DR.SC.-01 REQUEST FOR APPROVAL OF THE DISSERTATION TOPIC[1]			
GENERAL INFORMATION AND PERSONAL CONTACT INFORMATION OF THE DOCTORAL CANDIDATE			
First and last name, and title of the doctoral candidate:	Girgis Kalim Assaf		
Provider of the study programme:	Faculty of Kinesiology, University of Zagreb, Croatia		
Name of the study programme:	Doctoral study: Kinesiology		
Scientist ID of the doctoral candidate:	12733822179 homeland number		
Approval of topic for acquiring a PhD *(please fill in*	X within programme-based doctoral study	☐ on the basis of scientific achievement	☐ Dual doctorate (Cotutelle de these)
First and last name of mother and/or father:	Moulouk Licha / Kalim Assaf		
Date and place of birth:	25.10.1981, Kourayat, Lebanon		
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CURRICULUM VITAE OF THE DOCTORAL CANDIDATE			
Education *(in chronological order, with most recent first)*:	• Université Antonine Masters (5 years), Physical Education, Specialization In Performance and Health, 2006 • European diploma for strength and conditioning, Claude Bernard Lyon 1 (France), La Scuola Universitaria interfacolta in Science Motorié, Turin University(Italy), Lausanne Univesity (Suisse), Bruxelles University (Belgique): Graduated with high honors/major of promotion 2006		
Work experience *(in chronological order, with most recent first)*:	• Director of the European Diploma for strength and conditioning at Université Antonine (UA) in Lebanon in collaboration of three European universities: Claude Bernard Lyon1 France, Université de Lausanne and Université Libre de Bruxelles, 2005 to Present • Co-Founder and Technical director of Performance First Heath Club : First Club that provide athletes total physical assessments 2008 to Present • Co-Founder and Director of Sports Academy School: First Technical Baccalaureate in		

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[1] Please name file as: DR.SC.-01 – Last name and first name of Doctoral Candidate.doc
Please send the filled -out form DR.SC.-01, in electronic and written format, and signed, to the appropriate Registrar's Office.

	physical education in Lebanon 2015 to Present **GRADUATE COURSES TAUGHT** ● Periodization of training in Basketball, Claude Bernard Lyon1 France, 2015 to Present ● Applied Strength and Conditioning UA, 2007 to Present ● Methodology/ Periodization of training, 2007 to Present ● Performance Evaluation tests, 2007 to Present ● Techniques of Physical Fitness Assessment, 2007 to Present ● Training for Speed, Agility And Quickness,2007 to Present ● Strength and conditioning for soccer: Saudi Arabia, 2013 to Present ● Concepts of Fitness, Strength of Periodization, Military University 2013-14
Bibliography and active participation in conferences:	

TITLE OF THE PROPOSED TOPIC	
Croatian:	Učinci oporavka u hiperoksiji nakon intervalnog treninga visokog intenzitetau hipoksiji na transportni sustav za kisik i aerobne sposobnosti
English:	The effects of hyperoxic recovery following high intensity interval training in hypoxia on blood oxygen transport parameters and aerobic capacity.
Title in the language of the dissertation (if it is not Croatian or English)	The effects of hyperoxic recovery following high intensity interval training in hypoxia on blood oxygen transport parameters and aerobic capacity.
Area/field/branch (if the doctoral study is performed in a branch)**:**	Sports training

PROPOSED OR POTENTIAL MENTOR(S)

(name the second mentor in case of interdisciplinary research or if there is another reason for more than one mentor)

	First name and last name, title:	**Institution, country:**	**E-mail:**
First mentor:	prof. Lana Ružić, MD, PhD	University of Zagreb, Faculty of Kinesiology	lana.ruzic@kif.hr
Second mentor:			

MENTOR'S COMPETENCES – list of up to five relevant works published in the last five years

First mentor:	1. Sedlaček M 1, Ružić L 1, Cigrovski V. The effects of aerobic exercise in ski beginners at altitudes of 1250-2000m on blood oxygen transport parameters. Dtsch Z Sportmed. 2019; 70: *in press.* 2. Ruzic L, Cigrovski Berkovic M, Starcevic H, Lovrić D, Matković B.R. Male sex hormones response after a month long Himalayas trek in relation to hemoglobin oxygen saturation. Kinesiology, 2018; 50(2);157-164. 3. Orepic P, Mikulic P, Soric M, Ruzic L, Markovic G. Acute physiological responses to

recreational in-line skating in young adults. Eur J Sport Sci. 2014;14 Suppl 1:S25-31.
4. Radman I, Wessner B, Bachl N, Ruzic L, Hackl M, Prpic T, Markovic G. The acute effects of graded physiological strain on soccer kicking performance: a randomized, controlled cross-over study. Eur J Appl Physiol. 2016;116(2):373-82.
5. Vuletic L, Spalj S, Rogic D, Ruzic L, Alajbeg I. Effect of L-arginine dietary supplementation on salivary urea concentration and pH in physically active individuals. Aust Dent J. 2013;58(4):491-7.

Second mentor:

TOPIC OUTLINE

Summary in Croatian *(no more than 1000 characters with spaces):*

Sportski stručnjaci i treneri traže uvijek nove načine za poboljšanje izvedbe sportaša. Između različitih komplementarnih metoda treninga važno mjesto zauzimaju i hipoksične i hiperoksične metode. Hiperoksija je prethodno bila rezervirana samo za posebne klinike, ali je razvoj opreme koja se može koristiti na licu mjesta učinio njenu upotrebu dostupnom sportašima. Cilj ovog istraživanja je utvrđivanje učinaka intervalnog treninga visokog intenziteta (HIIT) u hipoksičnim uvjetima, nakon čega slijedi faza oporavka u hiperoksičnim uvjetima, kako bi se utvrdilo je li postoje povoljni učinci dodanih hiperoksičnih uvjeta u oporavku na aerobne sposobnosti i transportni sustav za kisik. Istraživanje će obuhvatiti 48 sportaša, u dobi između 18 i 20 godina, podijeljenih u 3 skupine, prema protokolu intervencije: visoko intenzitetni intermitentni trening u hipoksiji nakon čega slijedi oporavak u hiperoksiji ili za drugu grupu u normoksiji te treću kontrolnu skupinu. Uzorci krvi će se prikupljati od ispitanika prije i deset dana nakon ispitivanja kako bi se odredili pokazatelji iz crvene krvne slike tj. oni vezani uz transport kisika. Također će prije i nakon intervencije provesti mjerenje maksimalnog primitka kisika i time izmjeriti pokazatelji vezani uz aerobne sposobnosti . Intervencija će trajati 4 tjedna, a ispitanici dvije eksperimentalne skupine će trenirati 3x tjedno. Učinci kombinacije hipoksije, hiperoksije i HIIT-a nikada nisu proučavani u vezi s pokazateljima prijenosa kisika u krvi i aerobne izvedbe u sportaša. Stoga će ova studija doprinijeti biti korak saznanjima i programiranju treninga, osobito u disciplinama izdržljivosti, a u slučaju da se pozitivni učinci hiperoksije pokažu nepostojeći, to će uštedjeti novac sportašima i sportskim klubovima koji su stalno pod pritiskom tvrtki koje proizvode uređaje za hiperoksični trening.

Summary in English *(no more than 1000 characters with spaces):*

For a long time, sports experts and coaches have been looking for new ways to improve the athlete's performance in any given sport. Many methods were created, among which the hypoxic and hyperoxic training methods are recently becoming more and more popular. Hyperoxia was previously reserved to special clinics but development of the "on the spot" equipment made it more available to athletes. The aim of this study is to determine the possible enhancing effect of the added hyperoxic conditions during recovery after high-intensity interval training (HIIT) in hypoxic conditions. The study will include 48 athletes, between the ages of 18 and 20, divided into 3 groups according to the intervention protocol: high intensity intermittent training in hypoxia followed by a recovery in hyperoxia (or in normoxia for the other experimental group) and also a control group. The blood samples will be collected from the subjects before and ten days after the

intervention to measure the red blood cell parameters (oxygen transport related parameters). The aerobic capacity measured by all- out- treadmill test will also be determined before and after the intervention. The intervention will last 4 weeks and the subjects in two training groups will train 3x a week. The effects of combination of hypoxia, hyperoxia and HIIT has never been studied in regard to blood oxygen transport and aerobic performance in athletes. Therefore, this study, if it yields positive results, will be a step forward in the training process of many athletes, especially in endurance disciplines. In case that the positive effects prove to be non-existent, it will save money to many athletes and sports clubs who are constantly under the pressure of hyperoxia-product companies.

Introduction and overview of research conducted hitherto *(suggested length: 7000 characters with spaces)*

A lot of pressure is put on elite athletes to perform to the limits of their performance abilities in order to achieve outstanding results. The competitiveness among athletes, teams and countries has never been fiercer. Since doping is illegal, coaches and sports experts have long searched for various alternative ways to improve an athlete's performance legally. In the late sixties, and later especially in the nineties, a major attention was brought to a new method of training, known as "altitude training", and subsequently to its opposite, "hyperoxic training". Both those techniques were said to improve sea-level performance and endurance, especially in power sports (Lundby et al. 2012). The use of hypoxic and hyperoxic training has not beenconsidered illegal, and therefore, throughout the years, multiple variables of both have been developed to benefit the widest range of athletes across different sports.

Hypoxic training is a training method executed at high altitudes in training camps or in a simulated hypoxic environment (Feriche et al., 2014). Over the years, hypoxic training developed into multiple protocols, namely: Live high- train high (LHTH), Live high- train low (LHTL), Intermittent Hypoxic Exposure (IHE), and Intermittent Hypoxic Training (IHT) (Millet et al., 2010), as well as Repeated Sprint Training in Hypoxia (RSH). Although these five methods each have their own characteristics, they do share some common ground. The ideal altitude at which to conduct training is set between 2200 meters and 2500 meters and the exposure ought to last four weeks, for twelve hours a day (Millet et al. 2010). However, the results may start to be noticed starting day 18 (Millet et al. 2010). Those methods are all different and have different effects on the body and the performance.

The Live high-train high technique is considered one of the oldest and most famous forms of altitude training. Notable experiments were conducted on LHTH, such as one conducted by Mellerowicz, who gathered twenty-two East German police officers and exposed some of them to an altitude of 2020m for four weeks, while the others lived and trained at sea-level. The results showcased that the group living at altitude undoubtedly had a great boost in its running performance and their VO_{2max} increased significantly compared to the sea-level group. Mellerowicz was therefore able to prove that the LHTH trial is effective (cit. in Lundby et al. 2012).

The second technique is the Live high- train low technique (LHTL). Many experiments based on the LHTL method had also been conducted, the most notable being Levine et al. (2008). This method is favoured among others because the athlete doesn't have to change their training regimen or intensity. Their regular training at sea-level will remain unchanged. Levine et al. concluded that LHTL is an effective method for elite athletes. Indeed, the experiment consisted of athletes living for twenty-seven days at 2500m and training at 1250m, and the results were very promising: a rise in aerobic performance, as well as in O_2 transport capacity.

Intermittent Hypoxic Exposure (IHE) is the third technique in altitude training. It consists of exposure to hypoxic air at rest. Julian et al. (2004) conducted such an experiment, and the results were disappointing. IHE lead to no boost in any of the factors related to performance. But more experiments are needed in order to cement this conjecture.

Intermittent Hypoxic Training (IHT) is also known as Live low- train high. It is the exact opposite of LHTL: athletes live at sea-level, but train at higher altitudes. There is also a variation of this technique known as Voluntary Hypoventilation. Athletes simulate hypoxia by holding their breaths and keeping their inhalations at low volumes. According to Woorons et al., reducing breathing

frequency is effective in boosting anaerobic performance. IHT proved to have many benefits. First of all, compared to actual training in high altitudes, IHT doesn't force the athlete to change their training environment nor lifestyle, and it allows for muscle excitability to remain unchanged at sea-level. After experiments on different groups, it was noticed that IHT increased the performance of swimmers, cyclers, and runners compared to the normoxia training group results. One can thus conclude that IHT boosts performance compared to training in regular sea-level conditions. (Faiss et al. 2013). Last but not least, Repeated Sprint Training in Hypoxia (RSH). RSH is another training method that promises performance boosts. Indeed, RSH is identical to the performance demanded of athletes during matches, where they are required to perform intense effort during short spouts of time (Czuba et al. 2013). The additional benefits of altitude training are an increase in the maximal aerobic exercise capacity, exercise economy and increased muscle buffering capacity (Kasai et al., 2015,Millet et al, 2010).

On the other hand, in hyperoxic training the athletes are exposed to air that contains a high percentage of oxygen. Hyperoxia has been the focus of multiple studies as well, but it was not studied as much as hypoxia in regard to athletic performance. In one study the cyclists performed the exercise under hyperoxia (F_iO_2=0.36) and the others under normoxic conditions (F_iO_2=0.21). The study, which is a single-blinded, randomized, control trial, concluded that time to exhaustion is longer for the hyperoxic group compared to the normoxic group, and although the S_aO_2 levels decreased, as expected, for the normoxia group, they remained the same for the hyperoxia group. Since those levels remained unchanged, one can come to the conclusion that hyperoxia increases performance when applied during HIIT (Ohya et al., 2016). Breathing the hyperoxic air had an effect on S_aO_2, blood acidosis delay and heart rate recovery after the exercise in runners subjected to 3×3×300m runs in three different conditions: normoxia, hyperoxia during exercise and recovery and hyperoxia during recovery alone. The results showed that the ones in hyperoxia maintained the same S_aO_2 levels. As for the blood pH, blood lactate and heart rate, they all remained unchanged (Nummela, et al., H., 2002). Tucker et al. (2007) suggested that his suggests that improved exercise performance in hyperoxia may be the result of increased muscle activation leading to greater power outputs. It seems that the effects of hyperoxia supplementation during training are difficult to detect and further research is needed before hyperoxic-supplemented endurance training can be recommended for health purposes for the general population bit in elite athletes even small enhancements might be beneficial (Cardinale and Ekblom, 2018).

Beyond experiments regarding hypoxic training and hyperoxic training separately, only a very few have tried to combine the two modalities to achieve optimal results and mostly in patients. The studies focused on to their combined effects in cardiovascular or malignant diseases and rarely on athletic performance. The studies on cardiac patients showed that the combination of hypoxia and hyperoxia during rest gave the same benefits as standard training in regard to cardiorespiratory fitness and confirmed the hypoxia and hyperoxia gas breathing combination as a beneficial training method in cardiac patients (Dudnik et al. 2018; Syrkin et al. 2017). In healthy patients an experiment confirmed the original thesis meaning when the fraction of inspired oxygen reached 0.30 or more, the individuals had a better performance, and longer time to exhaustion (Mallette MM, et al., 2018.) Nevertheless, some studies doubt the hyperoxia influence (Winter et al, 1989, Robbins et al., 1992, White et al., 2013). Even though pure oxygen did not influence recovery and other parameters investigated, in those studies that it was mostly following normoxia training or it was supplemented during training, but none of those study designs searched into combination of hypoxia training and hyperoxia recovery and the effects on blood oxygen transport and aerobic performance. Hyperoxia might have some potential damaging but at the same time enhancing effects of adaptations because it increases the reactive oxygen species (ROS) production. A study by Wilber et al. (2004) showed no difference in ROS production supplementing hyperoxic training compared to normoxic conditions in welltrained cyclists and ROS was not different between FIO2 0.26 and 0.60 which indicates a quite large safe range of O2 supplementation pressure. That is why we hypothesise that supplementation in recovery, meaning hyperoxia, might be beneficial after hypoxic training as the athletes will have lower SO2 at the end of the training than the athletes in previously mentioned studies.

To the best of the author's knowledge, there has not been any studies or experiments conducted that combined high intensity interval training in hypoxia with exposure to hyperoxia at rest. Moreover, all previous studies either studied hypoxia or hyperoxia each on its own, or maybe even combined them but without using high intensity interval training procedure (HIIT) in healthy subjects. Therefore, the aim of the study is to search for the effects of the combination of: HIIT in hypoxia, followed by hyperoxia at rest during recovery.

Objective and hypotheses of research[2] *(suggested length: 700 characters with spaces)*

The main aim of the doctoral thesis is to determine the effects of combining two different environments for an athlete's training process: hypoxia during high-intensity interval training and hyperoxia during recovery, and their effects on blood oxygen transport parameters and an athlete's performance measured by aerobic capacity.

The main hypotheses of the research are set as:
H1: A combination of intermittent high intensity hypoxic training and recovery in hyperoxia significantly improves the aerobic capacity then when recovering in normoxia
H2. A combination of intermittent high intensity hypoxic training and recovery in hyperoxia significantly improves the oxygen transport parameters then when recovering in normoxia.

Material, participants, methodology and plan of research *(suggested length: 6500 characters with spaces)*

Sample

A priori power analysis in free G*Power software was used in order to calculate the minimal sample size for desired minimal power. The minimal acceptable power was set at 0.80. The group of Z tests, and ANOVA within-between effects was chosen. For the p set at p<0,05, the minimal total sample with expected moderate effect size and for two repeated measurements in three groups was calculated to be 42 total subjects (14 per group). A moderate effect size f =0.25 was chosen as in paper by Cardinale and Ekblom, (2018) the estimated hyperoxia training effects on VO2max and performance were 0.15 to 1.0 respectively, meaning small and large effects. As it was inconclusive we opted for moderate effect. So, it was decided that the sample will be comprised of 48 (15% more than required in case of a dropout) able-bodied male students age 18 to 20.

The subjects will be randomly assigned to one of the three groups and train 3 times per week for 4 weeks according to their intervention training protocol.

1. HIIT: High intensity interval training group, normoxia recovery
2. HIIT+O_2: High intensity interval training group training group, hyperoxia recovery
3. CTR: Control group, performing everyday activities

Equipment and protocol

Initial and final testing: The experiment will have two series of aerobic performance and blood testing, separated by four microcycles of training (4 weeks days). The first series of testing will be conducted initially before the intervention and finally, ten days after the last microcycle. It will consist of a blood test to determine the erythrocyte count, haemoglobin, haematocrit, reticulocyte, MCHC, MCH

[2] The sequence of listing the objective and hypotheses depends on the area of research.

and MVB parameters. Also, the aerobic capacity testing will be performed by means of all-out test with incremental intensity using treadmill and metabolic analyser (*Fitmate PRO*, COSMED, Italy). The analysed variables will comprise of parameters at maximal exertion (VO2max, maximal speed reached, HRmax) and parameters at anaerobic threshold (ANT) determined by v- slope method (VO2 at ANT, speed at ANT, HR at ANT) expressed as absolute values as well as relative values (percentage of maximum).

The training protocol in hypoxia will be performed for 4 weeks with *Everest 2 Summit generator* (Hypoxico, USA). Each microcycle will consist of 1 week with 3 training sessions. Each of 4 weeks the intensity of the HIIT and continuous training will increase by 5%. HIIT hypoxia exercise protocol will consist of 6 bouts of 1 minute at 80 to 95% of HRmax (each week higher,respectively) followed by 2 minutes at 60% of HR max

The recovery protocol for experimental group HIIT+O_2 will be 15 minutes at FiO2=0.40 as according to Cardinale and Ekblom (2018), 0.21. to 0.6 are safe ranges (equipment DeVilbiss, USA) while the recovery protocol for experimental group HIIT will be 15 minutes breathing ambient air at rest.

The protocol for control group: 4 weeks of continuing the everyday activities (no training involved).

Expected scientific contribution of proposed research *(suggested length: 500 characters with spaces)*

As opposed to the previous studies, this research will determine through scientific methods whether the combination of high-intensity interval training in hypoxia followed by hyperoxic recovery exposure provides additional beneficial effects of hyperoxia on aerobic endurance and the oxygen transport system. The results of this study will be one-of-a-kind to our best knowledge as the effects of combination of hypoxia, hyperoxia and HIIT has never been studied in regard to blood oxygen transport and aerobic performance in healthy patients. Therefore, this study, if it yields positive results, will be a step forward in the training process of many athletes, especially in endurance disciplines; but if the positive effects prove to be non-existent, it will save money to many athletes and sports clubs who are constantly under the pressure of hyperoxia-product companies.

List of literature cited (no more than 30 references)

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in female athletes. Springerplus. 2015 Jul 2;4:310.

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Total cost estimate of proposed research *(in kuna)*

Proposed sources of funding for research

Type of funding	Title of project	Project leader	Signature
National funding			
International funding			
Other types of projects			
Self funding			
Session of the Ethics Committee at which consent was given to the research proposal[3]			

Agreement of the mentor and the doctoral candidate to request for topic approval

I declare under responsibility that I agree with the topic whose approval is requested.

Signature

(first and last name of first proposed mentor)

Signature

(first and last name of second proposed mentor)

Signature

(first and last name of doctoral candidate)

STATEMENT

I declare under responsibility that I have not submitted a request for approval of an identical dissertation topic at any other university[4].

Zagreb, (date)

Signature

(first and last name of doctoral candidate)

Official stamp here

[3] Fill out only if needed
[4] Not required in case of dual doctorate (*Cotutelle de these*)