjects were aware of the randomization sequence. Blinding was not mentioned in all three studies. In one of the three studies it was explicitly mentioned that the effect assessors (the researchers who described satellite cells with immunofluorescent microscopy) were blinded for treatment. In the other two studies there was too little information to answer this question. Reliability of the measurements, including inter-rater and intra-rater reliability, was not mentioned. Follow-up was available for all three RCT's. Appropriate statistical analysis was used.

In general strengths and limitations were not discussed in any of the included studies. A common bias was the volunteer bias, whereby patients volunteered to participate in a study.

4.3. Results data-extraction

Table 5 shows the data-extraction overview, describing: aims of the study, sample size, included mean age, fitness level, sex, interventions, outcomes, results and conclusion of the included articles.

The target **population** was between 18-65 years old. Within the included studies, mostly young male adults were recruited between 20 and 31 years old. One study shows a female middle-aged population of 56 ± 5 years old (Murach et al., 2016). A small (n = ± 8) sample size was present in most studies with a population ranging from 5 (Kadi, Johansson, et al., 2004) to 34 (Herman-Montemayor et al., 2015) participants. All participants had a BMI of 25 or less. Participants were mainly moderate or recreationally active. There is an all-male patient population in 13 out of the 18 included studies. Two articles describe a mixed male-female patient population (Joanisse et al., 2015; Kadi, Johansson, et al., 2004) and 2 studies included an all-female population of untrained, inactive or sedentary women (Herman-Montemayor et al., 2015; Murach et al., 2016).

Twelve out of the 18 included studies describe a resistance training **intervention**, with intervention intensities going from 40% 1RM (Herman-Montemayor et al., 2015) to 85% 1RM (Wilborn, Taylor, Greenwood, Kreider, & Willoughby, 2009) or a maximal isokinetic, eccentric muscle-damaging exercise protocol was performed (Cermak et al., 2013; Crameri et al., 2004; Hyldahl, Olson, Welling, Groscost, & Parcell, 2014; McKay et al., 2008; O'Reilly et al., 2008; Toth et al., 2011) using the Biodex dynamometer (Biodex Medical Systems, Inc., Shirley, NY, USA).
Six out of the 18 included studies discuss endurance training, 3 have a continuous training protocol going from a 45 to 90-minute training duration at 60-65% VO_2max intensity (Babcock et al., 2012; Joanisse et al., 2015; Murach et al., 2016). The remaining 3 articles describe interval training with larger variations in the training intensities. An overview from the protocols can be found in table 5 in the appendix.

The **aim of the study** was to investigate the satellite cell response after resistance training in comparison with endurance or no training intervention.

Outcome measures and **results**. For this literature study the main outcome measure is the number of satellite cells expressed in number satellite cells (SC's) per fiber or per 100 fibers, the specified name 'satellite cell content' is applicable. The satellite cell number for resistance training can be found in table 6A and for endurance training in table 6B, in appendix. Primary outcome measures are Pax7 (or CD56 / NCAM); MyoD; Myf5; Myosin; heavy chain isoforms I, IIa, IIx; these are described below.
When type of training and its influence on satellite cells in the results was assessed, the main outcome was that resistance type exercise training provides muscle hypertrophy that is associated with a larger satellite cell content (Babcock et al., 2012; Cermak et al., 2013; Crameri et al., 2004; Hanssen et al., 2013; Herman-Montemayor et al., 2015; Hyldahl et al., 2014; Kadi, Schjerling, et al., 2004; Mackey, Holm, et al., 2011; McKay et al., 2008; O'Reilly et al., 2008; Toth et al., 2011; Wilborn et al., 2009). Eccentric but not concentric muscle contractions resulted in functional and histological evidence of muscle damage that is accompanied by increased satellite cell activity post-exercise in men (Cermak et al., 2013; Crameri et al., 2004; Hyldahl et al., 2014; McKay et al., 2008; O'Reilly et al., 2008; Toth et al., 2011). Satellite cells play an important role in non-hypertrophic stimuli. Six weeks of sprint interval training or moderate intensity continuous exercise did not result in an increase in the number of satellite cells in type I and II fibers in untrained healthy men and women. However, there was an increase in activated and differentiated satellite cells after six weeks of training (Joanisse et al., 2015).
Satellite cells have been shown to respond differently during post-exercise recovery depending on the muscle fiber type in which they are located. For mixed muscles, the number of satellite cells per muscle fiber did not change after 24 hours of recovery ($P = 0.15$) (Cermak et al., 2013).
Satellite cell content was expressed in a fiber type–specific manner, the number of satellite cells per type II muscle fiber increased significantly after 24 hours of recovery ($P < 0.05$), whereas no changes in type I muscle fiber satellite cell content were observed (Cermak et al., 2013). In contrast for the resistance training group, satellite cell content was significantly higher in type I compared with type II muscle fibers (Babcock et al., 2012; Snijders et al., 2012). The satellite cell density increased by 32%

(P < 0.05) in all fibers (Murach et al., 2016). This was also found in (Herman-Montemayor et al., 2015) where the satellite cell content increased in all fiber types (I, IIa and IIx) in traditional strength group and for only the fast subtype IIx in slow speed group. After endurance training the satellite cell density increased by 50% for the myo-heavy chain type I fibers (P < 0.05) but satellite cell density for the myo-heavy chain type II did not significantly change with acute resistance exercise or endurance training (Murach et al., 2016). No increase was found in the number of satellite cells after six weeks of training associated with either type I fibers in low-volume high-intensity sprint interval training (SIT-2) and moderate intensity continuous training (MICT) (P > 0.05) or type II fibers in SIT-2 and MICT (P > 0.05) (Joanisse et al., 2015).

When performing strength training, studies show that Pax7 is up-regulated. Following 300 eccentric contractions, Pax7+ cells increased 26.6% after 24 hours and Pax7+ cells per 100 myofibers increased from 15.5 at pre- to 19.6 (P < 0.05) 24 hours post-exercise (Toth et al., 2011). The same pattern is seen in (Hyldahl et al., 2014) were a significant effect of time (p = 0.028), but not mode or the time x mode interaction was found pre- to post-exercise in the eccentric group but not in the concentric group. When satellite cells were stained with CD56+ in resistance training studies, a time effect was found (Hanssen et al., 2013; Herman-Montemayor et al., 2015; Kadi, Schjerling, et al., 2004; Mackey, Holm, et al., 2011). A relative increase was found in satellite cell number post-training for the proportion of CD56+ cells (P = 0.117), CD56+ cells/fiber (P = 0.151) and CD56+ cells/mm^2 (P = 0.190). (Mackey, Holm, et al., 2011). Satellite cell content described by CD56+ increased by 19.3% at 30 days of training (P = 0.02) and significantly by 31.4% at 90 days of training (P = 0.0003). When pre-training satellite cell values are taken as a reference, the number of satellite cells remained statistically elevated at 3 (P = 0.003), 10 (P = 0.0001) and 60 (P = 0.02) days of detraining (Kadi, Schjerling, et al., 2004). Significant between-group differences were found, where post-training % satellite cells in traditional strength exceeded that of each other group. There was a significant main effect of group, training effect, and group by time interaction. Post-training satellite cell frequency in traditional strength was significantly greater than slow speed, traditional muscular endurance and non-training group. Traditional strength also showed significant within-group training-induced increases in both % satellite cells and satellite cell frequency for each fiber type (Herman-Montemayor et al., 2015). When describing NCAM, a significant increase was found (Crameri et al., 2004; O'Reilly et al., 2008). 24 hours after the training intervention an increase of 36% was found and after 72 hours an 80% increase. The increase in NCAM (% total myonuclei) peaked at 72 hours post-training, which was significantly higher than pre-, 4 hours, and 24 hours after the training intervention. NCAM expressed per 100 myofibers followed a similar trend by peaking at 72 hours post-exercise (P < 0.001). NCAM (per 100 myofibers) was elevated above baseline at 24 hours, 72 hours, and 120 hours (P < 0.001). At 4 hours, NCAM (%myonuclei or per 100 myofibers) was not different from pre-values (P = 0.99) (O'Reilly et al., 2008). A significant increase in cells positive for NCAM in the exercised leg was found on days 4 and 8 after exercise (P < 0.05) (Crameri et al., 2004).

When performing endurance training a significant increase of Pax7 was found (Joanisse et al., 2015; Macaluso, Brooks, Niesler, & Myburgh, 2013; Macaluso et al., 2012). A highly significant positive correlation (P = 0.009) was found between the number of Pax7+ cells per fiber and VO_2max (Macaluso et al., 2012). The number of Pax7 satellite cells per myofiber increased by a mean of 26% (P = 0.005)

after a week of recovery, this related to the baseline VO_2max, whether satellite cell number was expressed as Pax7 cells per fiber (P = 0.032) or as Pax7 cells relative to total nuclei (P = 0.011). Baseline VO_2max also correlated with the percentage change in satellite cells, whether calculated for the percent change in Pax7 cells per fiber (P = 0.037) or the percent change in Pax7 cells relative to total nuclei (P = 0.043) (Macaluso et al., 2013).

The myogenic regulatory factor MyoD per myofiber increased after exercise (Hyldahl et al., 2014; McKay et al., 2008; Wilborn et al., 2009). When performing eccentric exercises, a larger increase was found (Hyldahl et al., 2014; McKay et al., 2008). Contrary according to the following studies, MyoD did not change after strength exercises (Hanssen et al., 2013; Snijders et al., 2012). Also, in aerobic training studies there was no or a small change in MyoD (Kadi, Johansson, et al., 2004; Macaluso et al., 2013). Myf5 was up-regulated or tended to increase over time in a strength training protocol (McKay et al., 2008; Snijders et al., 2012; Toth et al., 2011; Wilborn et al., 2009) or combined with aerobic (Snijders et al., 2012). An increase of myogenin was observed in myonuclei of human muscle fibers in the endurance training leg and no increase in the resting leg (Kadi, Johansson, et al., 2004). (Macaluso et al., 2013; Macaluso et al., 2012) found the opposite pattern where there was no increase in myogenin when performing endurance training. Significant main effects over time were found (P = 0.001) for myogenin when performing strength training (Wilborn et al., 2009) and stays up-regulated after 24 hours (McKay et al., 2008; Toth et al., 2011).

5. Discussion

5.1. Reflection on the quality of the included studies

As mentioned above, the quality of each study has been determined depending on the type of article (RCT or Quasi-Experimental) with accompanying checklist ‘Dutch Cochrane Centre Checklist for a Randomized Controlled Trial’ and the ‘Joanna Briggs Institute checklist for Quasi-Experimental Studies’. (Appendix table 3A and 3B).

In general, the quality of the included studies is sufficient but rather low, as each article received a correspondingly calculated percentage of 50 or more, this could be seen as successful. However, there are also shortcomings in the included articles. For example the lack of information on some crucial aspects about validity, assessors, blinding, follow-up, adherence and or compliance in long-term studies. Muscle biopsy sampling, experimental protocol, exercise protocol and immunohistochemical analysis are well described parts in the included articles. Still, this information is incomplete if it is unknown whether the accessors had the adequate knowledge and training to apply the interventions mentioned above, if it was the same person for all participants and on which manner it was established. Precisely this information has not been described and could not be derived from the text. As a result, all articles scored a ‘not mentioned’, this is equal to a 0-point score, on the statement 'Were outcomes measured in a reliable way?' from the ‘Joanna Briggs Institute checklist for Quasi-Experimental Studies’. The randomized controlled trials also got a 0-point value as too little information was available to answer the question ‘Were the effect assessors blinded for treatment?’ from the ‘Dutch Cochrane Centre checklist

for an RCT'. This meant that a maximum score was no longer obtainable and the highest percentage achieved was 89.

The limited number of participants (n = ± 8) per intervention may be due to the nature of the measurement methods. Vastus lateralis skeletal muscle biopsies samples were taken 2-5 cm deep to the fascia, using the percutaneous needle biopsy technique under local anaesthesia. Since there was a baseline measurement and on average 2-3 days follow-up, samples were taken in a number of studies. This meant that in a short period of time a number of muscle biopsies must be taken, correctly stored and further processed into small slices for immunohistochemical staining and histological quantification. It is plausible that the muscle biopsy intervention is less pleasant for the participants. Another weakness is the generalizability, with a young and mainly male population described in the included studies, we cannot translate these obtained results with certainty to the originally intended population of healthy adults between 18 - 65 years old. In a number of studies there is a volunteer bias because mostly young people participated voluntarily in the studies. Furthermore, we must also be vigilant for a selective publication bias, as this is a recent research domain and perhaps only studies are published where a noticeable satellite cell response occurred. However, it must be said that these recent studies on humans are established after extensive research and knowledge of the satellite cell response on animal models.

Little information from the obtained articles was available on blinding, as discussed above. Blinding of patients and therapists was not possible due to the nature of the interventions. It seems acceptable that there was no effect on the outcomes even without blinding for patients or therapists, as long as effect assessors were blinded, since it is a cellular response under physiological conditions.

5.2. Reflection on the findings in function of the research question

Transcription factor and markers

Both pax7 and NCAM/CD56 are reliable and frequently used markers to identify satellite cells in human skeletal muscles, however studies show that there may be small fluctuations in their degree of identification. It is found that NCAM/CD56 can better perceive late-phase differentiating satellite cells (Snijders et al., 2015). Overall NCAM shows a (± 5%) higher percentage of satellite cell position expression in comparison to Pax7 (Lindstrom et al., 2010; Mackey et al., 2009).This has not been taken into account when describing the results.

There is mixed evidence about MyoD cell activity whether there is an accumulation of cells positive for MyoD when performing strength training or endurance training. This can be due to the fact that the satellite cells within the size pool are progenitors rather than a combination of progenitors and committed muscle precursor cells (Macaluso et al., 2013).

Training intervention SC response

In the present literature study, increased satellite cell activity and number when performing resistance training was found. Resistance training causes fiber damage and results in hypertrophy of the muscle which stimulates an inflammatory response and repair of the damaged muscle by forming new

myofibrils. In the included studies of this review, eccentric strength training is the most common training modality. Previous studies show that a single bout of maximal muscle damage by eccentric exercise is the way to cause structural damage so that muscle fiber repair can take place, and satellite cells can play their part (Lepper, Partridge, & Fan, 2011; Murphy et al., 2011). Heavy load isolated eccentric muscle contractions have been shown to be the biggest stimulator for muscle damage and is it is known that this activates the satellite cells more than concentric contractions. Also the availability of satellite cells in untrained muscles can be an important determinant of hypertrophic potential (Petrella et al., 2008). Also (Macaluso et al., 2012) showed that lower VO_2max baseline values were associated with a larger increase in satellite cells, this indicates that poor aerobic ability may have a greater acute effect on proliferation of satellite cells for example in sedentary people. This can be projected to an aged population or sedentary people, where exercise prescriptions should be applied to find a balance in muscle generation and degeneration with the aim of gaining more muscle mass.
The findings from the included articles in this literature study partly agree with previous reports. Exercise duration and intensity are important parameters that affect the satellite cell response in endurance training. Satellite cell content has shown to increase after 40-155 minutes of moderate to high intensity training (Parise et al., 2008). Another previous report affirmed that an increase in satellite cell content correlates more to the intensity than the duration of the intervention (Kurosaka, Naito, Ogura, Machida, & Katamoto, 2012).

Fiber type SC response

The study design in all studies is constructed in such a way that different muscle biopsies per individual have to be taken, this on the same leg, within the same muscle, at a standardized distance, what makes it difficult. Myofiber type-related differences exist in the satellite cell response to exercise. Satellite cells are more present in type I muscle fibers than in type 2, this means that type I muscle fibers have a lesser degree of adaptive potential (Babcock et al., 2012; Snijders et al., 2012). In contrast, (Cermak et al., 2013) revealed a greater satellite cell content in type II fibers. This process seems logical because type II has a greater contribution to muscle mass hypertrophy and higher responsiveness to resistance training.

Time course

The results obtained from this literature study are in the same trend and add strength to previous research (McKay et al., 2012) that states that there is a significant increase in the number of satellite cells and satellite cell content at 24 and 48 hours after one bout of eccentric resistance training. The increased satellite cell number becomes perceptible at 24h and peaks at 72h post-exercise recovery, on average it can be presumed that higher-force eccentric exercise is associated with a more fiber-type specific response for type II muscle fibers (Friden, Sjostrom, & Ekblom, 1983; Nardone, Romano, & Schieppati, 1989; Nardone & Schieppati, 1988; Vijayan, Thompson, Norenberg, Fitts, & Riley, 2001). Time course studies in human muscle show an expansion of the satellite cell content from 24- 72h post-exercise for up to 8 days (Crameri et al., 2004).

5.3. Reflection on the strengths and weaknesses of the literature study

Table 4 contains a detailed overview of the limitations and strengths of the included articles. The overall limitation is that the majority of the included studies are 'Quasi-Experimental' studies hence have a lower level of evidence. The low sample sizes are a limitation of the studies that may be caused by the study design. As a result, the studies have a reduced scientific power. The study design consisted of muscle biopsies in combination with strength, endurance training or a combination. Muscle biopsies were removed from the upper leg and an incision had to be made. This creates a small scar and that can deter people, especially women. In half of the studies there is a volunteer bias in which there is only a subset of the population, mostly young men who volunteered to participate in the study. Within the included studies mostly a male population, between 20-31 years old, participated with the exception of three studies (Herman-Montemayor et al., 2015; Joanisse et al., 2015; Murach et al., 2016) in which two studies included only women and one study in which there was an unevenly distributed mix between men (n = 16) and women (n = 3). This makes it difficult to generalize the results in this review to women and also to other age categories such as 40-65 years. Follow-up is not mentioned in most studies except for three studies (Hanssen et al., 2013; Herman-Montemayor et al., 2015; Hyldahl et al., 2014) where it was clearly described how many participants dropped out from the studies and the reasons why. Limitations and strengths are often not mentioned except for three studies (Hyldahl et al., 2014; Macaluso et al., 2013; Mackey, Andersen, et al., 2011) where limitations are discussed. A selection bias has been found in which a certain group (young men) is sampled in such a way that proper randomization is not achieved and therefore the sample is not representative.

A strength of the included articles is the standardized approach and tools such as Biodex, VO_2max and 1-RM to determine muscle strength and cardiorespiratory fitness and to set up and execute the training program. Another common strength is familiarization with the trainings protocol, this ensures that the participants are well prepared and know what to do, this may also prevent a possible learning bias.

5.4. Recommendations for further research

To increase the quality for further research, and to make a smoother transition to clinical practice following recommendations are made. In general, an RCT study design has a higher quality. To increase generalization, the patient population should be widened with participants of both sexes and all age groups between 18-65 years old. With a larger sample size, for example a minimum of 20 participants per intervention group, the statistical power also magnifies. Each intervention group should randomly be assembled. To get a correct and complete representation follow-up and adherence must be described. Based on the knowledge gained so far, it is best to opt for a baseline measurement and post-measurements at 24h, (48h,) 72h, 96h of recovery. To examine the effect for a longer time period, an additional post measurement after 10 days or 2 weeks of recovery could add new insights. All measurements should be taken by independent, trained and experienced effect assessors, who are blinded for the interventions.

In terms of intervention there are several options. Exercise protocols can consist of resistance training or endurance training. For resistance training, eccentric muscle work is preferred, a muscle-damaging exercise protocol has been developed, where unilateral eccentric contractions (180 deg s^{-1}) of the knee

extensors are performed with the use of a Biodex. For endurance training, higher intensities generate a larger satellite cell response, so the exercise protocol could consist of a high-intensity exercise training with intensities going up to 80-90% VO_2max. Training duration preferably exceeds 30 minutes.
Outcome measurements should at least describe satellite cell count and content. This data should also be available for the fiber-specific response. Furthermore, a description of activation, proliferation and differentiation could be made possible if following markers are investigated Pax7 (or CD56/NCAM); MyoD; Myf5 and Myogenin.
If more studies are available of higher quality, the next step may be that pathologies are included.
It would be interesting to investigate for a possible difference in satellite cell response between a healthy individual and for example a person with Multiple Sclerosis or another muscular disorder or a chronic pain patient. As mentioned above, satellite cell response is a fairly new research domain, but more and more research is being published and the quality is certainly increasing. It is known that satellite cells play an important role in the inflammatory response by release factors that attracted macrophages and monocytes (Chazaud et al., 2003). This could indicate that activated satellite cells in an injury or a pathological context could signal for the rapid, early invasion of macrophages and monocytes and promote recovery faster (Tidball, 2005). It is also known that satellite cells decrease in numbers with aging, sarcopenia and diseases such as muscular dystrophy (Bazgir, Fathi, Rezazadeh Valojerdi, Mozdziak, & Asgari, 2017; Snijders et al., 2015). Physical therapists can give the most adapted physiological stimuli such as resistance training and endurance training that will initiate compensatory adjustments in the inflammatory process and the satellite cell response, by increasing the satellite cell number or by suppressing the age-related reduction in satellite cell content. The knowledge about satellite cell research is growing and hopefully the insights of the satellite cell response can provide an added value in the future.

6. Conclusions

This literature review was based on 18 articles (RCT and Quasi-Experimental study design). Results show that for a healthy and young adult patient population satellite cell response increases significantly from pre- to post exercise intervention after 24 hours. When type of training and its influence on satellite cells was assessed in the results, the main outcome was that resistance training provided muscle hypertrophy with an accompanying larger satellite cell content. Eccentric training leads to more muscle damage and therefore an increased satellite cell activity post-exercise was established. Satellite cell content when expressed in a fiber type–specific manner, the number of satellite cells per type II muscle fibers increased significantly after 24 hours of recovery, whereas no changes in type I muscle fibers satellite cell content were observed. After endurance training the majority of articles show that the satellite cell density increased significantly for a mixed-fiber type and up to 50% for type I muscle fibers but satellite cell density did not significantly change for the myo-heavy chain type II fibers. When performing strength training, studies show that Pax7 is up-regulated. Both eccentric resistance training and endurance training show an increase in satellite cell activation, as described above, each of these training modalities have an accompanying fiber-type specific increase in satellite cell content. At this time, it's premature to make a statement about which training modality has a greater increase in satellite

cell response due to insufficient data and the difficulty to compare the outcomes. But it is clear that higher intensities cause more muscle damage and therefore a greater increase of satellite cell activation is associated as a natural response under these physiological conditions.

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Yin, H., Price, F., & Rudnicki, M. A. (2013). Satellite cells and the muscle stem cell niche. *Physiol Rev, 93*(1), 23-67. doi:10.1152/physrev.00043.2011

8. Appendix

Table 1A: Overview of the number of hits for different combinations of search terms in PubMed

	Search Builder PubMed	Hits 12/2017	Hits 05/2018
#1.1	satellite cells, skeletal muscle[MeSH Terms] OR satellite cells[Title/Abstract] OR muscle stem cells[Title/Abstract]	4 871	4975
#1.2	satellite cells, skeletal muscle[MeSH Terms] OR satellite cells[Title/Abstract] OR muscle stem cells[Title/Abstract] OR stem cells[MeSH Terms] OR stem cells[Title/Abstract]	235 428	240 289
#2.1	resistance training[MeSH Terms] OR resistance training[Title/Abstract] OR exercise therapy[MeSH Terms] OR exercise therapy[Title/Abstract]	45 183	46 308
#2.2	resistance training[MeSH Terms] OR resistance training[Title/Abstract] OR exercise therapy[MeSH Terms] OR exercise therapy[Title/Abstract] OR power training[Title/Abstract] OR exercise training[Title/Abstract] OR exercise[MeSH Terms]) OR training[Title/Abstract]	482 141	492 606
#3	skeletal muscles[MeSH Terms] OR fast twitch muscle fiber[MeSH Terms] OR slow twitch muscle fiber[MeSH Terms] OR muscle fiber[Title/Abstract] OR muscle fibre[Title/Abstract] OR skeletal muscles[Title/Abstract] OR fast twitch muscle fiber[Title/Abstract] OR slow twitch muscle fiber[Title/Abstract] OR fast twitch muscle fibre[Title/Abstract] OR slow twitch muscle fibre[Title/Abstract]	252 569	255 286
#4	#1.1 AND #2.1	88	93
#5	#1.1 AND #2.1 AND #3	74	76
#6	#1.1 AND #2.2	262	273
#7	#1.1 AND #2.2 AND #3	218	225
#8	#1.2 AND #2.1	166	173
#9	#1.2 AND #2.1AND #3	87	89
#10	#1.2 AND #2.2	903	939
#11	#1.2 AND #2.2 AND #3	285	293

PubMed:
1st category: satellite cells and derivatives
satellite cells, skeletal muscle[MeSH Terms] OR satellite cells[Title/Abstract] OR muscle stem cells[Title/Abstract] OR stem cells[MeSH Terms] OR stem cells[Title/Abstract]

2nd category: resistance training and derivatives
resistance training[MeSH Terms] OR resistance training[Title/Abstract] OR exercise therapy[MeSH Terms] OR exercise therapy[Title/Abstract] OR power training[Title/Abstract] OR exercise training[Title/Abstract] OR exercise[MeSH Terms]) OR training[Title/Abstract]

3rd category: skeletal muscles and derivatives
skeletal muscles[MeSH Terms]) OR fast twitch muscle fiber[MeSH Terms]) OR slow twitch muscle fiber[MeSH Terms]) OR muscle fiber[Title/Abstract]) OR muscle fibre[Title/Abstract]) OR skeletal muscles[Title/Abstract]) OR fast twitch muscle fiber[Title/Abstract]) OR slow twitch muscle

fiber[Title/Abstract]) OR fast twitch muscle fibre[Title/Abstract]) OR slow twitch muscle fibre[Title/Abstract]

#11= Combined search builder PubMed:
(((((((satellite cells, skeletal muscle[MeSH Terms]) OR satellite cells[Title/Abstract]) OR muscle stem cells[Title/Abstract]) OR stem cells[MeSH Terms]) OR stem cells[Title/Abstract])) AND (((((((((resistance training[MeSH Terms]) OR resistance training[Title/Abstract]) OR exercise therapy[MeSH Terms]) OR exercise therapy[Title/Abstract]) OR power training[Title/Abstract]) OR exercise training[Title/Abstract]) OR exercise[MeSH Terms]) OR training[Title/Abstract])) AND ((((((((((skeletal muscles[MeSH Terms]) OR fast twitch muscle fiber[MeSH Terms]) OR slow twitch muscle fiber[MeSH Terms]) OR muscle fiber[Title/Abstract]) OR muscle fibre[Title/Abstract]) OR skeletal muscles[Title/Abstract]) OR fast twitch muscle fiber[Title/Abstract]) OR slow twitch muscle fiber[Title/Abstract]) OR fast twitch muscle fibre[Title/Abstract]) OR slow twitch muscle fibre[Title/Abstract]))

➔ n = 285 hits (12/2017) ➔ filter ‘Humans’: n = 195 hits remain
➔ n = 293 hits (05/2018) ➔ filter ‘Humans’: n = 203 hits remain

Table 1B: Overview of the number of hits for different combinations of search terms in Web of Science

	Advanced search Web of Science	Hits 12/2017	Hits 05/2018
#1.1	TI=“satellite cell*” OR TI="Stem cell*" OR TI="muscle stem cell*"	169 834	173 652
#1.2	TI="satellite cell*" OR TI="skeletal muscle*" OR TO="satellite cell*" OR TI="muscle stem cell*" OR TI="stem cell*"	230 406	234 754
#2.1	TI=“training” OR TI="resistance training" OR TI="exercise training"	175 746	179 304
#2.2	TI=“training” OR TI="resistance training" OR TI="exercise training" OR TI="power training*" OR TI="exercise"	302 340	307 472
#3	TI="skeletal muscle*" OR TI="fast twitch muscle fib*" OR TI="slow twitch muscle fib*" OR TI="muscle fib*"	67 361	67 881
#4	TI=“animal*” OR TI=“mice*” OR TI=“mouse*”	601 826	800 123
#5	#1.1 AND #2.1	111	116
#6	#1.1 AND #2.1 AND TO=”human*”	30	31
#7	#5 NOT #4	109	116
#8	#1.1 AND #2.2	321	331
#9	#1.1 AND #2.2 AND TO=”human*”	67	69
#10	#8 NOT #4	302	320
#11	#1.1 AND #2.2 AND #3	49	49
#12	#1.2 AND #2.1	1 761	1 794
#13	#1.2 AND #2.1 AND TO=”human*”	491	502
#14	#1.2 AND #2.1 AND #3	1 595	1 622

Web of Science:
1st category: satellite cells and derivatives
TI=“satellite cell*” OR TI="Stem cell*" OR TI="muscle stem cell*"

2nd category: resistance training and derivatives
TI=“training” OR TI="resistance training" OR TI="exercise training" OR TI="power training*" OR TI="exercise"

Web of Science advanced search: (Web of Science Core Collection Database)
#10= combined search builder Web of Science:
(TI=“satellite cell*” OR TI="Stem cell*" OR TI="muscle stem cell*")
AND
(TI=“training” OR TI="resistance training" OR TI="exercise training" OR TI="power training*" OR TI="exercise")
NOT
(TI=”animal*” OR TI=”mice*” OR TI=”mouse*”)

➔ n = 302 hits (12/2017)
➔ n = 320 hits (05/2018)

Figure 1: Prisma Flow-Chart

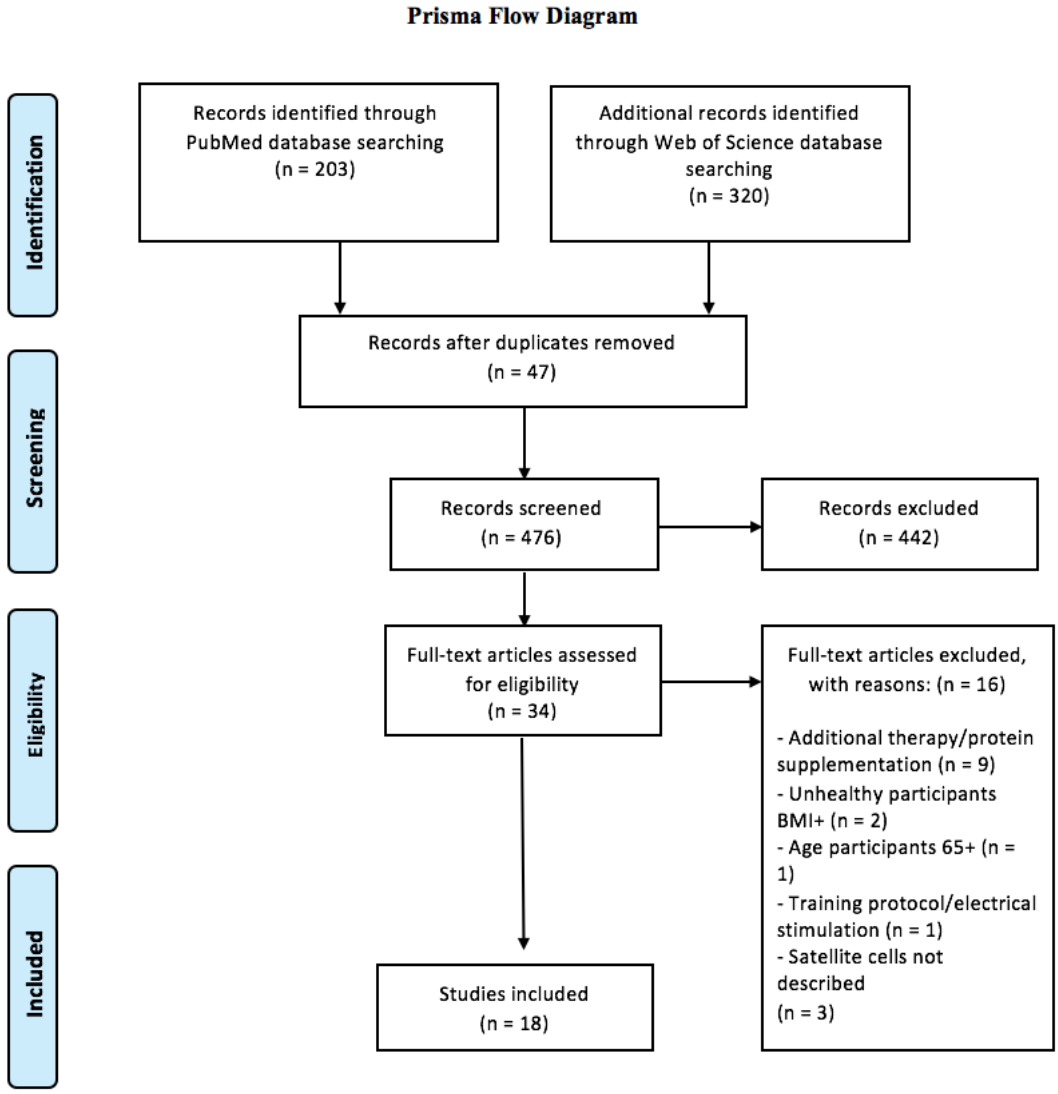

Table 2A: Overview exclusion criteria + number of studies

Exclusion criteria	Number of studies excluded
Additional therapy (Medication and/or supplementation that influences muscle physiology and trophy)	125
(Systematic) review	74
SC outcome not described	70
Animal study	64
Non-healthy participants (pathology or BMI > 25)	56
Age participants (<18 or >65yr.)	39
Article type (commentary, symposium, …, or no abstract/full text available)	15
Training protocol (Interventions other than resistance, endurance, aerobic, anaerobic and HIT training)	6
Vascularization impaired	5
Muscle pathology: traumatic lesions in the muscle (other than exercise induced)	2
No vastus lateralis skeletal muscle biopsies	2

Table 2B: Overview articles, source, included or excluded + reason

Article	Source, included or excluded + reason
Anonym, The impact of voluntary exercise on structure, function and stem cell activation in aging skeletal muscle. (2008). *Faseb Journal, 22*.	Source: WoK Excluded: Age participants
Aagaard, P. (2004). Making muscles "stronger": exercise, nutrition, drugs. *J Musculoskelet Neuronal Interact, 4*(2), 165-174.	Source: PubMed Excluded: Review
Aagaard, P., Jacobsen, M., Jensen, K. Y., Nielsen, J. L., Bulow, J., Rordam, L., . . . Frandsen, U. (2016). Effects of Chronic Blood-Flow Restriction Exercise on Skeletal Muscle Size and Myogenic Satellite Cell Expression. *Medicine and Science in Sports and Exercise, 48*(5), 1032-1033. doi:10.1249/01.mss.0000488106.09083.4f	Source: WoK Excluded: Vascularization impaired
Aagaard, P., Olsen, S., Kadi, F., Tufekovic, G., Verney, J., Olesen, J. L., . . . Kjaer, M. (2006). Changes in Satellite Cell and Myonuclei Number in Human Skeletal Muscle with Resistance Training: Effects of Creatine and Protein Supplementation. *Medicine and Science in Sports and Exercise, 38*(5), S9-S9. doi:10.1249/00005768-200605001-00055	Source: WoK Excluded: Additional therapy
Abreu, P., Mendes, S. V., Ceccatto, V. M., & Hirabara, S. M. (2017). Satellite cell activation induced by aerobic muscle adaptation in response to endurance exercise in humans and rodents. *Life Sci, 170*, 33-40. doi:10.1016/j.lfs.2016.11.016	Source: WoK & PubMed Excluded: Review
Adamakis, I., Vasileiou, I., & Constantinides, C. A. (2013). The treatment of iatrogenic male incontinence: latest results and future perspectives. *Rev Recent Clin Trials, 8*(1), 36-41.	Source: PubMed Excluded: SC outcome not described
Agha, N. H., Baker, F. L., Kunz, H. E., Graff, R., Azadan, R., Dolan, C., . . . Simpson, R. J. (2018). Vigorous exercise mobilizes CD34+hematopoietic stem cells to peripheral blood via the beta(2)-adrenergic receptor. *Brain Behavior and Immunity, 68*, 66-75. doi:10.1016/j.bbi.2017.10.001	Source: WoK Excluded: Additional therapy
Agha, N. H., Baker, F. L., Spielmann, G., Bigley, A. B., & Simpson, R. J. (2016). Can A Single Exercise Bout Increase The Yield Of Hematopoietic Stem Cells From Peripheral Blood? *Medicine and Science in Sports and Exercise, 48*(5), 86-86. doi:10.1249/01.mss.0000485266.85612.e4	Source: WoK Excluded: Article type: (not an article) Commentary
Aguayo, D., Mueller, S. M., Boutellier, U., Auer, M., Jung, H. H., Fluck, M., & Toigo, M. (2016). One bout of vibration exercise with vascular occlusion activates satellite cells. *Experimental Physiology, 101*(2), 295-307. doi:10.1113/ep085330	Source: WoK & PubMed Excluded: Training protocol, Vascularization impaired
Al-Hashem, F. H. (2013). Role of vitamins E and C in mitigating hypoxia- and exhaustive exercise-induced aberrant stem cell factor expression and impaired reproductive function in male Wistar rats. *Saudi Medical Journal, 34*(4), 354-363.	Source: WoK Excluded: Animal study
Alhashem, F., Alkhateeb, M., Alshahrani, M., Elrefaey, H., Alsunaidi, M., Alessa, R., . . . Khalil, M. A. (2014). Exercise protects against obesity induced semen abnormalities via downregulating stem cell factor, upregulating ghrelin and normalizing oxidative stress. *Excli Journal, 13*, 551-572.	Source: WoK Excluded: SC outcome not described
Allouh, M. Z., & Aldirawi, M. H. (2013). Sustanon Administration Induces Satellite Cell Proliferation and Giant Fiber Formation in Growing Skeletal Muscle without Exercise. *Faseb Journal, 27*.	Source: WoK Excluded: Additional therapy
Alway, S. E., & Siu, P. M. (2008). Nuclear apoptosis contributes to sarcopenia. *Exerc Sport Sci Rev, 36*(2), 51-57. doi:10.1097/JES.0b013e318168e9dc	Source: PubMed Excluded: Review
Ambrosio, F., Kadi, F., Lexell, J., Fitzgerald, G. K., Boninger, M. L., & Huard, J. (2009). The effect of muscle loading on skeletal muscle regenerative potential: an update of current research findings relating to aging and neuromuscular pathology. *Am J Phys Med Rehabil, 88*(2), 145-155. doi:10.1097/PHM.0b013e3181951fc5	Source: PubMed Excluded: Review
Antonio, J., & Gonyea, W. J. (1993). Skeletal muscle fiber hyperplasia. *Med Sci Sports Exerc, 25*(12), 1333-1345.	Source: PubMed Excluded: Review
Aoki, A., Murata, M., Asano, T., Ikoma, A., Sasaki, M., Saito, T., . . . Ishikawa, S. E. (2012). Prompt increases in retinol-binding protein 4 and endothelial progenitor cells during acute exercise load in diabetic subjects. *Endocr J, 59*(12), 1085-1091.	Source: PubMed Excluded: Non-healthy participants
Appell, H. J., Forsberg, S., & Hollmann, W. (1988). Satellite cell activation in human skeletal-muscle after training - evidence for muscle-fiber neoformation. *International Journal of Sports Medicine, 9*(4), 297-299. doi:10.1055/s-2007-1025026	Source: WoK & PubMed Excluded: Article type (no abstract or full-text)

Arisi, M. F., Chirico, E. N., Sebeny, R., Muthukumaran, G., Mu, A. B., De Jonghe, B. C., . . . Libonati, J. R. (2017). Myocardial apoptosis and mesenchymal stem cells with acute exercise. *Physiological Reports, 5*(11). doi:10.14814/phy2.13297	Source: WoK Excluded: SC outcome not described
Aufenacker-van Bethlehem, W. J. M. (2011). Training for a paediatric nurse to become a haematopoietic stem cell transplantation paediatric nurse: an important issue in the University Medical Centre Utrecht/Wilhelmina Children's Hospital, Netherlands. *Bone Marrow Transplantation, 46*, S441-S441.	Source: WoK Excluded: Additional therapy
Babcock, L., Escano, M., D'Lugos, A., Todd, K., Murach, K., & Luden, N. (2012). Concurrent aerobic exercise interferes with the satellite cell response to acute resistance exercise. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology, 302*(12), R1458-R1465. doi:10.1152/ajpregu.00035.2012	Source: WoK & PubMed Included
Babcock, L., Escano, M., D'Lugos, A., Todd, K., Murach, K., & Luden, N. (2012). Concurrent Aerobic Exercise Interferes With the Satellite Cell Response to Acute Resistance Exercise in MHC I Muscle Fibers. *Medicine and Science in Sports and Exercise, 44*, 353-353.	Source: WoK Excluded: Article type (not an article: no abstract or full text)
Balck, F., Zimmermann, A., & Neumann, A. (2015). Conception and Associated Evaluation of a Problem-Solving Training (PST) for Patients in the Hospital Context of Hematopoietic Stem Cell Transplantation (HSCT). *Journal of Psychosocial Oncology, 33*(3), 232-249. doi:10.1080/07347332.2015.1019659	Source: WoK Excluded: SC outcome not described
Baldwin, K. M., & Haddad, F. (2010). Research in the exercise sciences: where we are and where do we go from here--Part II. *Exerc Sport Sci Rev, 38*(2), 42-50. doi:10.1097/JES.0b013e3181d49644	Source: PubMed Excluded: SC oucome not described
Bamman, M. M. (2007). Take two NSAIDs and call on your satellite cells in the morning. *J Appl Physiol (1985), 103*(2), 415-416. doi:10.1152/japplphysiol.00536.2007	Source: PubMed Excluded: Additional therapy
Barfield, W. L., Uaesoontrachoon, K., Wu, C. S., Lin, S., Chen, Y., Wang, P. C., . . . Hoffman, E. P. (2014). Eccentric muscle challenge shows osteopontin polymorphism modulation of muscle damage. *Hum Mol Genet, 23*(15), 4043-4050. doi:10.1093/hmg/ddu118	Source: PubMed Excluded: SC outcome not described
Bargi, G., Guclu, M. B., Aribas, Z., Aki, S. Z., & Sucak, G. T. (2016). Inspiratory muscle training in allogeneic hematopoietic stem cell transplantation recipients: a randomized controlled trial. *Supportive Care in Cancer, 24*(2), 647-659. doi:10.1007/s00520-015-2825-3	Source: WoK Excluded: Additional therapy
Bargi, G., Guclu, M. B., Aribas, Z., Camcioglu, B., Karadalli, M. N., Aki, Z. S., . . . Sucak, G. T. (2013). Predictors of functional exercise capacity allogeneic hematopoietic stem cell transplantation recipients. *European Respiratory Journal, 42*.	Source: WoK Excluded: Additional therapy
Bargi, G., Guclu, M. B., Aribas, Z., Sakizli, E., Camcioglu, B., Karadalli, M. N., . . . Sucak, G. T. (2014). Functional exercise capacity, respiratory and peripheral muscle strength, pulmonary functions and dyspnea in allogeneic hematopoietic stem cell transplantation candidates. *European Respiratory Journal, 44*.	Source: WoK Excluded: Additional therapy
Barnett, D., Granger, V., Kraan, J., Whitby, L., Reilly, J. T., Papa, S., . . . European Working Grp Clinical, C. (2000). Reduction of intra- and interlaboratory variation in CD34(+) stem cell enumeration using stable test material, standard protocols and targeted training. *British Journal of Haematology, 108*(4), 784-792. doi:10.1046/j.1365-2141.2000.01932.x	Source: WoK & PubMed Excluded: Training protocol, SC outcome m. vastus lateralis not investigated
Bauer-Wu, S., Carmody, J., Cooley, M., Reed, G., Rosenbaum, E., Whitworth, R., . . . Flowers, C. (2011). A randomized controlled trial of mindfulness training for cancer patients undergoing stem cell transplant. *Annals of Behavioral Medicine, 41*, S241-S241.	Source: WoK Excluded: Non-healthy participants
Baumann, F. T., Kraut, L., Schule, K., Bloch, W., & Fauser, A. A. (2010). A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplantation, 45*(2), 355-362. doi:10.1038/bmt.2009.163	Source: WoK Excluded: Additional therapy
Baumann, F. T., Zopf, E. M., Nykamp, E., Kraut, L., Schule, K., Elter, T., . . . Bloch, W. (2011). Physical activity for patients undergoing an allogeneic hematopoietic stem cell transplantation: benefits of a moderate exercise intervention. *European Journal of Haematology, 87*(2), 148-156. doi:10.1111/j.1600-0609.2011.01640.x	Source: WoK Excluded: Additional therapy

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Wang, J. S., Lee, M. Y., Lien, H. Y., & Weng, T. P. (2014). Hypoxic exercise training improves cardiac/muscular hemodynamics and is associated with modulated circulating progenitor cells in sedentary men. *Int J Cardiol, 170*(3), 315-323. doi:10.1016/j.ijcard.2013.11.005	Source: PubMed Excluded: SC outcome not described
Waring, C. D., Papalambrou, A., Sharp, L., Smith, A. J., Purushothaman, S., Vicinanza, C., . . . Ellison, G. M. (2010). Cardiac Stem Cell Activation and Ensuing Myogenesis and Angiogenesis Contribute to Cardiac Adaptation following Intensity-Controlled Exercise Training. *Circulation, 122*(21).	Source: WoK Excluded: SC outcome not described
Waring, C. D., Papalamprou, A., Purushothaman, S., Smith, A. J., Vicinanza, C., Goldspink, D. F., . . . Ellison, G. M. (2012). Endogenous cardiac stem cell (eCSC) activation, myogenesis and angiogenesis contribute to cardiac remodelling following intensity-controlled exercise training. *Cardiovascular Research, 93*, S16-S16.	Source: WoK Excluded: SC outcome not described
Weis, J., Poppelreuter, M., Mumm, A., & Bartsch, H. (2006). Neuropsychological deficits after haematopoietic stem cell therapy and effects of systematic cognitive training. *Bone Marrow Transplantation, 37*, S59-S59.	Source: WoK Excluded: SC outcome not described
Wens, I., Farup, J., Keytsman, C., Eijnde, B. O., & Dalgas, U. (2015). High intensity training may reverse the fiber type specific decline in myogenic stem cells in multiple sclerosis patients. *Multiple Sclerosis Journal, 21*, 406-407.	Source: WoK Excluded: Non-healthy participants
Wernbom, M., Apro, W., Paulsen, G., Nilsen, T. S., Blomstrand, E., & Raastad, T. (2013). Acute low-load resistance exercise with and without blood flow restriction increased protein signalling and number of satellite cells in human skeletal muscle. *European Journal of Applied Physiology, 113*(12), 2953-2965. doi:10.1007/s00421-013-2733-5	Source: WoK & PubMed Excluded: Vascularization impaired
West, S. L., Gassas, A., Schechter, T., Egeler, R. M., Nathan, P. C., & Wells, G. D. (2014). Exercise Intolerance and the Impact of Physical Activity in Children Treated With Hematopoietic Stem Cell Transplantation. *Pediatric Exercise Science, 26*(3), 358-364. doi:10.1123/pes.2013-0156	Source: WoK Excluded: Additional therapy
Wilborn, C. D., Taylor, L. W., Greenwood, M., Kreider, R. B., & Willoughby, D. S. (2009). Effects of different intensities of resistance exercise on regulators of myogenesis. *J Strength Cond Res, 23*(8), 2179-2187. doi:10.1519/JSC.0b013e3181bab493	Source: PubMed Included
Wilkinson, D. J., Brook, M. S., Smith, K., & Atherton, P. J. (2017). Stable isotope tracers and exercise physiology: past, present and future. *J Physiol, 595*(9), 2873-2882. doi:10.1113/jp272277	Source: PubMed Excluded: SC outcome not described
Willkomm, L., Gehlert, S., Jacko, D., Schiffer, T., & Bloch, W. (2017). p38 MAPK activation and H3K4 trimethylation is decreased by lactate in vitro and high intensity resistance training in human skeletal muscle. *Plos One, 12*(5), e0176609. doi:10.1371/journal.pone.0176609	Source: PubMed Excluded: Additional therapy
Wilson, R. W., Jacobsen, P. B., & Fields, K. K. (2005). Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. *Bone Marrow Transplantation, 35*(7), 721-727. doi:10.1038/sj.bmt.1704815	Source: WoK Excluded: Additional therapy
Wiskemann, J. (2013). Exercise in the setting of hematopoietic stem cell transplantation. *European Review of Aging and Physical Activity, 10*(1), 15-18. doi:10.1007/s11556-012-0116-2	Source: WoK Excluded: Additional therapy
Wiskemann, J., Dreger, P., Schwerdtfeger, R., Bondong, A., Huber, G., Kleindienst, N., . . . Bohus, M. (2011). Effects of a partly self-administered exercise program before, during, and after allogeneic stem cell transplantation. *Blood, 117*(9), 2604-2613. doi:10.1182/blood-2010-09-306308	Source: WoK Excluded: Additional therapy
Wiskemann, J., & Huber, G. (2008). Physical exercise as adjuvant therapy for patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplantation, 41*(4), 321-329. doi:10.1038/sj.bmt.1705917	Source: WoK Excluded: Additional therapy
Wiskemann, J., Jaeger, D., Ulrich, C. M., Huber, G., Dreger, P., Schwerdtfeger, R., & Bohus, M. (2012). Individual Training Response In Allogeneic Stem Cell Transplant	Source: WoK Excluded: Additional therapy

Patients Depending On Baseline Fitness Level. *Medicine and Science in Sports and Exercise, 44*, 891-891.	
Wiskemann, J., Kleindienst, N., Kuehl, R., Dreger, P., Schwerdtfeger, R., & Bohus, M. (2015). Effects of physical exercise on survival after allogeneic stem cell transplantation. *International Journal of Cancer, 137*(11), 2749-2756. doi:10.1002/ijc.29633	Source: WoK Excluded: Additional therapy
Wiskemann, J., Kuehl, R., Dreger, P., Huber, G., Kleindienst, N., Ulrich, C. M., & Bohus, M. (2015). Physical Exercise Training versus Relaxation in Allogeneic stem cell transplantation (PETRA Study) - Rationale and design of a randomized trial to evaluate a yearlong exercise intervention on overall survival and side-effects after allogeneic stem cell transplantation. *Bmc Cancer, 15*. doi:10.1186/s12885-015-1631-0	Source: WoK Excluded: Additional therapy
Wright, C. R., Brown, E. L., Della Gatta, P. A., Fatouros, I. G., Karagounis, L. G., Terzis, G., . . . Russell, A. P. (2015). Regulation of Granulocyte Colony-Stimulating Factor and Its Receptor in Skeletal Muscle is Dependent Upon the Type of Inflammatory Stimulus. *J Interferon Cytokine Res, 35*(9), 710-719. doi:10.1089/jir.2014.0159	Source: WoK & PubMed Excluded: SC outcome not described
Xie, J., & Liu, R. L. (2012). *Bone Mesenchymal Stem Cells Transplantation and Exercise-induced Spinal Cord Injury*.	Source: WoK Excluded: Non-healthy participants, Additional therapy
Yamada, S., Kimura, H., Fujimaki, A., & Strohman, R. (1992). *Expression of fibroblast growth-factors in exercise-induced muscle hypertrophy with special reference to the role of muscle satellite cells* (Vol. 37).	Source: WoK Excluded: Animal study
Yan, Z. (2000). Skeletal muscle adaptation and cell cycle regulation. *Exerc Sport Sci Rev, 28*(1), 24-26.	Source: PubMed Excluded: Review
Yang, C. C., Hsieh, Y. L., & Ou, H. C. (2010). Transplantation of mesenchymal stem cells fails to provide a synergistic effect on functional recovery of transected nerve with exercise-treated rats. *Faseb Journal, 24*.	Source: WoK Excluded: Animal study
Yang, X. Y., Zhu, F., Zhang, X. M., Gao, Z., & Cao, Y. P. (2012). Ipsilateral versus bilateral limb-training in promoting the proliferation and differentiation of endogenous neural stem cells following cerebral infarction in rats. *Neural Regeneration Research, 7*(34), 2698-2704. doi:10.3969/j.issn.1673-5374.2012.34.007	Source: WoK Excluded: Animal study
Yildiz, V., Duger, T., Nevin, C., & Cetinkaya, D. U. (2015). Effects of the Exercise Programme on Childrens' Fatigue and Quality of Life Level During and After Pediatric Hematopoietic Stem Cell Transplantation. *Bone Marrow Transplantation, 50*, S468-S469.	Source: WoK Excluded: Additional therapy
Zaldivar, F., Eliakim, A., Radom-Aizik, S., Leu, S. Y., & Cooper, D. M. (2007). The effect of brief exercise on circulating CD34(+) stem cells in early and late pubertal boys. *Pediatric Research, 61*(4), 491-495. doi:10.1203/pdr.0b013e3180332d36	Source: WoK Excluded: Age participants
Zangari, M., Platnick, J., Croft, L., Ross, V., Ahmad, S., Scigliano, E., . . . Fruchtman, S. (1997). Predictive value for survival using gated blood pool imaging at rest and with exercise (EX) in stem cell transplantation (SCT). *Blood, 90*(10), 1105-1105.	Source: WoK Excluded: Additional therapy
Zhang, J. Y., & Wang, J. H. C. (2015). Moderate Exercise Mitigates the Detrimental Effects of Aging on Tendon Stem Cells. *Plos One, 10*(6). doi:10.1371/journal.pone.0130454	Source: WoK Excluded: Age participants
Zhang, Y. X., Yuan, M. Z., Cheng, L., Lin, L. Z., Du, H. W., Chen, R. H., & Liu, N. (2015). Treadmill exercise enhances therapeutic potency of transplanted bone mesenchymal stem cells in cerebral ischemic rats via anti-apoptotic effects. *Bmc Neuroscience, 16*. doi:10.1186/s12868-015-0196-9	Source: WoK Excluded: Animal study
Zou, K., De Lisio, M., Huntsman, H. D., Pincu, Y., Mahmassani, Z., Miller, M., . . . Boppart, M. D. (2014). Laminin-111 Improves Skeletal Muscle Stem Cell Quantity and Function Following Eccentric Exercise. *Stem Cells Translational Medicine, 3*(9), 1013-1022. doi:10.5966/sctm.2014-0044	Source: WoK Excluded: Additional therapy
Zou, K., Huntsman, H. D., Valero, M. C., Adams, J., Skelton, J., De Lisio, M., . . . Boppart, M. D. (2015). Mesenchymal Stem Cells Augment the Adaptive Response to Eccentric Exercise. *Medicine and Science in Sports and Exercise, 47*(2), 315-325. doi:10.1249/mss.0000000000000405	Source: WoK Excluded: Animal study

Table 3A: Quality-assessment quasi-experimental studies

Yes (Y) → 1-point value
No (N) → 0-point value
Not mentioned (NM) → 0-point value
Not applicable (NA) → Not included in the scoring

Quasi-experimental studies (The Joanna Briggs Institute checklist for Quasi-Experimental Studies)										
	Is it clear in the study what the cause is and what the effect is? (i.e. there is no confusion about which variable comes first)?	Were the participants included in any comparisons similar?	Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Was there a control group?	Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?	Total score
Babcock, L., Escano, M., D'Lugos, A., Todd, K., Murach, K., & Luden, N. (2012). Concurrent aerobic exercise interferes with the satellite cell response to acute resistance exercise.	Y	Y	Y	N	Y	Y	NA	NM	Y	6/8 = 75%
Cermak, N. M., Snijders, T., McKay, B. R., Parise, G., Verdijk, L. B., Tarnopolsky, M. A., . . . Van Loon, L. J. (2013). Eccentric exercise increases satellite cell content in type II muscle fibers.	Y	Y	Y	N	Y	Y	NA	NM	Y	6/8= 75%
Crameri, R. M., Langberg, H., Magnusson, P., Jensen, C. H., Schroder, H. D., Olesen, J. L., . . . Kjaer, M. (2004). Changes in satellite cells in human skeletal muscle after a single bout of high intensity exercise.	Y	Y	Y	Y	Y	Y	Y	NM	Y	8/9= 89%
Joanisse, S., McKay, B. R., Nederveen, J. P., Scribbans, T. D., Gurd, B. J., Gillen, J. B., . . . Parise, G. (2015). Satellite cell activity, without expansion, after nonhypertrophic stimuli.	Y	Y	Y	Y	Y	Y	Y	NM	Y	8/9= 89%
Kadi, F., Johansson, F., Johansson, R., Sjostrom, M., & Henriksson, J. (2004). Effects of one bout of endurance exercise on the expression of myogenin in human quadriceps muscle.	Y	Y	Y	Y	Y	Y	Y	NM	Y	8/9= 89%

Kadi, F., Schjerling, P., Andersen, L. L., Charifi, N., Madsen, J. L., Christensen, L. R., & Andersen, J. L. (2004). The effects of heavy resistance training and detraining on satellite cells in human skeletal muscles.	Y	Y	Y	N	Y	NM	NA	NM	Y	5/8= 63%
Macaluso, F., Brooks, N. E., Niesler, C. U., & Myburgh, K. H. (2013). Satellite cell pool expansion is affected by skeletal muscle characteristics.	Y	Y	Y	Y	Y	N	Y	NM	Y	7/9= 78%
Macaluso, F., Brooks, N. E., van de Vyver, M., Van Tubbergh, K., Niesler, C. U., & Myburgh, K. H. (2012). Satellite cell count, VO(2max) , and p38 MAPK in inactive to moderately active young men.	Y	Y	Y	N	Y	NM	NA	NM	Y	5/8= 63%
Mackey, A. L., Holm, L., Reitelseder, S., Pedersen, T. G., Doessing, S., Kadi, F., & Kjaer, M. (2011). Myogenic response of human skeletal muscle to 12 weeks of resistance training at light loading intensity.	Y	Y	NM	N	Y	Y	NA	NM	Y	5/8= 63%
McKay, B. R., O'Reilly, C. E., Phillips, S. M., Tarnopolsky, M. A., & Parise, G. (2008). Co-expression of IGF-1 family members with myogenic regulatory factors following acute damaging muscle-lengthening contractions in humans.	Y	Y	Y	N	Y	NM	NA	NM	Y	5/8= 63%
Murach, K. A., Walton, R. G., Fry, C. S., Michaelis, S. L., Groshong, J. S., Finlin, B. S., . . . Peterson, C. A. (2016). Cycle training modulates satellite cell and transcriptional responses to a bout of resistance exercise.	Y	Y	NM	N	Y	NM	NA	NM	Y	4/8= 50%
O'Reilly, C., McKay, B., Phillips, S., Tarnopolsky, M., & Parise, G. (2008). Hepatocyte growth factor (HGF) and the satellite cell response following muscle lengthening contractions in humans.	Y	Y	Y	N	Y	NM	NA	NM	Y	5/8= 63%
Petrella, J. K., Kim, J. S., Mayhew, D. L., Cross, J. M., & Bamman, M. M. (2008). Potent myofiber hypertrophy during resistance training in humans is associated with satellite cell-mediated myonuclear addition: a cluster analysis.	Y	Y	Y	N	Y	NM	NA	NM	Y	5/8= 63%
Snijders, T., Verdijk, L. B., Beelen, M., McKay, B. R., Parise, G., Kadi, F., & van Loon, L. J. (2012). A single bout of exercise activates skeletal muscle satellite cells during subsequent overnight recovery.	Y	Y	Y	N	Y	NM	NA	NM	Y	5/8= 63%
Toth, K. G., McKay, B. R., De Lisio, M., Little, J. P., Tarnopolsky, M. A., & Parise, G. (2011). IL-6 induced STAT3 signalling is associated with the proliferation of human muscle satellite cells following acute muscle damage.	Y	Y	Y	N	Y	Y	NA	NM	Y	6/8= 75%
Wilborn, C. D., Taylor, L. W., Greenwood, M., Kreider, R. B., & Willoughby, D. S. (2009). Effects of different intensities of resistance exercise on regulators of myogenesis.	Y	Y	Y	Y	Y	Y	Y	NM	Y	8/9 = 78%

Table 3B: Quality-assessment RCT

Yes (Y) → 1-point value
No (N) → 0-point value
Too little information in the article to answer this (TLI) → 0-point value
Question 13: not included in the scoring

Randomized controlled trials (Dutch Cochrane Centre checklist for a Randomized Controlled Trial)														
	Was allocation of the intervention randomized for the patients?	The person who includes patients in the study should not be aware of the randomization sequence. Was that the case here?	Were the patients blinded for treatment?	Were the therapists blinded for the treatment?	Were the effect assessors blinded for treatment?	Were the groups comparable at the beginning of the trial?	A full follow-up is available from a sufficient proportion of all patients included?	Are all the included patients analyzed in the group in which they were randomized?	Have the groups been treated equally, apart from the intervention?	Are the results of the research valid and applicable?	Results	Can the result found be applied to the Dutch situation?	On which echelon (s) can the result be applied?	Total score
Hanssen, K. E., Kvamme, N. H., Nilsen, T. S., Ronnestad, B., Ambjornsen, I. K., Norheim, F., . . . Raastad, T. (2013). The effect of strength training volume on satellite cells, myogenic regulatory factors, and growth factors.	Y	TLI	N	N	TLI	Y	Y	Y	TLI	Y, valid and aplicapble	Yes, shown in study	Y	Second -line care	7/1 =58 %
Herman-Montemayor, J. R., Hikida, R. S., & Staron, R. S. (2015). Early-Phase Satellite Cell and Myonuclear Domain Adaptations to Slow-Speed vs. Traditional Resistance Training Programs.	Y	TLI	N	N	TLI	Y	Y	Y	TLI	Yes, valid and applicable	Yes, shown in study	Y	Second -line care	7 /12 =58 %
Hyldahl, R. D., Olson, T., Welling, T., Groscost, L., & Parcell, A. C. (2014). Satellite cell activity is differentially affected by contraction mode in human muscle following a work-matched bout of exercise.	Y	TLI	N	TLI	Y	Y	Y	Y	Y	Yes, valid and applicable	Yes, shown in study	Y	Second -line	9/12 =75 %

Table 4: Strengths and weaknesses of the included studies

	Reference	Strenghts	Limitations
1	Babcock, L., Escano, M., D'Lugos, A., Todd, K., Murach, K., & Luden, N. (2012). Concurrent aerobic exercise interferes with the satellite cell response to acute resistance exercise. Am J Physiol Regul Integr Comp Physiol, 302(12), R1458-1465. doi:10.1152/ajpregu.00035.2012	- Complete description of methods interventions. - Subject characteristics are described at baseline. - Longer time course/duration. - Multiple interventions compared. - Standardized approaches for muscle strength measure: 1RM. - Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max.	- Low sample size: 8 college-aged males - Only men participated in the study ⇒ difficult generalization to women (external validity). - No blinding mentioned of effect assessors. - No follow-up flow chart. - No limitations and strengths shown. - Selection bias. - Volunteer bias: subjects volunteered to participate in the study. - No randomization. - No (non-intervention) control group.
2	Cermak, N. M., Snijders, T., McKay, B. R., Parise, G., Verdijk, L. B., Tarnopolsky, M. A., . . . Van Loon, L. J. (2013). Eccentric exercise increases satellite cell content in type II muscle fibers. Med Sci Sports Exerc, 45(2), 230-237. doi:10.1249/MSS.0b013e318272cf47	- All image recordings and analyses (effect assessors) were performed by an investigator blinded to subjects. - Randomization intervention leg. - Standardized approaches for muscle strength measure: Biodex. - Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max.	- Low sample size, nine healthy, active men (23±1yr.). - Only men participated in the study ⇒ difficult generalization to women (external validity). - Selection bias. - In 20% of the study participants results from 2 out of the 4 SC-markers were not reliable. ⇒ low statistical power - No control group. - Inter/intra rater reliability is not mentioned. - No limitations and strengths shown.
3	Crameri, R. M., Langberg, H., Magnusson, P., Jensen, C. H., Schroder, H. D., Olesen, J. L., . . . Kjaer, M. (2004). Changes in satellite cells in human skeletal muscle after a single bout of high intensity exercise. J Physiol, 558(Pt 1), 333-340. doi:10.1113/jphysiol.2004.061846	- Contralateral leg being the control. - Standardized approaches for muscle strength measure: Biodex.	- Low sample size, eight healthy sedentary male subjects age (25±3 yr.). - Only men participated in the study ⇒ difficult generalization to women (external validity). - No limitations and strengths shown. - Inter/intra rater reliability is not mentioned. - No blinding mentioned of effect assessors. - No randomization. - Volunteer bias.
4	Hanssen, K. E., Kvamme, N. H., Nilsen, T. S., Ronnestad, B., Ambjornsen, I. K., Norheim, F., . . . Raastad, T. (2013). The effect of strength training volume on satellite cells, myogenic regulatory factors, and growth factors. Scand J Med Sci Sports, 23(6), 728-739. doi:10.1111/j.1600-0838.2012.01452.	- Control group. - Follow-up mentioned. - Randomization. - Standardized approaches for muscle strength measure: 1RM. - Larger sample size (24 participants).	- Strengths and limitations not mentioned. - No blinding mentioned of effect assessors. - Inter/intra rater reliability not mentioned. - Only men participated in the study → difficult generalization to women (external validity).

5	Herman-Montemayor, J. R., Hikida, R. S., & Staron, R. S. (2015). Early-Phase Satellite Cell and Myonuclear Domain Adaptations to Slow-Speed vs. Traditional Resistance Training Programs. J Strength Cond Res, 29(11), 3105-3114. doi:10.1519/jsc.0000000000000925	- Drop-outs mentioned. - Multiple training speeds. - Larger sample size (34 subjects). - The first 2 weeks of the study involved familiarization with the training protocol, pretraining testing, anthropometric measures, and muscle biopsies. - Standardized approaches for muscle strength measure: 1RM.	- No blinding mentioned of effect assessors. - No limitations and strengths of the study shown. - Volunteer bias. - Selection bias. - Only women participated in the study → difficult generalization to men (external validity).
6	Hyldahl, R. D., Olson, T., Welling, T., Groscost, L., & Parcell, A. C. (2014). Satellite cell activity is differentially affected by contraction mode in human muscle following a work-matched bout of exercise. Frontiers in Physiology, 5. doi:10.3389/fphys.2014.00485	- Randomization patients for CON or ECC group. - Quantification of immunofluorescent images was carried out by an investigator that was blind to both condition and time point. - Limitations discussed. - Familiarization with the training protocol. - Standardized approaches for muscle strength measure: Biodex. - Drop-outs mentioned.	- Total sample size, 14 untrained young men. Small sample size of 7 subjects per group. This sample size likely contributed to the discrepant results between MyoD DNA binding activity (ELISA) and MyoD nuclear accumulation (IHC). - Only men participated in the study ⇒ difficult generalization to women (external validity). -Single sampling point of 24 h post-exercise, in as much as robust changes in muscle satellite cell content occur at later time points (48–72 h post-exercise). - Inter/intra rater reliability is not mentioned. - Significant variability that existed in CON due to disparities in the strength of subjects in that group. - Strengths of the study not shown.
7	Joanisse, S., McKay, B. R., Nederveen, J. P., Scribbans, T. D., Gurd, B. J., Gillen, J. B., . . . Parise, G. (2015). Satellite cell activity, without expansion, after nonhypertrophic stimuli. Am J Physiol Regul Integr Comp Physiol, 309(9), R1101-1111. doi:10.1152/ajpregu.00249.2015	- Control group. - Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max. - Larger sample size.	- No mentioning of blinding effect assessor. - No limitations and strengths shown. - Volunteer bias. - Selection bias. - Inter/intra rater reliability not mentioned. - Blinding not mentioned. - Uneven distribution of men (16) and women (3).
8	Kadi, F., Johansson, F., Johansson, R., Sjostrom, M., & Henriksson, J. (2004). Effects of one bout of endurance exercise on the expression of myogenin in human quadriceps muscle. Histochem Cell Biol, 121(4), 329-334. doi:10.1007/s00418-004-0630-z	- All subjects were familiarised to the one-leg exercise cycling protocol before the actual test. - Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max.	- Volunteer bias → Selection bias. - Low sample size: 5 healthy young volunteers, 4 men and 1 woman. - Inter/intra rater reliability not mentioned. - Blinding not mentioned. - No strengths and limitations shown.
9	Kadi, F., Schjerling, P., Andersen, L. L., Charifi, N., Madsen, J. L., Christensen, L. R., & Andersen, J. L. (2004). The effects of heavy resistance training and detraining on satellite cells in human skeletal muscles. J Physiol, 558(Pt 3), 1005-1012. doi:10.1113/jphysiol.2004.065904	- Standardized approaches for muscle strength measure: 1RM but not in %. - Larger sample size for typical biopsy studies, but still fairly low.	- No randomization. - No control group. - Blinding not mentioned. - Inter/intra rater reliability not mentioned. - No limitations and strengths mentioned. - Follow-up not mentioned.

			- Only men (15) participated in the study ⇒ difficult generalization to women (external validity).
10	Macaluso, F., Brooks, N. E., Niesler, C. U., & Myburgh, K. H. (2013). Satellite cell pool expansion is affected by skeletal muscle characteristics. Muscle Nerve, 48(1), 109-116. doi:10.1002/mus.23721	- Extra control slide for immunofluorescence. - Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max. - Limitations discussed.	- Small control group. - Volunteer bias. - Inter/intra rater reliability not mentioned. - Blinding not mentioned. - No use of a sophisticated exercise mode for isolated muscle groups. ⇒ downhill running is a form of exercise that may be recommended to the general population. - Strengths of the study not shown.
11	Macaluso, F., Brooks, N. E., van de Vyver, M., Van Tubbergh, K., Niesler, C. U., & Myburgh, K. H. (2012). Satellite cell count, VO(2max) , and p38 MAPK in inactive to moderately active young men. Scand J Med Sci Sports, 22(4), e38-44. doi:10.1111/j.1600-0838.2011.01389.x	- Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max. - Extra control slide for immunofluorescence.	- Low sample size 8 inactive to moderately active men. - Only men participated in the study ⇒ difficult generalization to women (external validity). - Blinding not mentioned. - Volunteer bias. - Selection bias. - No randomization. - No strengths and limitations mentioned.
12	Mackey, A. L., Holm, L., Reitelseder, S., Pedersen, T. G., Doessing, S., Kadi, F., & Kjaer, M. (2011). Myogenic response of human skeletal muscle to 12 weeks of resistance training at light loading intensity. Scand J Med Sci Sports, 21(6), 773-782. doi:10.1111/j.1600-0838.2010.01178.x	- Before sectioning, the biopsies were coded by randomly assigning a unique identification number from 1 to 48 to each biopsy such that all samples were blinded with regard to subject, time point and leg. All subsequent analyses were performed blinded. - Limitations discussed. - Standardized approaches for muscle strength measure: 1RM.	- Only men (12) participated in the study ⇒ difficult generalization to women (external validity). - No randomization. - Volunteer bias. - Selection bias. - No control group. - Double labeling with laminin and not CD56; they cannot be certain that the stained nuclei are satellite cells and not myonuclei. - Training loads were not sufficient to induce differentiation of satellite cells to a detectable level at 12 weeks, or that the new satellite cells detected are programmed to remain as satellite cells. - Strengths of the study not shown.
13	McKay, B. R., O'Reilly, C. E., Phillips, S. M., Tarnopolsky, M. A., & Parise, G. (2008). Co-expression of IGF-1 family members with myogenic regulatory factors following acute damaging muscle-lengthening contractions in humans. J Physiol, 586(22), 5549-5560. doi:10.1113/jphysiol.2008.160176	- Familiarization with the training protocol. - Standardized approaches for muscle strength measure: Biodex. - For each subject, one leg was selected randomly to perform the exercise protocol. - Longer time course/duration.	- Low sample size, 8 healthy males. - Only men participated in the study ⇒ difficult generalization to women (external validity). - No control group. - No strengths and limitations mentioned.
14	Murach, K. A., Walton, R. G., Fry, C. S., Michaelis, S. L., Groshong, J. S., Finlin, B. S., . . . Peterson, C. A. (2016). Cycle training	- Standardized approaches for muscle strength measure: 1RM. - Familiarization with the training protocol.	- Low sample size, 7 healthy inactive middle-aged women. - Only women participated in the study → difficult generalization to men (external validity).

	modulates satellite cell and transcriptional responses to a bout of resistance exercise. Physiological Reports, 4(18). doi:10.14814/phy2.12973	- Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max. - Standardized approaches for body composition: DEXA scan. - Longer time course/duration.	- No control group. - No strengths and limitations mentioned. - Inter/intra rater reliability not mentioned. - Blinding not mentioned. - No randomization.
15	O'Reilly, C., McKay, B., Phillips, S., Tarnopolsky, M., & Parise, G. (2008). Hepatocyte growth factor (HGF) and the satellite cell response following muscle lengthening contractions in humans. Muscle Nerve, 38(5), 1434-1442. doi:10.1002/mus.21146	- Standardized instrument for muscle strength measure: Biodex. - Familiarization. - Investigators provided verbal encouragement for the subjects to complete and exert maximal force during each contraction. - Longer time course/duration.	- Low sample size, 8 healthy recreationally active men. - Only men participated in the study → difficult generalization to women (external validity). - No control group. - Inter/intra rater reliability not mentioned. - Blinding not mentioned. - No randomization. - Follow-up not mentioned. - Selection bias. - No strengths and limitations mentioned.
16	Snijders, T., Verdijk, L. B., Beelen, M., McKay, B. R., Parise, G., Kadi, F., & van Loon, L. J. (2012). A single bout of exercise activates skeletal muscle satellite cells during subsequent overnight recovery. Exp Physiol, 97(6), 762-773. doi:10.1113/expphysiol.2011.063313	- Familiarization with the training protocol. - Standardized approaches for cardiorespiratory fitness: bicycle ergometer VO2max and workload capacity. - Standardized approaches for muscle strength measure: 1RM.	- Low sample size, 8 healthy, recreationally active men. - Only men participated in the study → difficult generalization to women (external validity). - Inter/intra rater reliability not mentioned. - Volunteer bias. - Blinding not mentioned. - Follow-up not mentioned. - No randomization. - No strengths and limitations mentioned.
17	Toth, K. G., McKay, B. R., De Lisio, M., Little, J. P., Tarnopolsky, M. A., & Parise, G. (2011). IL-6 induced STAT3 signalling is associated with the proliferation of human muscle satellite cells following acute muscle damage. PLoS One, 6(3), e17392. doi:10.1371/journal.pone.0017392	- Control leg. - Standardized instrument for muscle strength measure: Biodex. - Two separate blinded reviewers quantified the co-localization of Pax7 and cMyc.	- Low sample size, 12 healthy but sedentary males. - Only men participated in the study → difficult generalization to women (external validity). - No randomization. - Inter/intra rater reliability not mentioned. - Follow-up not mentioned. - No strengths and limitations mentioned.
18	Wilborn, C. D., Taylor, L. W., Greenwood, M., Kreider, R. B., & Willoughby, D. S. (2009). Effects of different intensities of resistance exercise on regulators of myogenesis. J Strength Cond Res, 23(8), 2179-2187. doi:10.1519/JSC.0b013e3181bab493	- All participants acted as their own controls in a cross-over design. - Patients were randomly assigned. - Standardized approaches for muscle strength measure: 1RM.	- Low sample size, 13 recreationally active but non resistance-trained men. - Only men participated in the study → difficult generalization to women (external validity). - Blinding not mentioned. - Reliability not mentioned. - Follow-up not mentioned. - No strengths and limitations mentioned.

Table 5: Data-extraction

	Reference	Aim study	Sample size	Training intervention	Time course	Outcomes	Results	Conclusion
1	Babcock, L., Escano, M., D'Lugos, A., Todd, K., Murach, K., & Luden, N. (2012). Concurrent aerobic exercise interferes with the satellite cell response to acute resistance exercise. Am J Physiol Regul Integr Comp Physiol, 302(12), R1458-1465. doi:10.1152/ajpregu.00035.2012	The aim of this study was to assess the influence of acute resistance exercise (RE), aerobic exercise (AE) or concurrent exercise (CE) program on the VL satellite cell population.	8 recreationally active, college-aged males (age: 23 ± 1 yr.)	- RE= 4 sets 10 repetitions leg extensions and presses: 75% 1RM - AE/CE= 4 sets 10 repetitions: 75% 1RM + 90 min of cycling (60% Wmax) RE= resistance exercise AE= aerobic exercise CE= concurrent exercise	- PRE - 4d. - 10d. - 14d.	- Pax7: / - CD56 (=NCAM): / - MyoD: / - Myf5:/ - Myogenin: / - Myonuclei: / - MHC I: ✓ - MHC IIa /MHC IIx: ✓ - SC number: ✓ ⇒ (SC density = #SC /fiber) - SC activation - SC density combined muscle fiber - SC density MHC I and MHC II muscle fibers	- The number of active satellite cells per muscle fiber was unaffected by exercise. - There was a time x mode interaction for satellite cell density (P = 0.021). - The relative increase in satellite cell density with RE was greater than CE (P = 0.012) - There were no other differences in combined muscle fiber satellite cell proliferation. - There was a time x mode interaction in MHC I (P = 0.050), but not MHC II muscle fibers (P = 0.121). - RE increased satellite cell density of MHC I fibers more than CE (P = 0.028) and AE (P= 0.030). - Time x mode interaction for MHC II muscle fibers was modest and did not reach significance, inclusion of the aerobic exercise comparison appears to have masked meaningful interactions between CE and RE. - RE increased satellite cell density of MHC II fibers more than CE (P = 0.025), we must note that MHC II satellite cell density was elevated at pre-CE compared with pre-AE (P = 0.036). - Satellite cell activation was not different between the RE time points (pre-exercise, 4 days post, and 10 days post-exercise). - Satellite cell density of combined fibers was different across the three time points (P = 0.004). - SC density in both MHC type I & II were significant increased in 4 days post RE but less 10 days post RE. (P < 0,05), this is a transient pattern in the SC response (up at 4 days and back to baseline at 10 days).	A single bout of traditional (concentric and eccentric contractions) RE transiently increases satellite cell density. Satellite cells increased to a greater extent following RE (resistance exercise), compared with CE (concurrent exercise). This result was evident in combined, MHC I muscle fibers, and MHC II fibers. We must note that an elevated MHC II satellite cell count prior to CE may have softened the potential for further increases following CE and, therefore, may not reflect true interference. The current data suggest that the physiological environment evoked by AE might attenuate the eventual addition of myonuclei important for maximum muscle fiber growth and consequent force-producing capacity.
2	Cermak, N. M., Snijders, T., McKay, B. R., Parise, G., Verdijk, L. B., Tarnopolsky, M. A., . . . Van Loon, L. J. (2013). Eccentric exercise increases satellite cell content in type II muscle fibers. Med Sci Sports Exerc, 45(2), 230-237. doi:10.1249/MSS.0b013e318272cf47	The aim of this study is to demonstrate that a single bout of high-force eccentric exercise activates SCs and augments SC content after 24 h of post exercise recovery in a muscle fiber type–specific manner.	9 healthy, active men (age: 23 ± 1 yr.)	15 sets of 20 eccentric actions of the knee extensors performed on an isokinetic at a speed of 0.52 rad·s^{-1} with 1-min rest intervals between sets.	- PRE - 24h.	- Pax7: ✓ - CD56 (=NCAM): ✓ - MyoD: / - Myf5:/ - Myogenin: / - Myonuclei: ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	- Muscle fiber type composition in vastus lateralis muscle was 44% ± 5% Type I and 56% ± 5% Type II muscle fibers. The proportion of muscle fiber area occupied by Type I and Type II muscle fibers was 37% ± 5% and 63% ± 5%. - Muscle fiber area was significantly greater in Type II compared with type I fibers (P < 0.05) - For mixed muscle, the number of SCs per muscle fiber did not change after 24 h of recovery (P = 0.15). SC content was expressed in a fiber type–specific manner, the number of SC's per Type II muscle fiber increased significantly after 24 h of recovery (P < 0.05), whereas no changes in Type I muscle fiber SC content were observed.	A single bout of high-force eccentric exercise increases muscle fiber SC content and activation status in Type II but not Type I muscle fibers within 24 h of post exercise recovery in young, healthy men.
3	Crameri, R. M., Langberg, H., Magnusson, P., Jensen, C. H., Schroder, H. D., Olesen, J. L., . . . Kjaer, M. (2004). Changes in satellite cells in human skeletal muscle after a single bout of high intensity exercise. J Physiol, 558(Pt 1), 333-340. doi:10.1113/jphysiol.2004.061846	The aim of this study is to report activation of satellite cells in vivo in human muscle after a single bout of high intensity exercise. In this investigation, eight individuals performed a single bout of high intensity exercise with one leg, the	8 healthy sedentary men (age: 25 ± 3 yr.)	Exercise group: (3 exercise phases) - (1) 50 one-leg 'drop down' jumps were performed from a stable platform of 45 cm. - (2) 8 sets of 10 maximal eccentric knee extensions at −30 deg s−1 using an isokinetic dynamometer. - (3) 8 sets of 10 maximal eccentric knee extensions at −180 deg s−1 using an isokinetic dynamometer. -30 s rest phase between each set	- PRE - 5h. - 2d. - 4d. - 8d.	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: / - Myf5:/ - Myogenin: ✓ - Myonuclei: ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓ - Ki-67: proliferation/differentiation markers of active nuclei - FA-1: fetal antigen 1 protein growth factor	A significant increase in cells positive for NCAM in the exercised leg was found in the histological sections taken from all subjects, on days 4 and 8 after the cessation of exercise (P < 0.05).	This study shows that an increase in the number of satellite cells is possible with a single bout of voluntary high intensity exercise. However, a single bout of exercise is not sufficient for the satellite cell to undergo terminal differentiation.

		contralateral leg being the control.		-5 min rest period between each exercise phase. Control group: - Non-exercising contralateral leg		- CD-68: inflammatory marker		
4	Hanssen, K. E., Kvamme, N. H., Nilsen, T. S., Ronnestad, B., Ambjornsen, I. K., Norheim, F., . . . Raastad, T. (2013). The effect of strength training volume on satellite cells, myogenic regulatory factors, and growth factors. Scand J Med Sci Sports, 23(6), 728-739. doi:10.1111/j.1600-0838.2012.01452.x	The aim the study was to investigate the satellite cell response in upper and lower body muscles to single- and multiple-set strength training during a period of 11 weeks. In addition, changes in fiber area and the number of myonuclei were measured.	24 healthy untrained men (age: 26 ± 2 yr.)	Group 3L-1UB (n = 10): 3 sets of the leg exercises and a single-set upper body exercises Group 1L-3UB (n = 11): single-set leg exercises and 3 sets of the upper body exercises (1L-3UB) → 11-week training period: - 3 workouts/week on non-consecutive days. - Standardized warm-up including three sets with gradually increasing load (40–75–85% of expected one RM) and decreasing number of repetitions (12–7–3) - leg press - leg extension - leg curl - seated chest press - seated rowing - latissimus pull- down, - biceps curl - shoulder press. -Training intensity (RM) was similar for the 2 groups. -Week 1-2: trained with 10 RM sets in all exercises. -Week 3-4: increased intensity to 8 RM sets. -Week 5-1: trained with 7 RM sets.	- PRE - 2w. (3–4 days after the fifth training session) - 11w. (2–5 days after the final training session = Post-intervention)	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: ✓ - Myf5: / - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	Baseline values - No statistically significant differences between m. vastus lateralis and m.trapezius in the measured immunohistochemical variables at baseline. - No statistically significant differences found between groups in the number of satellite cells in m. vastus lateralis or in m. trapezius. Fiber and muscle CSAs - The two-way ANOVA showed an overall time effect ($P < 0.05$) for the changes in fiber area in m. vastus lateralis. - No significant changes in fiber CSA were observed in the 3L-1UB group. CSA of knee extensors increased more in the 3L-1UB group than in the 1L-3UB group ($P < 0.05$). Myonuclei - The two-way ANOVA showed an overall time effect ($P < 0.05$) in m. vastus lateralis and m. trapezius, but no group effect or interaction effect was shown. - The two-way ANOVA showed an overall group effect ($P = 0.05$) and a tendency toward a time effect ($P = 0.07$) in m. vastus lateralis. In m. vastus lateralis, an 18 7% reduction in myonuclear domain was observed during the first 2 weeks of training in the 3L-1UB group ($P < 0.05$). - No other significant changes were observed in the myonuclear domain throughout the training period. Effects of strength training on satellite cells - The two-way ANOVA showed a time effect ($P < 0.05$), a group effect ($P < 0.05$), and an interaction effect ($P < 0.05$) for the satellite cell number in m. vastus lateralis. - The number of satellite cells increased more in the 3L-1UB group than in the 1L-3UB group after 2 weeks of training ($P < 0.05$) as well as after 11 weeks of training ($P < 0.05$). - The two-way ANOVA showed no significant effects on the proportion of MRF positive satellite cells in m. vastus lateralis. MyoD and myogenin protein levels in muscle homogenate - The two-way ANOVA showed no significant effects on the protein levels of MyoD or myogenin analyzed in the cytosolic and nuclear fractions. Correlations - No significant correlation was found between the number of satellite cells at baseline and changes in fiber CSA during the training period. - No significant correlations were observed between the proportion of activated satellite cells (MRF-positive satellite cells) and changes in the number of satellite cells or changes in fiber CSA during the training period.	Strength training resulted in an early increase in activated satellite cells and total number of satellite cells. The larger satellite cell response with high training volume in thigh muscles corresponded to a larger increase in knee extensor muscle CSA and strength as compared with the group training with a low volume. This strengthens the hypothesis that satellite cell activation, proliferation, and later fusion with growing myofibers are important for muscle growth in response to strength training.
5	Herman-Montemayor, J. R., Hikida, R. S., & Staron, R. S. (2015). Early-Phase Satellite Cell and Myonuclear Domain Adaptations to Slow-Speed vs. Traditional Resistance Training Programs. J Strength Cond Res, 29(11), 3105-3114.	The aim of this study was to identify adaptations in satellite cell (SC) content and myonuclear domain (MND) after 6-week slow-speed vs. “normal-speed” resistance training programs.	34 healthy untrained women (age:21.1 ± 2.7 yr.)	Training session: 3 sets of 3 exercises targeting the quadriceps muscle group: leg press, squat, and knee extension. Week 0-2: Familiarization training protocol. Week 3: 2 Resistance training sessions/week. week 4-8: 3 Training sessions/ week. ⇒ Total 17 sessions.	- PRE - POST (after 6 intervention weeks)	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: / - Myf5:/ - Myogenin: / - Myonuclei: ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓ (Relative percentage of satellite cells % SC and satellite cell	Baseline: - At baseline (i.e., before training), SC frequency was greater in type I and IIA fibers than in type IIX fibers, and type IIA SC frequency was greater than type IIAX. - There were significant differences between fiber type in myonuclear number at baseline. The myonuclear number of type IIX fibers was significantly less than that of type I, IIA, and IIAX fibers. The myonuclear number of type IIAX fibers was less than that of type I and IIA fibers. - There was no significant difference in MND of fiber types I, IIA, IIAX, or IIX at baseline	-Heavy-load resistance training was found to induce a number of fiber type–specific changes in SC content and MND size. Compared with the other groups, the high-intensity training of TS induced the greatest increase in SC numbers. When specified by fiber type, the SC content increased in all fiber types (I, IIA, IIAX, and IIX) in TS and for only the fast subtypes IIAX and IIX in SS. -Resistance training did not change the myonuclear number of any fiber type in any of the groups in this study.

	doi:10.1519/jsc.0000000000000925			- Slow speed (SS): 10-second con/4-second ecc contractions for 6–10RM. (40–60% 1RM). - Traditional strength (TS): 1–2 seconds of concentric/eccentric (1–2 seconds con/ecc) contractions for 6–10 repetitions to failure (80–85% 1RM). - Traditional muscular endurance (TE): 1-2 seconds of con/ecc contractions for 20– 30RM. (40–60% 1RM) - Non-training control group (C)		frequency (SC frequency)	Satellite cell population: - %SC and SC frequency increased after training in TS only. Significant between-group differences were found where post training %SC in TS exceeded that of each other group. - There was a significant main effect of group, training effect, and group by time interaction. - Post-training SC frequency in TS was significantly greater than each other group. - TS showed significant within-group training-induced increases in both %SC and SC frequency for each fiber type. - Significant between-group differences were also detected for both %SC and SC frequency variables within the post-training time point. - TS group is significantly different from pretraining value within group and of control group (P<0.05). 7,4% increase in SC. -Satellite cell content of type I, IIA, IIAX, and IIX fibers significantly increased in TS (traditional speed). - SC content of only type IIAX and IIX fibers increased in SS, and there was no change in TE or C. - The myonuclear number (number of nuclei per muscle fiber cross-section) in TS was less than C. - Myonuclear number did not change in any group. - TS had significant fiber hypertrophy of type I, IIA, and IIX fibers after training, and SS had significant fiber hypertrophy of type IIA and IIX fibers after training. There were no changes in fiber size of any fiber type in TE or C.	⇒ Slow-speed resistance training increased SC content and MND more than training with a similar resistance at normal speed. However, high-intensity normal-speed training produced the greatest degree of fiber adaptation for each variable.
6	Hyldahl, R. D., Olson, T., Welling, T., Groscost, L., & Parcell, A. C. (2014). Satellite cell activity is differentially affected by contraction mode in human muscle following a work-matched bout of exercise. Frontiers in Physiology, 5. doi:10.3389/fphys.2014.00485	The aim of the present study was to determine how contraction mode, when matched for total work, influenced indices of muscle damage and satellite cell activity in humans. The primary objectives of the study were to assess (1) functional and histological markers of muscle damage, and (2) satellite cell content and activation status before and 24h following a single bout of either eccentric or concentric contractions.	14 untrained young men ECC: 7men (age: 22.6 ± 2.1 yr.) CON: 7men (age: 23.5 ± 1.1 yr.)	- Concentric (7 subjects): maximally kick on Biodex at a rate of 60.sec−1 self-selected ROM (90° - 20° of knee flexion), total range of motion of 70°. - Eccentric (7 subjects): maximally resist on Biodex at 120°.sec−1, resist lever from 40° of knee flexion (where 0° is full extension) to 115° of knee flexion, a total range of motion (ROM) of 75°. → Multiple sets of concentric or eccentric contractions until approximately 40 kJ of work was achieved. → 2 kJ of work with a 1 min rest between sets.	- PRE - 24h.	- Pax7: ✓ - CD56 (=NCAM): / - MyoD: ✓ - Myf5: / - Myogenin: / - Myonuclei (DAPI): ✓ - MHC I: ✓ - MHC IIa/MHC IIx: / - SC number: ✓	Exercise performance - No significant differences between ECC and CON for anthropometric measures - No difference in the amount of total work completed for ECC or CON. - Average peak torque was 44% greater for ECC compared to CON, individuals in CON performed a significantly higher number of maximal muscle contractions to maintain an equivalent workload. - Significant variability existed in CON due to disparities in the strength of subjects in that group. - Over the course of the exercise protocol only CON experienced significant decreases in average peak torque achieved during each 2 kJ set, indicating greater fatigue in this group. SC - For total mixed fiber satellite cell content, ANOVA revealed a significant effect of time (p = 0.028), but not mode or the time × mode interaction. - Pre- to post-exercise, total satellite cell content per muscle fiber increased in ECC but not CON. - Total satellite cell number increased in all but 1 study participant in the ECC group. - No differences in the number of type I fiber-associated satellite cells pre- to post-exercise for ECC or CON. - No differences in the number of type II fiber-associated satellite cells pre- to post-exercise for ECC or CON. MyoD - There were no changes in MyoD DNA binding activity pre- to post-exercise for ECC or CON as assessed by a transcription factor ELISA - A statistically relevant trend was noted for the main effect of time (P = 0.10). - MyoD immunoreactivity in muscle cross sections was found in only 5 of 14 pre-exercise biopsies (3 from ECC and 2 from CON), whereas we found MyoD+ cells in all biopsies post-ECC and in only 3 out of 7 biopsies post-CON. - MyoD+ cells per myofiber increased pre- to post-ECC and was unchanged pre- to post-CON. MyoD+ cells per myofiber revealed a significant effect of time (P < 0.05), mode (P < 0.05), and the interaction (P < 0.05). In conclusion, ECC but not CON results in functional and histological evidence of muscle damage that is accompanied by increased satellite cell activity 24 h post-exercise.	ECC but not CON results in functional and histological evidence of muscle damage that is accompanied by increased satellite cell activity 24 h post-exercise.

7	Joanisse, S., McKay, B. R., Nederveen, J. P., Scribbans, T. D., Gurd, B. J., Gillen, J. B., . . . Parise, G. (2015). Satellite cell activity, without expansion, after nonhypertrophic stimuli. Am J Physiol Regul Integr Comp Physiol, 309(9), R1101-1111. doi:10.1152/ajpregu.00249.2015	The purpose of the present studies was to determine the effect of various non-hypertrophic exercise stimuli on satellite cell (SC) pool activity in human skeletal muscle.	Study 1 (n=19) recreationally active men (n= 16) & women (n= 3): - SIT 2 age: 21 ± 2 yr.) - MICT age 21 ± 4 yr.)	Study 1: SIT-2: low-volume high-intensity sprint interval training: - 4 days/week for 6 wk. - 8 20-s intervals at 170% of VO2peak separated by 10 s of rest eight times, for a total of 4 min. - During rest periods, subjects cycled against no load at a self-selected cadence. MICT: moderate-intensity continuous exercise training: - 30 min of continuous cycling at 65% of VO2peak. A standardized warmup of descending and ascending four flights of stairs was completed before all training sessions.	- PRE - 48h. - 72h. (after last training session)	- Pax7: ✓ - CD56 (=NCAM): / - MyoD: ✓ - Myf5:/ - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	Fiber CSA and Myonuclear Domain - Six weeks of training did not lead to a significant increase of CSA of either type I or II fibers with SIT-1, SIT-2, or MICT. - Training did not result in an increase in the number of nuclei per fiber for either SIT-1, SIT-2 or MICT. The myonuclear domain, defined as the CSA per myonuclei, was determined, and consistent with CSA and nuclei per fiber, it remained unchanged after training for all three groups. Fiber Type-Specific SC Response to Training - 6 weeks of training did not increase the number of SCs associated with either type I fibers in SIT-1, SIT-2 and MICT ($P > 0.05$) or type II fibers in SIT-1, SIT-2 and MICT ($P > 0.05$). SC Activity After Training - A significant increase in activated SCs was observed after SIT-1, SIT-2 and MICT ($P \leq 0.05$). - A significant increase in the number differentiating SCs was observed after 6 wk of either SIT-1, SIT-2 and MICT ($P \leq 0.05$). - In the subset of subjects from the SIT-2 group (n=3), the proportion of $Pax7^+$ cells expressing MyoD ($Pax7^+/MyoD^+$) was 60.8%. - Muscle sections of the SIT-2 and MICT groups were also stained for myogenin, a MRF expressed during terminal differentiation. In accordance with the increase in differentiating SCs as assessed with MyoD staining, an increase in the number of cells stained positive for myogenin was observed after SIT-2 and MICT.	- When faced with a non-hypertrophic stimulus, SCs may still play a role, although likely different than that associated with resistance training, as training did not lead to an increase in nuclear content. - The activation status of the SC pool when describing their contribution to various stimuli in humans, as simply enumerating SC content using various markers of SCs, such as Pax7 or neural cell adhesion molecule, may not be sufficient in fully describing the response of the SC to a given stimulus.
8	Kadi, F., Johansson, F., Johansson, R., Sjostrom, M., & Henriksson, J. (2004). Effects of one bout of endurance exercise on the expression of myogenin in human quadriceps muscle. Histochem Cell Biol, 121(4), 329-334. doi:10.1007/s00418-004-0630-z	The objective of this study was to investigate the cellular localization of MyoD and myogenin in human skeletal muscle fibres as well as the possible alterations in the expression of MyoD and myogenin in response to a single bout of endurance exercise at 40% and 75% of maximum oxygen uptake (VO2 max).	5 healthy young participants men (n=4) & women (n=1) (age: 26 ± 5 years)	- The VO2 max for one-leg and two-leg cycle ergometry was determined 1–2 weeks before the experimental protocol was undertaken (familiarization). - The ergometer used for one-leg cycling being equipped with an extra heavy wheel in order to create momentum for returning the pedal for subsequent pedaling movements. - Right (one-)leg cycling at a pedaling rate of 60 rpm to different exercise intensities: 40% and 75% of the one-leg VO2 max. - The total duration of the one-leg cycle ergometry exercise bout was 30 min. - Subjects were instructed to relax the resting leg during the exercise bout.	Right leg: - PRE - 10s. after exercise Left resting leg: - 1 min after the exercise bout. - Before the second exercise bout. Left & right leg: - 6–9 days after second bout.	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: ✓ - Myf5:/ - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: / - MHC IIa/MHC IIx: ✓ - SC number: ✓	MyoD and myogenin - A single bout of one-leg cycle exercise at either 40% or 75% of VO2 max did not induce changes in the expression and the distribution of MyoD. - No changes in the expression pattern of MyoD in the resting leg following these exercise bouts. - Analysis of muscle biopsies from the exercised leg following exercise at 40% and 75% of VO2 max showed a fine rearrangement of myogenin expression; an accumulation of myogenin was observed in myonuclei of human muscle fibres. - There was no accumulation of myogenin at the level of myonuclei in biopsies from the resting legs following these exercise bouts.	The present study showed that an increase in the expression of myogenin occurs in the myonuclei of human skeletal muscle fibers following a single bout of one-leg cycle ergometry.
9	Kadi, F., Schjerling, P., Andersen, L. L., Charifi, N., Madsen, J. L., Christensen, L. R., & Andersen, J. L. (2004). The effects of heavy resistance training and detraining on satellite cells in human skeletal muscles. J Physiol, 558(Pt 3), 1005-1012.	The aim of this study was to investigate the modulation of satellite cell content and myonuclear number following 30 and 90 days of resistance training and 3, 10, 30, 60 and 90 days of detraining.	15 young healthy men (age: 24 ± 1yr.)	- 3 months 3 times a week, 4 different resistance-training exercises for the legs were performed: hack squat, incline leg press, knee extensions and hamstring curl. - 4–5 series of 6–12 repetitions, corresponding to 6–12 RM. - Additionally, a number of upper body exercises were performed. - After the training period the subjects entered a 3	- PRE - 30d. after RE - 90d. after RE. - 3d. detraining - 10d. detraining - 60d. detraining - 90d. detraining	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: / - Myf5: / - Myogenin: / - Myonuclei: ✓ - MHC I: / - MHC IIa/MHC IIx: / - SC number: ✓	- The number of satellite cells increased gradually during the training period. By 30 days of resistance training, the number of satellite cells was significantly enhanced ($P = 0.02$). At 90 days, the number of satellite cells was further enhanced ($P = 0.0003$) as compared with the increase observed at 30 days of resistance training. - Satellite cell content increased by 19.3% at 30 days of training and by 31.4% at 90 days of training. - When pre-training satellite cell values are taken as a reference, the number of satellite cells remained statistically elevated at 3 ($P = 0.003$), 10 ($P = 0.0001$) and 60 ($P = 0.02$) days of detraining. The difference in satellite cell frequency between pre-training values and the 30 days of detraining time point approached the significance level ($P = 0.07$). - Compared to the values observed at the end of the resistance-training period, the number of satellite cells per fibre decreased gradually in the detraining period.	The present results clearly demonstrate the high plasticity of satellite cells in response to exercise training and provide new insights into the long-term effects of training followed by detraining. Moderate changes in the size of skeletal muscle fibres can be achieved without the addition of new myonuclei, which indicates that existing myonuclei are able to support a certain level of muscle fibre hypertrophy.

	doi:10.1113/jphysiol.2004.065904			month detraining period, in which they returned to their everyday life with an activity level as prior to entering the study, meaning that the subjects did not perform any resistance (or endurance) exercises during the detraining period.			- There were no significant alterations in the number of myonuclei following the resistance and the detraining periods. The mean number of myonuclei per cross-sectional area of myofibre averaged 2.85 before training and 2.82 by the end of the third month of resistance training. The myonuclear number remained constant throughout the entire detraining period. We noted that both the mean value and the standard deviation for myonuclei at the end of the detraining period (2.99 ± 0.19) were higher than pre-training values (2.85 ± 0.08). - The training period induced a gradual increase in the cross-sectional area of muscle fibres. The increase in fibre area reached 6% at 30 days and 17% at 90 days. The enhancement of the area of muscle fibres reached the significance level at 90 days of training. During the detraining period, the area of muscle fibres gradually decreased. - Before the training period, the area controlled by each myonucleus averaged 1522 μm^2.	
10	Macaluso, F., Brooks, N. E., Niesler, C. U., & Myburgh, K. H. (2013). Satellite cell pool expansion is affected by skeletal muscle characteristics. Muscle Nerve, 48(1), 109-116. doi:10.1002/mus.23721	The aim of this study was therefore to investigate the change in SC count after an acute bout of strenuous exercise in a heterogeneous group of inactive to moderately active young men.	8 inactive to moderately active young men (age: 24 ± 2 yr.)	- Blood samples were collected 1 month before exercise intervention (muscle soreness). 1, 2, 7, and 9 days after the exercise intervention. -V_{O2max} testing: 5-min warm-up prior to beginning the incremental maximal V_{O2max} test on a treadmill. Each individual started at 10 km/h, after which the speed increased by 0.5 km/h every 30 s. until exhaustion. The test was accepted if 2 of the following criteria were met: (1) heart rate within 5 beats/min of theoretical maximum heart rate (220 - age); (2) RER >1.10; and (3) a plateau in V_{O2}. - 5 subjects performed downhill running (DHR): 5-min warm up, 40-min intermittent downhill run, consisting of five 8-min bouts of running with a slope of 10% (-5.7° slope) on a treadmill. Each 8-min bout was followed by a 2-min standing rest period. The speed of the treadmill was set at 80% of each individual's own peak treadmill speed. - 2 individuals, who did not participate in the DHR, agreed to a muscle biopsy, which was used to assess SC count variability within subjects without an exercise intervention.	- PRE - 7d. (n=2) - 9d.	- Pax7: ✓ - CD56 (=NCAM): / - MyoD: ✓ - Myf5:✓ - Myogenin: ✓ - Myonuclei: ✓ - MHC I: / - MHC IIa/MHC IIx: ✓ - SC number: ✓	Skeletal muscle. - There was no change in myonuclear number at baseline compared with after a week of recovery (P = 0.648). - The number of SCs (i.e., $Pax7^+$) per myofiber increased by a mean of 26% (P = 0.005) after a week of recovery. - The percentage increase ranged from 14% to 91%. - By expressing SCs as a percentage of total nuclei, there was also a significant increase after a week of recovery. - No change was evident in the 2 individuals who did no exercise. - Almost no muscle precursor cells were observed expressing myogenic regulatory factors MyoD ($MyoD^+$/m-$cadherin^+$) or myogenin ($myogenin^+$/m-$cadherin^+$) at baseline (n = 7, observed with analysis of 1272 fibers) or at the later time-point in the 2 individuals who did no exercise. - In the second biopsy taken after a week of muscle recovery in the DHR group, we observed very low levels of $MyoD^+$ cells (n = 2 $MyoD^+$/m-$cadherin^+$/$Hoechst^+$ SCs observed with analysis of 753 fibers) and myogenin (n = 3 $myogenin^+$/m-$cadherin^+$/$Hoechst^+$ SCs observed with analysis of 753 fibers). - The extremely low number of positive cells for MyoD and myogenin confirmed that all the SCs within the increased pool size were progenitors rather than a combination of progenitors and committed muscle precursor cells. Correlations. - Highly significant positive correlation between the number of Pax7 cells per fiber and VO2max in inactive to moderately active young men. - Despite some inter-individual differences in the SC response to DHR, the correlation with VO2max was still evident after a week of muscle recovery. - More important was the observation that the number of SCs after a week of muscle recovery was related to the baseline VO2max, whether SC number was expressed as Pax7 cells per fiber (r = 0.908, P = 0.032) or as Pax7 cells relative to total nuclei (r = 0.956, P = 0.011). Baseline VO2max also correlated with the percentage change in SC, whether calculated for the percent change in Pax7 cells per fiber (r = 0.899, P = 0.037) or the percent change in Pax7 cells relative to total nuclei (r = 0.889, P = 0.043). - The number of SCs at baseline was positively correlated with SC number after the exercise intervention (r = 0.979, P = 0.003). -The data also reveal a trend for a correlation between the change in SC pool size (Pax7 cells relative to total nuclei: 1-week post-DHR minus baseline) and myosin heavy chain (MHC) type II percentage expressed in the skeletal muscle (r = 0.848, P = 0.06). This trend was less clear when SC count was expressed per fiber (P = 0.10).	The SC pool increased (26%) after DHR (P= 0.005). SCs/total myonuclei after recovery correlated with baseline SCs and VO2max, whereas change in SC pool (Pax7 cells/total myonuclei: recovery minus baseline) tended to correlate with percent MHC II. Interindividual physiological characteristics affect SC pool expansion after a single bout of DHR and are influenced by VO2max.

11	Macaluso, F., Brooks, N. E., van de Vyver, M., Van Tubbergh, K., Niesler, C. U., & Myburgh, K. H. (2012). Satellite cell count, VO(2max) and p38 MAPK in inactive to moderately active young men. Scand J Med Sci Sports, 22(4), e38-44. doi:10.1111/j.1600-0838.2011.01389.x	The aims of the present study were therefore to: (1) compare the fitness level of inactive to moderately active subjects (estimated by VO2max), with the SC pool size (as measured by the number of quiescent/activated satellite cells); and (2) demonstrate an association between SC pool size and the stress-activated p38 MAPK phosphorylation state in rested muscle.	8 inactive to moderately active men (age: 24 ± 3 yrs.)	- During the first visit, blood sample and skeletal muscle biopsy was taken from the vastus lateralis muscle. Two weeks after the first visit, subjects underwent an incremental treadmill test to exhaustion to determine VO_{2max}. - Subjects completed an incremental maximal exercise test to fatigue on a treadmill. Heart rate (Polar), oxygen uptake (VO_2), carbon dioxide production (VCO_2) respiratory exchange ratio (RER), and minute ventilation (VE) were continuously measured throughout the test. Subjects underwent a 5-min warm-up prior to beginning the test, which started at 10 km/h after which the speed increased 0.5 km/h every 30 s until exhaustion. Subjects were verbally encouraged to continue as long as possible. - Maximal effort was attained when two of the following criteria were fulfilled: (1) heart rate within 5 beats/min of theoretical maximum heart rate (220 – age); (2) RER > 1.10; and (3) a plateau in VO2.	- PRE= 2 weeks before VO_{2max} testing - POST= immediately after the VO_{2max} testing.	- Pax7: ✓ - CD56 (=NCAM): / - MyoD: / - Myf5:/ - Myogenin: ✓ - Myonuclei: ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	Skeletal muscle - The number of quiescent/activated SCs per myofiber was determined following immunohistochemical analysis and ranged from 0.030 SC/fiber to 0.080 SC/fiber (0.056 ± 0.022 SC/ fiber). - The subjects had heterogenous fiber type distribution based on MHC percentage (MHC I: 24–71%; MHC II: 29–76%) and varied considerably in the phospho- p38/p38 MAPK ratio (1.35 0.30 arbitrary unit). - Myogenin levels were very low but similar in all the muscle samples. This result was confirmed by immunofluorescence, where no myogenin-positive nuclei were observed in any cryosections. Correlations - A highly significant positive correlation (P = 0.009) was found between the number of Pax7+ cells per fiber and VO2max. - A significant negative correlation (P = 0.002) was observed between Pax7+ cell count and the ratio of phospho-p38/p38 MAPK expression. - No correlation was observed between the proportion of MHCI or MHCII and VO2max or Pax7+ cell counts.	Inter- individual variability in the SC pool of inactive to moderately active subjects is positively correlated with VO2max, and negatively correlated with activated p38 MAPK, an intracellular stress signaling kinase that enhances the differentiation of SC.
12	Mackey, A. L., Holm, L., Reitelseder, S., Pedersen, T. G., Doessing, S., Kadi, F., & Kjaer, M. (2011). Myogenic response of human skeletal muscle to 12 weeks of resistance training at light loading intensity. Scand J Med Sci Sports, 21(6), 773-782. doi:10.1111/j.1600-0838.2010.01178.x	The aim of this study was to investigate if very light load-resistance training could enhance the satellite cell pool.	12 young healthy men (age: 25 ± 3 yr.)	- Unilateral leg extensions were performed three times a week for 12 weeks, with one leg working with a heavy load (H) and the other leg with a lighter load (L). The number of repetitions was adjusted such that the work lifted by the two legs was equal. H was thus calculated to be 10 sets of eight repetitions at 70% of 1-repetition maximum (1RM), and L was 10 sets of 36 repetitions at 15.5% 1 RM. 1 RM was determined before the 10th, 20th and 30th training sessions and the loads adjusted accordingly.	- PRE - 3d. (after final exercise)	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: / - Myf5:/ - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	Fiber type and size - No statistically significant changes were detected for fiber area. - A significant training time interaction (P=0.007) was observed for the percentage of type IIx fibers, decreasing significantly with Heavy intensity but not with Low intensity training (P= 0.046 and 0.498, respectively) Satellite cells and myonuclei - For all three variables (CD56+ cells, CD56+ cells/fiber, CD56+ cells/mm^2, the two-way repeated measures ANOVA detected a significant effect of time (P 0.005), but not training mode or time x training interaction. - The software program G*Power was used to carry out post hoc power calculations based on these data and revealed that, at a level of 0.05, inclusion of 12 subjects resulted in a power level (1-) of 0.99 with a large effect size (d) of 1.08 for H, and a power level of 0.64 with a moderate effect size of 0.49 for L. - Relative increase in satellite cell number post training in the two legs was similar, for the proportion of CD56+ cells (P = 0.117), CD56+ cells/fiber (P = 0.151) and CD56+ cells/mm^2 (P =0.190) - Occasional CD56+ cells located outside the basement membrane, i.e. in the interstitial space between the muscle fibers, were observed. However, these cells were rare. Post training, this value was 300 fibers for H and 177 fibers for L. Differentiation of satellite cells - Immunohistochemical staining for myogenin was performed in an attempt to follow differentiation of satellite cells with training. Given the low number of F5D1 cells, the values were expressed per 100 fibers.	An 18% increase in satellite cell (CD56+) number with 12 weeks of light intensity (15.5% 1 RM) resistance training.

							- The number of F5D1 nuclei expressed per 100 fibers did not change significantly. - Positive cells were observed in both groups at baseline (Heavy: 0.20 0.27; Light: 0.14 0.13 cells per 100 fibers) and post training (H: 0.17 0.28; L: 0.31 0.58 cells per 100 fibers). Centrally located nuclei - Centrally located nuclei were evident in half of the biopsies. - Present in H in a mean of 2.3% (± 5.0) of fibers at baseline and 0.1% (±0.2) post training. - Values in L were 0.4% (± 0.4) at baseline and 0.5% (± 0.5) post training. - Statistical analyses did not reveal any significant effect of time, training or training time interaction. - Of the total number of 154 fibers observed with internal nuclei in all of the biopsies assessed, 51 of these fibers demonstrated positive cytoplasmic staining for CD56.	
13	McKay, B. R., O'Reilly, C. E., Phillips, S. M., Tarnopolsky, M. A., & Parise, G. (2008). Co-expression of IGF-1 family members with myogenic regulatory factors following acute damaging muscle-lengthening contractions in humans. J Physiol, 586(22), 5549-5560. doi:10.1113/jphysiol.2008.160176	The aims of the current study were to: (1) investigate the time course of expression for IGF-1Ea, IGF-1Eb and MGF in human muscle following intense damaging muscle contractions; (2) investigate the time course of expression for MyoD, Myf5, MRF4 and myogenin in human muscle following damaging exercise; and (3) determine if there were any relationships between the temporal expression of the IGF-1 isoforms and MRF in the post-exercise period.	8 healthy males (age: 20.6 ± 2.1 yr.)	-300 maximal MLC (muscle-lengthening contractions) - Unilateral isokinetic eccentric contractions of the quadriceps femoris using a Biodex dynamo- meter. - 180°/s. - 5–10 submaximal lengthening contractions of the leg to be exercised. - 30 sets of 10 maximal knee extensions. - 1 min rest between sets.	- PRE - 4h. (T4) - 24h. (T24) - 72h. (T72) - 120h. (T120) - 3d. - 5d.	- Pax7: ✓ - CD56 (=NCAM): / - MyoD: ✓ - Myf5:✓ - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: / - MHC IIa/MHC IIx: / - SC number: ✓	MRF mRNA - Following muscle-lengthening expression of MyoD and Myf5 increased early following exercise, while MRF4 and myogenin increased at later approximately 2-fold by T4 (P = 0.001) with a trend to remain elevated at T24 (P = 0.07). - There were no significant differences between MyoD mRNA expression from PRE-at T72 or T120. Myf5 mRNA expression peaked at T24 (P < 0.05), followed by a gradual return to PRE-expression levels by T120. MRF4 mRNA expression increased ∼2.3-fold at T72 (P = 0.039) and remained ∼1.5-fold higher than PRE-at T120. - Myogenin mRNA expression increased at T4 and T24 (P < 0.05) and peaked at T72 (P = 0.009). - Myogenin expression remained ∼2.5-fold higher than PRE (P = 0.015) at T120.	MGF expression is related to the activation and proliferative phase of the myogenic programme, as marked by a significant increase in MyoD and Myf5 mRNA which is strongly correlated with MGF expression and the timing of which is in line with the coexpression of IGF-1 protein with Pax7 in muscle cross-sections. The expression of IGF-1Ea and IGF-1Eb are temporally related to myogenic differentiation as marked by increased myogenin and MRF4 expression which is strongly correlated with increased IGF-1Ea and -Eb expression. The exact mechanisms of MGF and IGF-1Eb signalling are currently unknown.
14	Murach, K. A., Walton, R. G., Fry, C. S., Michaelis, S. L., Groshong, J. S., Finlin, B. S., . . . Peterson, C. A. (2016). Cycle training modulates satellite cell and transcriptional responses to a bout of resistance exercise. Physiological Reports, 4(18).	The aim of this investigation is to evaluate whether moderate-intensity cycle ergometer training affects satellite cell and molecular responses to acute maximal concentric/ eccentric resistance exercise in	7 healthy inactive middle-aged women (age: 56 ± 5 yr.)	Resistance training: - Acute resistance exercise bout, subjects performed 10 min of light cycling as a warm-up. - 5 sets of 8 repetitions and a sixth set to volitional fatigue on the leg extension, all at 80% 1 RM. - 2minutes of rest between sets. 12 weeks aerobic exercise training: - 3 days/week for 45 min per session at an intensity	- PRE: 72h. (after resistance training) but before and after the start of a 12week aerobic intervention program. - POST: 72h. after resistance training and after a 12week	- Pax7: ✓ - CD56 (=NCAM): ✓ - MyoD: / - Myf5:✓ - Myogenin: / - Myonuclei (DAPI): ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	Fiber size, and fiber type distribution - Fiber cross sectional area of all fibers increased (3571 µm2 to 4313 µm2, P = 0.052), - MyHC I (3756 µm2 to 4430 µm2, P = 0.058) and MyHC IIa (3472 µm2 to 4183 µm2, P = 0.073) fiber cross-sectional area tended to increase. - MyHC IIa percentage tended to increase with cycle training (31% to 38%, P = 0.056) - MyHC I (53% to 49%, P = 0.07) and MyHC IIa/IIx (14% to 11%, P = 0.11) tended to decrease. Fiber type-specific and overall satellite cell responses to acute resistance exercise and endurance exercise training - Satellite cell changes in response to acute resistance exercise, and the effects of endurance training on that response. - MyHC I satellite cell density increased by 29% (0.068 ±0.021 to 0.088 ± 0.031 satellite cells per fiber) in the untrained state but declined by 13% in	The satellite cell and gene expression data presented here indicate that moderate intensity endurance cycle training modulates the response to acute resistance exercise, potentially conditioning the muscle for more intense concentric/eccentric activity. These data also provide further evidence that the cellular microenvironment influences satellite cell behavior in humans.

	doi:10.14814/phy2.12973	middle-aged women.		corresponding to 65% VO2max. Post 12-week intervention training: - Acute resistance exercise bout, subjects performed 10 min of light cycling as a warm-up. - 5 sets of 8 repetitions and a sixth set to volitional fatigue on the leg extension, all at 80% 1 RM. - 2 minutes of rest between sets.	aerobic intervention program.		the endurance trained state (0.102 ± 0.025 to 0.089 ± 0.020 satellite cells per fiber, acute resistance x training interaction, P < 0.05). - Satellite cell density in all fibers showed a trend for a similar pattern of satellite cell response as MyHC I fibers, but the interaction effect for satellite cell density in all fibers did not reach significance (P = 0.13). - MyHC I satellite cell density increased by 50% after endurance training (0.068 ± 0.021 to 0.102 ± 0.025 satellite cells per fiber, P < 0.05) and satellite cell density in all fibers increased by 32% (P < 0.05). - MyHC II satellite cell density did not change with acute resistance exercise or endurance training. - After endurance training, the number of satellite cells per muscle fiber cross- sectional area tended to increase in MyHC I fibers (19.6 ± 6.5 to 26.5 ± 7.7 satellite cells per mm2, P = 0.097), and remained stable in MyHC II fibers (17.2 ± 6.9 vs. 17.6 ±7.1 satellite cells per mm2, P > 0.05) as well as all fibers (17.9 ± 5.9 vs. 21.1 ± 7.1 satellite cells per mm2, P > 0.05).	
15	O'Reilly, C., McKay, B., Phillips, S., Tarnopolsky, M., & Parise, G. (2008). Hepatocyte growth factor (HGF) and the satellite cell response following muscle lengthening contractions in humans. Muscle Nerve, 38(5), 1434-1442. doi:10.1002/mus.21146	The purpose of this study was to investigate the response of HGF family members in the post-exercise period in the context of the muscle SC response	8 healthy, recreationally active men (age: 20.6 ± 2.1 yr.)	- 30 sets of 10 knee extensions ⇒ 300 maximal isokinetic unilateral eccentric contractions (lengthening) of the quadriceps femoris. -1minute rest between. -fixed velocity of 180°/s (using a Biodex dynamometer). -60° ROM.	- PRE - 4h. (T4) - 24h. (T24) - 72h. (T72) - 120h. (T120)	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: / - Myf5:/ - Myogenin: / - Myonuclei: ✓ - MHC I: / - MHC IIa/MHC IIx: / - SC number: ✓	Satellite cell enumeration: - NCAMcells, expressed as a percentage of total myonuclei, increased significantly at both T24 (36% increase vs. PRE) and T72 (80% increase vs. PRE). - The increase in NCAMcells (% total myonuclei) peaked at T72, which was significantly higher than PRE, T4, and T24. - NCAM cells expressed per 100 myofibers followed a similar trend by peaking at T72 [PRE vs. T72: 5.73± 0.59 vs. 14.19 ± 0.32 NCAMcells per 100 myofibers (P < 0.001)]. - NCAMcells (per 100 myofibers) were elevated above baseline at T24 (13.66 ± 0.28), T72, and T120 (12.54 ± 0.32; P < 0.001). - At T4, NCAMcells (%myonuclei or per 100 myofibers) were not different from PRE-values [PRE vs. T4: 3.90 ± 0.50 vs. 4.04±0.59% myonuclei (P = 0.99); and 5.73 ± 0.59 vs. 7.41 ± 0.67 NCAMcells per 100 myofibers (P = 0.094)]. - The number of nuclei per myofiber was not different at any time-point following lengthening contractions.	SCs were activated in human skeletal muscle as early as 24 h following an acute bout of eccentrically biased exercise. An increased number of NCAM-labeled cells were observed at 24 h (36% greater than PRE), which increased further at 72 h (80% greater than PRE) before decreasing at 120 h in the post-exercise period. ⇒ They conclude that a single bout of lengthening muscle contractions is sufficient to activate SCs, which may involve both a local and systemic HGF response to contraction-induced injury.
16	Snijders, T., Verdijk, L. B., Beelen, M., McKay, B. R., Parise, G., Kadi, F., & van Loon, L. J. (2012). A single bout of exercise activates skeletal muscle satellite cells during subsequent overnight recovery. Exp Physiol, 97(6), 762-773. doi:10.1113/expphysiol.2011.063313	The objective of the study was to determine the impact of a single bout of exercise on muscle fibre type-specific SC content and activation status following subsequent overnight recovery.	8 healthy, recreationally active men (age: 20 ± 1 yr.)	Cardio: - 10min. warming up on the cycle ergometer (50% Wmax). - 4 x 5 min cycle at 65% W max, alternating with 4 times for 2.5 min at 45% W max. - 5 min rest. Resistance training (upper and lower body): - UB = (chest-press, shoulder press and vertical lateral pull- down) 5 sets, 10 reps workload 40% of the total body weight. Resting period of 1 min between sets. - LB = (leg-press machine, horizontal leg press) 9 sets of 10 repetitions (3 sets at 55% of 1-RM, 3 at 65% 1-RM and 3sets of 75% 1-RM). 2 min rest periods between sets - 2 sets of 30 abdominal crunches. ⇒ Total work-out time = 120min.	- PRE - immediate after exercise - 9h. post exercise	- Pax7: / - CD56 (=NCAM): ✓ - MyoD: ✓ - Myf5: ✓ - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	Muscle fibre-type distribution and fibre area - No changes were observed in fibre-type distribution and/or muscle fibre size after 9h of post exercise recovery. - Muscle fibre area was significantly greater in type II compared with type I fibres (P < 0.05) Myonuclear number and satellite cell number - The number of myonuclei did not differ between type I and II muscle fibres. - Fibre area per nucleus was significantly larger in type II compared with type I muscle fibres (P < 0.05). - Satellite cell content was significantly higher in type I compared with type II muscle fibres (0.08 ± 0.01 versus 0.07 ± 0.01, respectively; P < 0.05). ⇒ in accordance, the number of SCs per square millimeter fibre area was significantly higher in type I compared with the type II muscle fibres (13.7 ± 1.4 versus 10.2 ± 1.0, respectively; P < 0.05). - No significant differences were observed in the number of SCs relative to the number of nuclei between fibre types. - The number of myonuclei and/or fibre area per nucleus did not change over time. - No significant changes were found in SC number per muscle fibre and per square millimeter fibre area over time. - Significant increase in the number of SCs when expressed relative to the number of nuclei in both type I and type II muscle fibres. Expression of mRNA - MyoD mRNA expression did not change following the single bout of exercise. - Myf5 mRNA expression tended (P = 0.088) to increase over time.	The present study shows that a single bout of combined resistance- and endurance-type exercise activates skeletal muscle SCs in both type I and II muscle fibres during subsequent overnight recovery in healthy, young men.

17	Toth, K. G., McKay, B. R., De Lisio, M., Little, J. P., Tarnopolsky, M. A., & Parise, G. (2011). IL-6 induced STAT3 signalling is associated with the proliferation of human muscle satellite cells following acute muscle damage. PLoS One, 6(3), e17392. doi:10.1371/journal.pone.0017392	The purpose of this study is to illustrate the potential of STAT3 signaling in promoting SC proliferation following acute muscle damage in humans. This study aimed to quantify SC localized p-STAT3 signaling over a time course.	12 healthy, but sedentary males (age: 21.2 ± 1.6 yr.)	- 300 maximal MLC. (muscle-lengthening contractions) - unilateral isokinetic eccentric contractions of the quadriceps femoris using a Biodex dynamometer. - 180°/s. - Over a 55° ROM.	- PRE - 1h. (T1) - 2h. (T2) - 24h. (T24)	- Pax7: ✓ - CD56 (=NCAM): ✓ - MyoD: / - Myf5:✓ - Myogenin: ✓ - Myonuclei (DAPI): ✓ - MHC I: / - MHC IIa/MHC IIx: / - SC number: ✓	- In response to acute muscle damage we observed a 26.6% increase in Pax7+ cells 24 hours following the MLC protocol. - Pax7+ cells per 100 myofibers increased from 15.5 at PRE to 19.6 ($P < 0.05$) 24 hours post exercise. When expressed as a percentage of total myonuclei we observed a 60.3% increase in satellite cell number (± 3% at PRE to ± 4.5% 24 hours post) ($P < 0.05$). -Myogenic regulatory factor 5 (Myf5), known for its role in SC proliferation was significantly up-regulated 1.8-fold 24 hours following the MLC ($P < 0.05$).	We demonstrate that IL-6 induction of STAT3 signaling occurred exclusively in the nuclei of SCs in response to MLC. An increase in the number of cMyc+ SCs indicated that human SCs were induced to proliferate under the control of STAT3 signaling.
18	Wilborn, C. D., Taylor, L. W., Greenwood, M., Kreider, R. B., & Willoughby, D. S. (2009). Effects of different intensities of resistance exercise on regulators of myogenesis. J Strength Cond Res, 23(8), 2179-2187. doi:10.1519/JSC.0b013e3181bab493	The specific aim of this study was to investigate the role, if any, that differing intensities of resistance exercise intensity has on markers of myogenesis and the expression of various genes involved in muscle hypertrophy.	13 recreationally active but nonresistance trained men (age: 21. ± 2.9 yr.)	2 separate bouts of resistance exercise separated by 2 weeks: - Bout 1: 65%1RM, 4 sets of 18–20 repetitions with 60–65% 1RM. 120 sec rest between sets and 150 sec rest between 2 exercises. - Bout 2: 85%1RM, 4 sets of 8–10 repetitions with 80–85% 1RM. 15-20 sec each set, 150 seconds of rest between sets and 150 seconds of rest between two exercises. → Cross-over design	- PRE; - 0.5h. (PST) - 2h. (2HPST) - 6h. (6HPST)	- Pax7: / - CD56 (=NCAM): / - MyoD: ✓ - Myf5: ✓ - Myogenin: ✓ - Myonuclei: / - MHC I: ✓ - MHC IIa/MHC IIx: ✓ - SC number: ✓	MHC Isoform mRNA Expression - No significant Intensity x Time interactions were observed for MHC I mRNA; MHC IIA mRNA and MHC IIX mRNA. - Significant main effects for time were observed for MHC I mRNA ($P = 0.028$), MHC IIA mRNA ($P = 0.008$), and MHC IIX mRNA ($P = 0.010$) - MHC I expression was significantly greater at 2HPST ($P = 0.032$) compared to PRE. -Compared to PRE, MHC IIA was significantly greater at PST ($P = 0.046$), 2HPST ($P = 0.012$), and 6HPST ($P = 0.048$). - MHC IIX, PST ($P = 0.041$) and 2HPST ($P = 0.015$) were significantly different from PRE. MRF mRNA Expression - No significant Intensity x Time interactions were observed for Myo-D, myogenin, MRF-4 and myf5. - Significant main effects for time were observed for Myo-D ($P = 0.001$), myogenin ($P = 0.001$), MRF-4 ($P = 0.002$), and myf5 ($P = 0.001$). - Myo-D expression was significantly greater at PST ($P = 0.001$), 2HPST ($P = 0.001$), and 6HPST ($P = 0.001$) compared to PRE. - Compared to PRE, myogenin was significantly greater at PST ($P = 0.001$), 2HPST ($P = 0.001$), and 6HPST ($P = 0.001$). - MRF-4, PST ($P = 0.021$) 2HPST ($P = 0.004$), and 6HPST ($P = 0.019$) were significantly different from PRE. - Compared to PRE, myf5 was significantly greater at PST ($P = 0.001$), 2HPST ($P = 0.001$), and 6HPST ($P = 0.002$).	For both intensities 65% 1RM & 85%1RM, MHC type IIX, IGF-1, IGF-R1, MGF, Myo-D, myogenin, MRF-4, and myf5 mRNA were all significantly increased in response to resistance exercise by 2 hours after exercise, whereas myostatin and the cyclin-dependent kinase inhibitor p27kip were decreased at 2 hours after exercise. Resistance exercise between 60–85% 1RM upregulates the mRNA expression of MHC and factors involved in myogenic activation of satellite cells while concomitantly decreasing expression of myogenic inhibitors.

Table 6A: Resistance training satellite cell content

Article	Sex	Age	N	Exercise protocol	Fiber type	PRE	24h	72h	96h	2w	4w	6w	11w	12w
Babcock, L et al., 2012	M	23 ± 1	8	RE= 4 sets 10 reps at 75%1RM AE/CE= 4 sets 10 reps 75% 1RM + 90 min of cycling (60% Wmax)	Mixed I II	SC/100FIBERS 6.13 ± 0.54 6.71 ± 1.42 6.09 ± 0.46			8.54 ± 1.11 8.90 ± 0.92 8.65 ± 1.51					
Cermak, N.M. et a.l, 2013	M	23 ± 1	9	15 sets 20 at - 30deg/s	Mixed I II	SC content = number of SC per fiber 0.085 ± 0.012	no changes 0.133 ± 0.016*							
Crameri, R. M. et al., 2004	M	25 ± 3	8	-50 one-leg 'drop down' jumps -8 sets 10 reps at - 30deg/s -8 sets of 10 reps at -180deg/s	Mixed	n.a.								
Hanssen, K. E. et al., 2013	M	26 ± 2	24	3L-1UB: - 3 sets: leg press, leg extension and leg curl. - 1 set: seated chest press, seated rowing, latissimus pull- down, biceps curl and shoulder press. <->1UB-3L	Mixed	SC/fiber 0.14 ± 0.01				37 ± 7%			44 ± 7%	
Herman-Montemayor, J. R. et al., 2015	F	21.1± 2.7	34	Slow speed: - 10-sec con/4-sec ecc 6–10RM. (40–60% 1RM). Traditional speed:: - 1-2s conc/ecc contractions for 6–10 reps to failure at 80–85% 1RM Traditional muscular endurance: - 1-2s of con/ecc contractions at 40–60% 1RM	Mixed I IIa IIx	%SC's (TS group only) 3.7 ± 2.0 3.9 ± 1.5 2.4 ± 1.0						%SC's (TS group only) 7.3 ± 3.6* 7.8 ± 1.8* 6.5 ± 2.6*		
Hyldahl, R. D. et al., 2014	M	22.6 ± 2	14	Conc: 60.sec−1 90° - 20° of knee flexion, total ROM of 70°. Eccentric: 120°.sec−1, resist lever from 40° of knee flexion to 115° of knee flexion, a total ROM of 75°. Total 40 kJ ecc and con.	Mixed I	ECC pre 0.101 ± 0.031 CON 0.099 ± 0.027 * ECC 0.08 ± 0.039 CON 0.107 ± 0.33	ECC 0.127 ± 0.041 (27%)* CON 0.102 ± 0.029* ECC 0.104 ± 0.046 CON 0.096 ± 0.063							

					II	ECC 0.106 ± 0.027 CON 0.10 ± 0.053	ECC 0.133 ± 0.056 CON 0.117 ± 0.055							
Kadi, F. et al., 2004b	M	24 ± 1	15	4–5 series of 6–12 repetitions, corresponding to 6–12 RM.	/	SC content n.a.					↑19.3%*			↑31.4%*
Mackey, A. L. et al., 2011	M	25 ± 3	12	HI: 10 sets 8 reps at 70% 1RM LI: 10 sets 36 reps at 15% 1RM	Mixed	SC/100 fibers HI: 0.20 ± 0.27 LI: 0.14 ± 0.13								HI: 0.17 ± 0.28 LI: 0.31 ± 0.58
McKay, B. R. et al., 2008	M	20.6 ± 2.1	8	10 sets 30 reps ecc at -180deg/s	/	n.a.								
O'Reilly, C. et al., 2008	M	20.6± 2.1	8	10 sets 30 reps ecc at 180deg/s	Mixed	SC/100 fibers 5.72 ± 0.59 SC/total myonulcei	13.66 ± 0.28* ↑36%*	14.19 ± 0.32* ↑80%*						
Toth, K. G. et al., 2011	M	21.2 ±1.6	12	10 sets 30 reps ecc at -180deg/s	/	Overall sc activity Pax7+/100 15.5 Total myonuclei %	26,6% 9.6* 60.3%							
Wilborn, C. D. et al., 2009	M	21 ± 2.9	13	4 sets 19 reps at 65% 1RM 4 sets 9 reps at 85% 1RM	Mixed, I & II	n.a.								

* Significant difference found ($P < 0.05$)

Table 6B: Endurance training satellite cell content

Article	Sex	Age	N	Exercise protocol	Fiber type	PRE	1-5'	72h	96h	1w	12w
Babcock, L et al, 2012	M	23 ± 1	8	AE: 90 min of cycling (60% Wmax)	Mixed I II	6.18 ± 1.22 6.67 ± 1.49 5.62 ± 0.22			6.09 ± 0.42* 4.95 ± 0.65* 6.66 ± 0.55		
Joanisse, S. et al, 2015	M+ W	21 ± 4	16M 3W	- SIT-2: 4x/week (6 wk) 8 x 20-s intervals at 170% of VO2peak separated by 10 s of rest (self-selected cadence) - MICT: 30 min of continuous cycling at 65% of VO2peak	SIT-2: I II MICT: I II	(SC/100fibers) 10.7 ± 5.5 7.2 ± 2.8 9.2 ± 3.7 8.8 ± 3.5		 11.5 ± 6.7 9.2 ± 5.7 7.5 ± 4.2 9.3 ± 3.5			
Kadi, F. et al, 2004a	M+ W	26 ± 5	4M 1W	Right (one-)leg cycling at a pedalling rate of 60 rpm to different exercise intensities: 40% and 75% of the one-leg VO2 max. The total duration exercise 30 min.	/						
Macaluso, F. et al, 2013	M	24 ± 2	8	Downhill running (DHR): 5-min warm up, 40-min intermittent downhill run, (5 sets of 8-min bouts of running with a slope of 10% (-5.7° slope) on a treadmill. 2-min standing rest between bouts. (Speed treadmill was at 80% of each individual's own peak treadmill speed.)	Mixed	(SC/fiber) 0.065 ± 0.020				0.082 ± 0.014*	
Macaluso, F. et al, 2012	M	24 ± 3	8	5-min warm-up, test which started at 10 km/h after which the speed increased 0.5 km/h every 30 s until exhaustion.	Mixed		(SC/fiber) 0.056 ± 0.022				
Murach, K. A. et al, 2016	W	56 ± 5	7	3x/week (12wk), 45 min/ session at 65% VO2max.	I		(SC/fiber) 0.068 ± 0.021				0.102 ± 0.025 (50%)*

* Significant difference found ($P < 0.05$)

PART 2: RESEARCH PROTOCOL

1. Introduction

Satellite cells are skeletal muscle precursor cells and facilitate muscle fiber repair, adaptation and regeneration following physiological (Parise et al., 2008) and pathological stimuli (Murphy et al., 2011). Under normal conditions, these satellite cells are mitotically quiescent. Injury of the muscle fiber causes activation, proliferation (slow and fast), fusion, early differentiation of the satellite cells to myoblasts, then to myocytes and in the late differentiation to myofibers (Almeida et al., 2016). These processes involve inflammatory responses, myofiber necrosis (in severe condition) and the self-renewing of the satellite cells. Satellite cells are examined via muscle biopsies. These muscle biopsies are placed under the microscope and the satellite cells are stained (immunostaining), this is called immunofluorescent microscopy. Using this technique, we can study the processes of satellite cells using specific markers. A characteristic of human satellite cells is their expression of the Pax7 gene (Bellamy et al., 2014; Cermak et al., 2013; Farup, Rahbek, Knudsen, et al., 2014; Farup, Rahbek, Riis, et al., 2014; Fry et al., 2014; Joanisse et al., 2013; Mackey, 2013; Mackey, Andersen, et al., 2011; Mackey, Esmarck, et al., 2007; Mackey, Holm, et al., 2011; Mackey et al., 2014; Mackey et al., 2009; McKay et al., 2008; McKay et al., 2013; McKay et al., 2012; Menon et al., 2012; Nielsen et al., 2012; Snijders et al., 2014; Toth et al., 2011; Walker et al., 2012). This gene is mostly used to identify muscle satellite cells, although others exist such as NCAM and CD56 (Charifi et al., 2003; Crameri et al., 2007; Crameri et al., 2004; Dreyer et al., 2006; Kadi et al., 1999; Kadi, Johansson, et al., 2004; Kadi, Schjerling, et al., 2004; Kadi & Thornell, 2000; Lindstrom et al., 2010; Mackey, Andersen, et al., 2011; Mackey, Esmarck, et al., 2007; Mackey et al., 2014; Mackey et al., 2009; Mackey, Kjaer, et al., 2007; O'Reilly et al., 2008; Petrella et al., 2006; Snijders et al., 2014; Verdijk et al., 2014; Verdijk et al., 2016; Verney et al., 2008). Other proteins called myogenic regulatory factors orchestrate the process of satellite cell activation to fusion or congregation. The most important regulatory factors are MyoD, Myf5 and Myogenin. These factors together with Pax7 can be used to determine the phase of myoblast formation.

The role of satellite cells in Multiple Sclerosis is a new topic in a little explored research domain.

Multiple Sclerosis (MS) is an auto-immune demyelinating disorder of the central nervous system that mostly affects young middle-aged adults. There are different forms of the disease including relapsing-remitting, secondary progressive and primary progressive depending on the time course and inflammatory surge. MS is characterized with neurodegeneration, inflammation, axonal demyelination and transaction problems. The chronic course of this disease can result in significant mental and physical symptoms and irreversible neurologic deficits including muscle weakness, tremor, ataxia, spasticity, paralysis, balance disorder, cognitive impairment, dysfunctions of vision, vertigo, impaired swallowing and speech, sensory deficits, incontinence, bowel dysfunctions, pain, fatigue, and depression (Halabchi, Alizadeh, Sahraian, & Abolhasani, 2017). The treatment consists mainly of disease-modifying drugs against inflammation, neurodegeneration, pain, motor impairments, etc.

Recent research also indicates positive effects on a non-pharmacological level with physical therapy by exercise interventions. Exercise training limits the deconditioning process and activates the patients

which provides many physical and mental health benefits (Halabchi et al., 2017). Most therapists tend to focus on physical and neurologic deficits only, and thus prefer to prescribe rehabilitation programs specifically to counteract these deficits. In addition to the positive effects, MS patients also experience muscular, cardiac, ventilatory and metabolic dysfunction which significantly contribute to exercise intolerance. These anomalies may also increase the risk for frequent hospitalization and morbidity and can reduce life expectancy. For this the MS patients must be screened in order to detect anomalies to prescribe the best possible exercise training intervention (Wens, Eijnde, & Hansen, 2016).

It is known that resistance type exercise training provides muscle hypertrophy that is associated with a larger satellite cell content (Babcock et al., 2012; Cermak et al., 2013; Crameri et al., 2004; Hanssen et al., 2013; Herman-Montemayor et al., 2015; Hyldahl et al., 2014; Kadi, Schjerling, et al., 2004; Mackey, Holm, et al., 2011; McKay et al., 2008; O'Reilly et al., 2008; Toth et al., 2011; Wilborn et al., 2009). When type of muscle contraction was examined, results show that eccentric but not concentric muscle contractions resulted in functional and histological evidence of muscle damage that is accompanied by increased satellite cell activity post-exercise in men (Cermak et al., 2013; Crameri et al., 2004; Hyldahl et al., 2014; McKay et al., 2008; O'Reilly et al., 2008; Toth et al., 2011).

Within this protocol, the focus is mainly on resistance training in persons with Multiple Sclerosis in comparison to healthy individuals. We want to provide insights in the most ideal resistance training stimulus that is being safe and adapted for the patient. The satellite cell response is investigated based on this resistance stimulus.

2. Aim of the study

This master thesis is part of a broader research project, a doctoral study on satellite cells, led by Mr. Sjoerd Stevens at the rehabilitation research center REVAL of UHasselt. The aim of the study is to investigate and compare the satellite cell response between healthy individuals and a population diagnosed with multiple sclerosis. The comparison is twofold, the first part is type of intervention and the corresponding satellite cell response in high resistance exercise training and a no-intervention (rest) control group. The second part is the investigation for a possible correlation between satellite cell response in adults with Multiple Sclerosis compared to a healthy control group.

2.1. Research question

“What is the effect of a single bout of high intensity resistance training in comparison to a no-training intervention on the number of satellite cells within skeletal muscle fibers (fast - and slow twitch) in healthy adults in comparison to adults with Multiple Sclerosis between 18-65 years old?”

2.2. Hypotheses

First hypothesis (H1): Satellite cell response is significantly greater for a high-intensity eccentric training program in comparison to a no-intervention (rest) program in a healthy adult population.

The first hypothesis is based on the prior composed literature study and very likely since it has been shown in several studies (Cermak et al., 2013; Crameri et al., 2004; Hyldahl et al., 2014; McKay et al., 2008; O'Reilly et al., 2008; Toth et al., 2011).

Second hypothesis (H2): Satellite cell response is significantly lower for a high intensity eccentric training program compared to no-intervention (rest) in adults with Multiple Sclerosis.
This second hypothesis is based on the idea that MS, a chronic inflammatory disease, and it's response to exercise can vary in inflammatory responses in comparison to healthy persons, this may reduce the satellite cell response and encourage fibrosis. Inflammatory-related problems that are present in ms may have a negative influence on muscle regeneration and repair and will not occur in the same manner for adults with Multiple Sclerosis as for healthy controls (Ploeger, Takken, de Greef, & Timmons, 2009). However exercise is considered as a safe and effective mean of rehabilitation in MS patients. Research on MS has shown that training programs adjusted to the individual can improve fitness, functional capacity and have a positive effect on the modifiable impairments (Gutierrez et al., 2005; Kjolhede, Vissing, & Dalgas, 2012; Surakka et al., 2004; White et al., 2004).

Third hypothesis (H3): Baseline number of satellite cells for healthy adults and adults with Multiple Sclerosis significantly greater in healthy adults compared to Multiple Sclerosis patients.
The third hypothesis is based on the so far known physiological profile of MS patients. Indirectly the reduced aerobic capacity and an average of 30% decrease in cardiorespiratory fitness (Feltham et al., 2013; Gallien et al., 2007; Sandoval, 2013; White et al., 2004) can play a role. Satellite cells from the vastus lateralis skeletal muscle are investigated and retrieved from biopsies. Multiple Sclerosis is often accompanied by a decrease in muscle strength and endurance capacity, specifically the lower extremities are affected by this defect (Dalgas, Stenager, & Ingemann-Hansen, 2008; White et al., 2004). Total muscle mass is reduced and muscle atrophy is often clear (Dalgas et al., 2008; Formica, Cosman, Nieves, Herbert, & Lindsay, 1997; Lambert, Lee Archer, & Evans, 2002; Sandoval, 2013) in Multiple Sclerosis patients. The reasons mentioned above can all contribute to possible differences in the number of satellite cells, fiber-specific distributions between a healthy population and a population diagnosed with Multiple Sclerosis.

Fourth hypothesis (H4): Satellite cell response after an eccentric training program is significantly lower for the healthy population compared to patients with Multiple Sclerosis.
The fourth hypothesis is based on the same idea as the second hypothesis, that MS and the inflammatory-related problems that are present in ms may have a negative influence on muscle regeneration and repair and so will not occur in the same manner for adults with Multiple Sclerosis as for healthy controls (Ploeger et al., 2009). It may also be possible that the degree of recovery can be significantly different, due to the reduced aerobic capacity and decrease in cardiorespiratory fitness in persons with MS (Feltham et al., 2013; Gallien et al., 2007; Sandoval, 2013; White et al., 2004). Little or no data or previous research has been done on this topic hence makes it difficult to predict.

3. Methods

3.1. Research design

A randomized controlled trial is set up. Two groups are formed ‘healthy adults’ and ‘Multiple Sclerosis patients’. The aim is to recruit a minimum of 20 adults (both male and female) for each group. The goal is to have an age-spread sample ranging from 18 to 65 years old. Left and right leg are randomly assigned which leg becomes the intervention or control leg. After recruitment, participants are screened and baseline characteristics are established which include age, height, weight, BMI, fitness level and 1-RM strength test, performed on a Biodex. A familiarization protocol will take place one week before the intervention. One hour before the exercise bout of eccentric training or rest (contralateral leg) muscle biopsy will be obtained, post-measurements are taken at 24, 72 and 96 hours. Guidelines for nutrition and physical activity during the course of the study are communicated to the participants. Effect assessors are blinded.

3.2. Participants

Healthy men and women aged between 18-65 years old in one group and men and women with MS aged between 18-65 years old in the other group.

3.2.1. Inclusion criteria

- Human population.
- Age participants between 18-65 years old.
- Healthy individuals.
- Patients with MS.
- Quadriceps manual muscle strength score 5.

3.2.2. Exclusion criteria

- BMI > 25.
- Other pathologies than MS (diabetes, cancer, cardiovascular diseases, pulmonary diseases and metabolic diseases).
- Resistance training performed in the last two weeks before the exercise protocol.

3.2.3. Patient recruitment

- University of Hasselt.
- MS hospital Overpelt.

3.3. Intervention

For the MS population in the protocol a multidisciplinary screening of the patient performed by a physical therapist, a rehabilitation physician and a psychologist all with proper expertise on MS patients. The screening for the MS participants but also the healthy participants should include an anamnesis in combination with a clinical examination. All participants should be screened for risk factors, red flags and yellow flags but also cardiovascular, respiratory and metabolic disorders.

The next step is to use a proper fitness test like 1-RM testing on a Biodex to measure the baseline values for resistance training. Subjects will be reported one week before the start of the protocol to the laboratory to become familiar with the experimental protocol and the Biodex device.
When performing the resistance training protocol, patients will be supervised by a physical therapist. It has been shown that supervision when performing strength training is more effective than non-supervised training (Dalgas et al., 2008; Mazzetti et al., 2000).
For the 24 hours preceding exercise and the day of the trial, the subjects consumed a standard diet and abstained from alcohol, caffeine, tobacco and additional exercise.
The exercise protocol consists of a warming-up, a resistance training bout and a cooling-down. The warming-up starts with 15 minutes of cycling on the ergometer against 20 Watt.
Training intensity should be set on 15 sets of 20 repetitions at 80% of 1repetition maximum (RM) with 30 seconds rest interval. In total 300 high-force eccentric contractions of one randomized knee extensor performed on the isokinetic dynamometer Biodex system 4 Pro^{TM}. The contralateral leg serves as a control group. Consistent verbal encouragement will be provided throughout each repetition.
Percutaneous muscle biopsy samples will be obtained by a doctor from the exercised and non-exercised (control) leg. A standardized depth and distance from the middle region of the vastus lateralis muscle 10 cm above the patella and approximately 2 cm deep to the fascia will be executed. One muscle biopsy will be obtained one hour before the start of the resistance training protocol and the others 24, 72 and 96 hours after performing the eccentric resistance training. Immediately after removal, the biopsy sample was frozen at -80°C for subsequent histochemical analysis to determine myocellular characteristics. To minimize the potential for inflammation arising from the biopsy procedure itself, biopsies are collected from separate incisions at least 3 cm distal from previous biopsy incisions in the same leg.
Immunohistochemical analysis performed by blinded assessors under immunofluorescence microscopy. Muscle cross sections are stained for satellite cell content and activation status using the following markers: Pax7, NCAM, CD56, MyoD, Myf5 and myogenin.

3.4. Outcome measures

3.4.1. Primary outcome measures

Number satellite cells: Pax7 or CD56/NCAM in healthy and MS participants in control and intervention leg.

3.4.2. Secondary outcome measures

MyoD, Myf5, Myogenin, Myosin heavy chain isoforms I, IIa, IIx and myofiber size/type distribution. Differences between healthy individuals and Multiple Sclerosis patients. Differences between eccentric training intervention and the control (rest).

3.5. Data analysis

Compare satellite cell response between the types of intervention (eccentric training and rest).
Possible differences in satellite cell response (number of SC's) between a healthy population and MS patients at baseline, 24, 72 and 96 hours. Look for a potential correlation for the above mentioned data.

Data analysis with ANOVA for between-group differences and Mixed-models for the repeated and dependent measurements.

4. Time planning

The study will be executed from September 2018 till February 2019.

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VOORTGANGSFORMULIER WETENSCHAPPELIJKE STAGE DEEL 1

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
27/10	- Bespreking onderwerp - Opstel PICO	Promotor: Copromotor: Student(e): Student(e):
29/11	- Overlopen: • PICO • In- en exclusiecriteria • Zoekstrategie	Promotor: Copromotor: Student(e): Student(e):
22/01	- Presentatie zoekstrategie	Promotor: Copromotor: Student(e): Student(e):
12/03	- Presentatie introductie, materiaal en methoden.	Promotor: Copromotor: Student(e): Student(e):
03/04	- Methode - Data-extractie - Kwaliteitscontrole	Promotor: Copromotor: Student(e): Student(e):
13/04	- Data-extractie - Outcomes - Bespreking resultaten tabellen	Promotor: Copromotor: Student(e): Student(e):
26/04	- Resultaten - Discussie - Protocol	Promotor: Copromotor: Student(e): Student(e):
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ZELFEVALUATIERAPPORT **WETENSCHAPPELIJKE STAGE - DEEL 1** **RWK**

Naam & Voornaam STUDENT: Nuyan Gillen

Naam & Voornaam (CO)PROMOTOR & PROMOTOR: PhD Femke Vandenabeele en dr. Anouk Aptem

TITEL masterproef (Nederlandstalig of Engels): The effect of exercise training on volleyball cell response within skeletal muscles.

LITERATUURSTUDIE	Gestelde deadline	Behaald op	Reflectie
De belangrijkste concepten en conceptuele kaders van het onderzoekdomein uitdiepen en verwerken	7/10/17	7/10/17	zeer goed
De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie	29/11/17	29/11/17	zeer goed
De opzoekbare onderzoeksvraag identificeren en helder formuleren in functie van de literatuurstudie	29/11/17	29/11/17	goed
De zoekstrategie op systematische wijze uitvoeren in relevante databanken	22/01/18	22/01/18	zeer goed
De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren	13/04/18	13/04/18	zeer goed
De data-extractie grondig uitvoeren	13/04/18	13/04/18	zeer goed
De bevindingen integreren tot een synthese	20/05/18	20/05/18	goed

Behaald

ONDERZOEKSPROTOCOL	Gestelde deadline	Behaald op	Reflectie
De onderzoeksvraag in functie van het onderzoeksprotocol identificeren	26/04/18	26/04/18	zeer goed
Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign	10/05/18	10/05/18	zeer goed
De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken	15/05/18	15/05/18	goed

Behaald

ACADEMISCHE SCHRIJVEN	Gestelde deadline	Behaald op	Reflectie
Het abstract tot he point schrijven	15/05/18	15/05/18	zeer goed
De inleiding van de literatuurstudie logisch opbouwen	12/03/18	12/03/18	goed
De methodesectie van de literatuurstudie transparant weergegeven	03/04/18	03/04/18	goed
De resultatensectie afstemmen op de onderzoeksvragen	26/04/18	26/04/18	zeer goed
In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren	26/04/18	26/04/18	zeer goed
Het onderzoeksprotocol deskundig technisch uitschrijven	15/05/18	15/05/18	zeer goed
Referenties correct en volledig weergeven	20/05/18	20/05/18	zeer goed

Behaald

ZELFSTUREND EN WETENSCHAPPELIJK DENLEN EN HANDELEN	Aanvangsfase	Tussentijdse fase	Eindfase
Een realistische planning opmaken, deadlines stellen en opvolgen	goed	goed	zeer goed
Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage	zeer goed	zeer goed	zeer goed
Kritisch wetenschappelijk denken	zeer goed	zeer goed	zeer goed
De contacten met de promotor voorbereiden en efficiënt benutten	goed	goed	zeer goed
De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen	goed	goed	zeer goed

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KNOWLEDGE IN ACTION

De communicatie met de medestudent helder en transparant voeren	goed	zeer goed	zeer goed
De communicatie met de promotor/copromotor helder en transparant voeren	zeer goed	zeer goed	zeer goed
Andere verdiensten:			