

I research the effects of exercise and exercise training on the human body or with the use of experimental models that mimic the human condition. This approach allows for a more detailed investigation and knowledge-generation of the function of the body systems, organs and cells, including their integration.

### Experimental Studies of Heart, Vasculature and Muscle

These studies bridge and integrate basic cardiovascular and physiologic sciences with exercise physiology and sports and exercise sciences. Focus of research is on understanding and deciphering the cellular and molecular determinants of cardiovascular performance and the subcellular adaptations following exercise training. This includes studying the cellular and molecular mechanistic events that underlie and translate into improved cardiac function and clinical outcome in health and disease, with the use of appropriate experimental exercise and disease models and physiologic, biophysical, and biochemical research techniques. As a more recent extension, these techniques have also been used to assess the skeletal muscle, which also undergoes changes in response to disease or exercise training.

The rationale for this line of studies is that heart disease is the biggest killer and the leading cause of disability in the society today, and there is a limited scope of treatment. The 5-year mortality of heart failure; a severe form of heart disease is 50-70%, of which ~50% die of progressive pump failure chiefly caused by abnormal contractile function and ~50% of sudden arrhythmic events. Both abnormal contractile function and many arrhythmic events are further mechanistically explained by abnormalities in cardiomyocyte excitation-contraction coupling and cell function. As such, the heartbeat, the rhythm, the force of the contraction, and irregularities thereof are controlled by the network of cells that make up the heart. In my laboratory, we therefore study the heart muscle and its constituent cells under normal conditions, during pathologic conditions such as heart disease, and after exercise training in both health and disease. We do this to understand the heart better, and therefore be able to generate better therapies for the heart when something goes wrong. Ultimately, this will reduce the impact of heart disease to the patient as well as to the society at large. Importantly, and in contrast to other interventions, exercise and exercise training provides a cheap, but underdeveloped means to improve mortality, morbidity, quality of life, function and physical capacity.

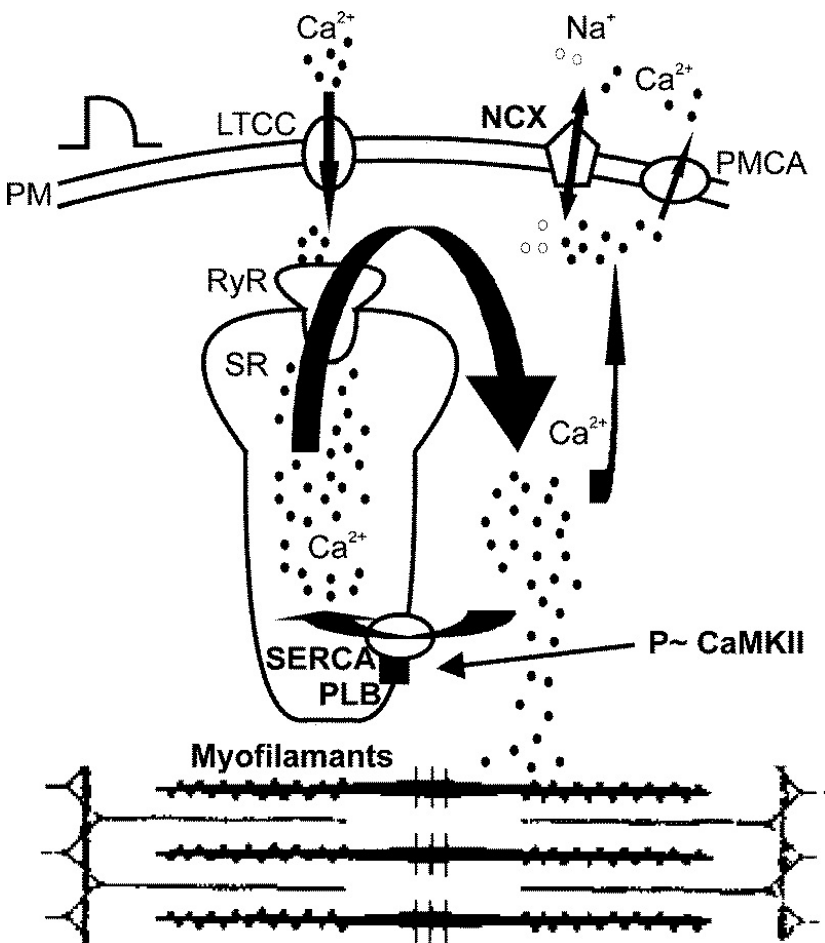


Figure 1 - From Kemi and Wisloff (*Acta Physiologica* 2010) and Wisloff, Ellingsen and Kemi (*Exercise and Sports Science Reviews* 2009): A schematic model of excitation-contraction coupling in muscle cells; broad arrows indicating cellular loci where exercise training induces beneficial adaptations that improve cellular function and contraction capacity.

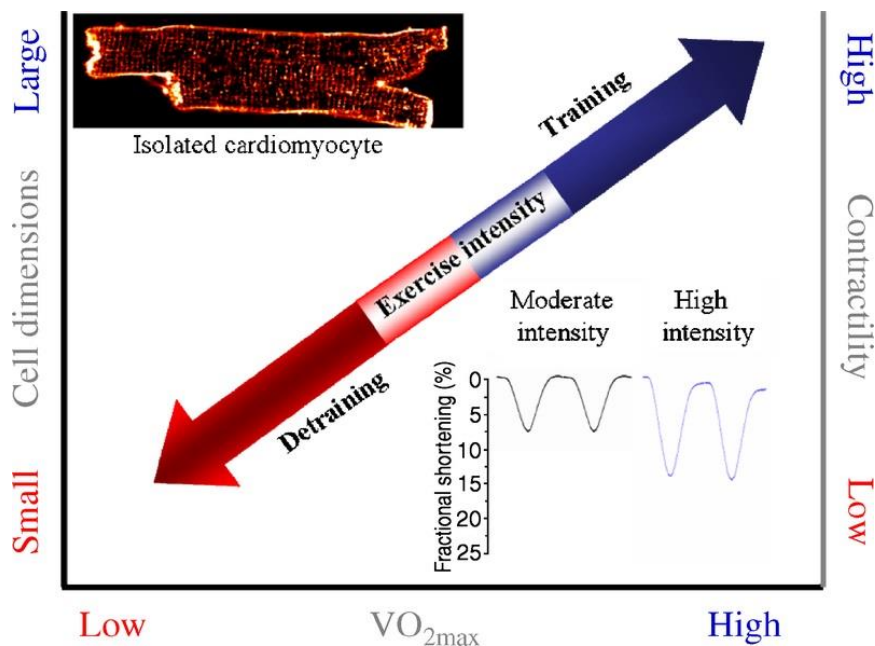


Figure 2 - From Wisloff, Ellingsen and Kemi (Exercise and Sports Science Reviews 2009): The extent of exercise training-induced adaptation of maximal oxygen uptake (as a measure of integrated human exercise and work capacity) and cardiomyocyte contractility and size (as a measure of cellular function in heart) are closely linked together and in fact depend on each other, whereas the response to training depends on the exercise intensity of the training sessions.

### Exercise Physiology, Sports Science and Performance

These experiments are carried out in voluntary human subjects in the sports science or exercise physiology laboratories or out in the field, such as professional and elite training and competition or match grounds, where the subject characteristics vary depending on the purpose of the study; some times they may be healthy young adults such as sports science students, other times they may be elite athletes competing at the highest level in their sport, and yet another time they may be subjects suffering from a dysfunction or disease that we may seek to remedy via exercise interventions. Recent examples of these experiments include:

Figure 3 - Exercise testing with assessment of various physiologic parameters from the lab.



**Active recovery** at a high intensity is superior for removing lactate in the muscle and facilitate readiness for the next exercise bout or session. Lactate has a long and interesting history of controversy, but a bit overlooked is the fact that lactate provides a proxy measure of fatigue in the working muscle. In a series of experiments, I and a number of students working on the project recruited healthy, normally active young adults, often sports science students, to the lab for a series for tests and measurements. Subjects first underwent an incremental exercise test where lactate threshold and maximal oxygen uptake was measured, after a health check and a proper warm-up. Each subsequent test, with each separated by several days, then continued with the subject undertaking really strenuous exercise by fast, intense running to exhaustion on a treadmill. This exercise was designed to raise muscle lactate production and blood lactate concentration to high and very high levels: in some experiments to a level of 5-6 mM, and in other experiments to the even higher levels of around 10-12 mM. Immediately following exhaustion, the subjects then began a recovery procedure that in the different experiments ranged from passive sit-down recovery (perhaps the most pleasant for the subjects) to active recovery consisting of walking to a pace that was more and more intense, by the highest intensity active recovery trial reaching the intensity of lactate threshold. During all this, blood lactate, lactate clearance, heart rate, and oxygen uptake were determined. These experiments

showed that active recovery was clearly superior to passive recovery for removing muscle and blood lactate and therefore facilitating recovery. Moreover, the experiments showed that the optimal active recovery intensity was at or close to the individual's lactate threshold intensity. This makes great sense, because this is the highest intensity that the subject may sustain without any further excess production and accumulation of lactate, and we know that lactate is best and most usefully eliminated by conversion to glucose in the muscle itself in a manner dependent on the rate of work by the muscle or by the liver in a process known as the Cori cycle, and we in this study were glad to show that the rate of lactate elimination is highest when the muscle is working at its highest rate it can achieve, before it topples over and starts to produce excess lactate again, which thereby must be avoided for active recovery.

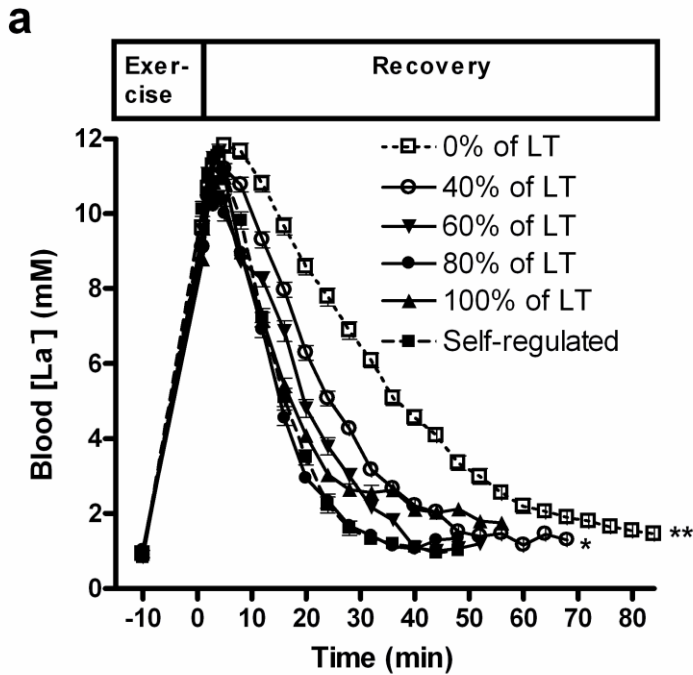
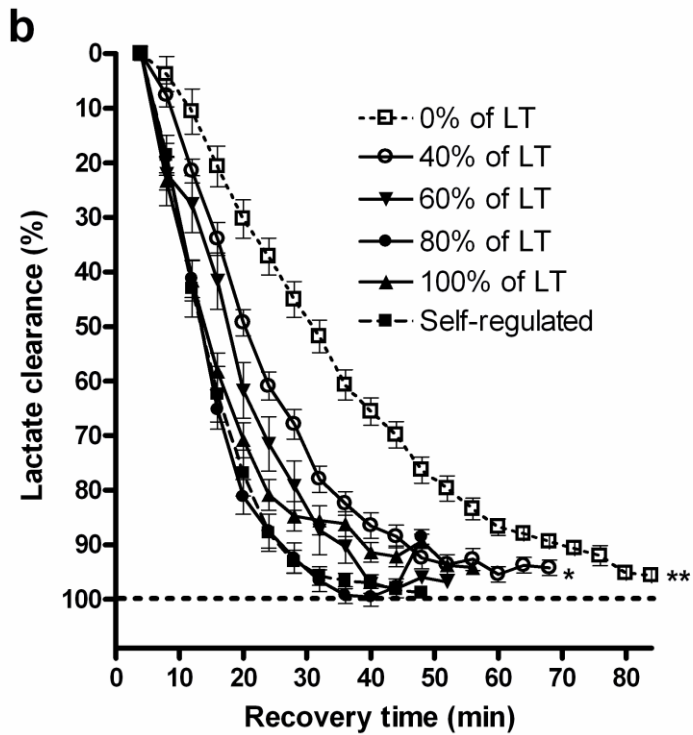


Figure 4 – From Devlin et al 2014 (Journal of Sports Medicine and Physical Fitness): Lactate concentrations (top) and clearance (bottom) during different intensities of active recovery following a supra-maximal bout of exercise, showing that active recovery is superior to passive recovery, and that active recovery is optimal at an exercise intensity close to one's individual lactate threshold intensity.



**Critical speed and the speed-tolerable duration relationship** is another concept of exercise physiology my studies have sought to investigate and utilize, as a determinant of endurance exercise performance and therefore a really useful characteristic of physical capacity. Critical speed during running (critical power if cycling) is a measure that relatively recently both has been established as an exercise intensity demarcator alongside more traditional measures such as lactate or anaerobic threshold, as it distinguishes between heavy aerobic oxidative exercise and severe anaerobic non-oxidative exercise domains, and it as well also measures the relationship between speed and maximal attainable duration (speed-tolerable duration) above the critical speed, which because it can be calculated allows us to very accurately predict how long a subject or an athlete can sustain the severe non-oxidative exercise at given speeds above the critical speed, which helps for both optimizing high-intensity training as well as competition pacing.

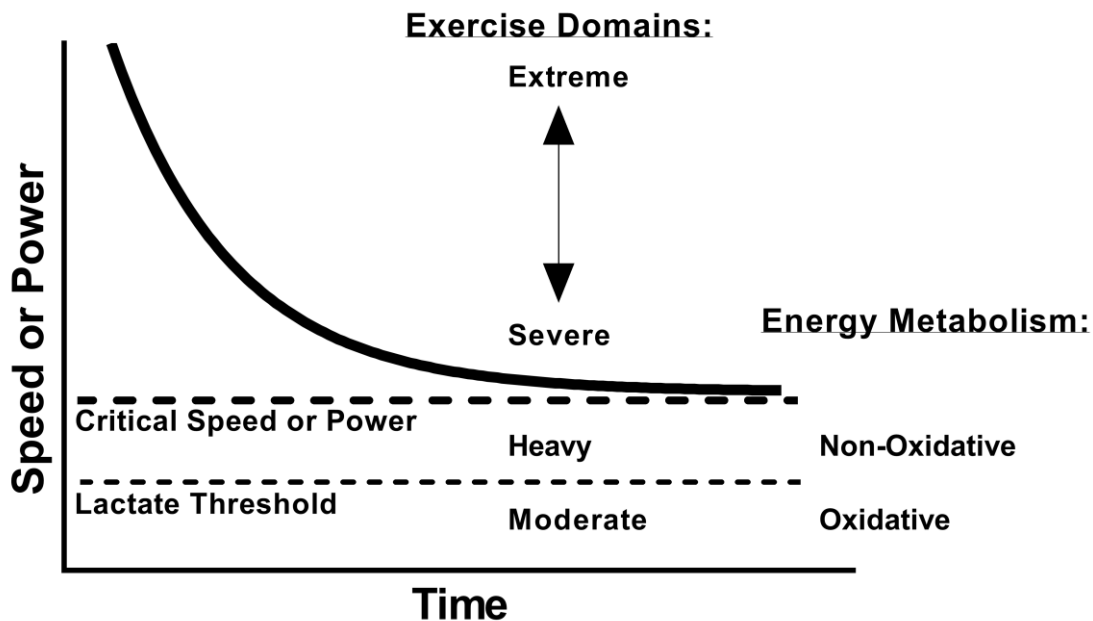


Figure 5 – Overview of critical speed and the speed-tolerable duration relationship. Critical speed distinguishes high-intensity exercise domains fueled by aerobic oxidative energy production and metabolism (heavy exercise) versus exercise that also must be fueled by significant anaerobic non-oxidative energy production (severe to extreme exercise, with a limit of approximately 30 minutes), such that exercise at or above this intensity threshold will be inexorably limited to the period of time of less than 30 minutes that this exercise may be upheld by rate-limiting glycolytic and phosphocreatine energy production. The duration of this rate-limited exercise may be very predictably established and accurately calculated by the hyperbolic speed-tolerable duration relationship above the critical speed threshold.

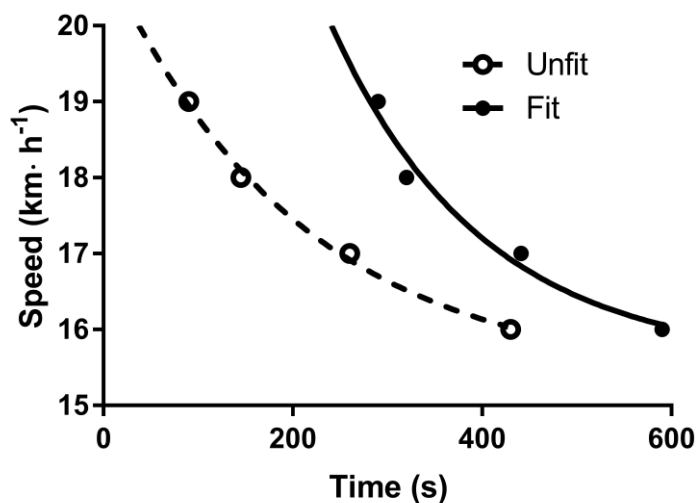
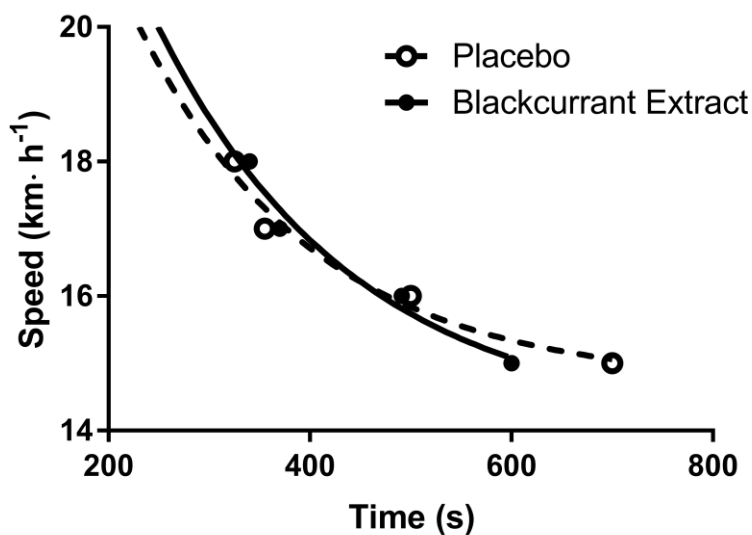


Figure 6 – From Kemi Lab: Critical velocity and the speed-tolerable duration relationship in a well-trained fit and an untrained unfit person, established during constant speed testing where subjects run at different pre-determined treadmill speeds to complete exhaustion. Treadmill speed on the Y-axis, and time to exhaustion on the X-axis; the graphs show that the well-trained fit person can run at high speeds for a longer period of time; for example, the unfit subject can run at 18 km/h for <200 seconds, whereas the fit athlete can run at the same speed for ~350 seconds.

In a very recent study, a postgraduate student in the lab undertook such experiments, where she established critical speed and speed-tolerable duration, along with measurements of maximal oxygen uptake, lactate or anaerobic threshold, running economy, and metabolic energy expenditure and substrate utilization. This was done under normal conditions and after supplementation of anthocyanin-rich blackcurrant extract, in a cross-over, placebo-controlled and randomized double-blind research design. Blackcurrant extract was chosen because experiments elsewhere had indicated that it may have ergogenic effects that potentially could improve high-intensity exercise. However, in our experiments, we found no such effect. The results from our experiments showed that supplementation of blackcurrant extract did not enhance or improve endurance exercise performance or the physiologic or metabolic parameters we measured, and hence provided no ergogenic effect. This was perhaps a little bit disappointing, but on the other hand, it is also important to show if a product may have ergogenic potential and when it may not have so.

Figure 7 – From Kemi Lab (Pastellidou et al, European Journal of Sports Science 2020): The technique of measuring the speed-tolerable duration relationship and critical speed, along with measurements of maximal oxygen uptake, lactate or anaerobic threshold, running economy, and metabolic substrate utilization assays, was used to show that ergogenic supplementation of blackcurrant extract does not enhance or improve endurance exercise performance or related physiologic and metabolic parameters.



**Physiology of Rock Climbing and Mountaineering** is an up-and-coming area of sports and exercise science, for several reasons. First, climbing, especially indoor roped climbing and bouldering, is rising in popularity these days. It has appeal to a variety of people as their chosen form of exercise and physical activity, and climbers cite a wide variety of reasons and motivations for why they climb, but important for many is the exercise training, physical capacity and the strength and conditioning aspect of it that improves fitness, health and well-being. This type of climbing has also a very strong competitive aspect to it, where competition climbing in line with most other sports sees athletes and competitions ranging in level from local club or community events to the international circuits of World Cups, World Championship, and most recently, its inclusion as an Olympic sport. The characteristics of upward and often overhanging climbing that taxes upper body and core strength as well as endurance, and with each event being time-limited to a range of seconds to minutes, this sets up a distinct bioenergetic scenario not found elsewhere.

In parallel to the above are the related activities of mountaineering, hiking and backcountry skiing or ski touring, but which in contrast to climbing are characterized by long to ultra-long endurance events. Here, the aerobic component prevails in a needs analysis of physical and physiologic determinants, but the strength contribution for successful completion is often also large and significant, though it may also be effectively non-existent, depending on the nature and chosen course of the activity. Moreover, the environmental challenges of exercising or

performing outdoors, often with a significant extra load to carry, often in cold conditions, and often at elevated altitude must also be considered. Like climbing however, there are important benefits to consider, such as the exercise training, improvement of physical capacity and the strength and conditioning aspects of it that improve fitness, health and well-being.

The above therefore make rock climbing and mountaineering interesting and really useful avenues to research from an exercise physiology perspective and promote from a public health perspective. As an example of this, in a recent study, a group of students and I set up a research study investigating the determinant factors for rock climbing performance. Effectively, the study boiled it down to one question: from a physical capacity and exercise physiologic point of view, what makes one climber better than the other? To answer this question, we recruited and tested climbers of all levels of achievement, from the beginners who had never climbed before to the best climbers we could get our hands on, climbers at a high national level. Climbing achievement is graded on an open-ended scale from 0 (everyone can do it) to the current top standard of 9c (only a couple climbers in the world have been able to successfully climb at this level). In our study, we were able to include subject and athletes of every level up to 8a, of both sexes. All participating climbers were brought to the sports science laboratory where a wide range of physical and physiologic parameters of strength, power, aerobic and anaerobic endurance, flexibility and other factors were assessed in each part of the body that we had surmised may affect climbing performance. The participants were then also tested for climbing-specific capacities in the same muscles while performing climbing-specific exercises or while actually climbing on standardized but specific climbing routes set up for this purpose. Subsequently, principal component and multiple regression analysis showed that there is not one, but several factors related to physical capacity that set the best climbers apart from the rest. One important finding was specifically that shoulder power and endurance, and arm and finger strength account for almost 60-70% of the variation between different climbers' peak performances, and as such provide a reason for why some climbers are better than others. Other parameters were also relevant, but not as important as the above, for determining climbing performance.

Knowing the above, we now are in a position to better and in a more informed manner tell what and how to train to progress in climbing and reach that next level of climbing. Specific training in response to this needs analysis would include specific dynamic exercises like pull-ups, static hangs with bent arms, and finger strength training, alongside more climbing and bouldering at climbing centers and locations.

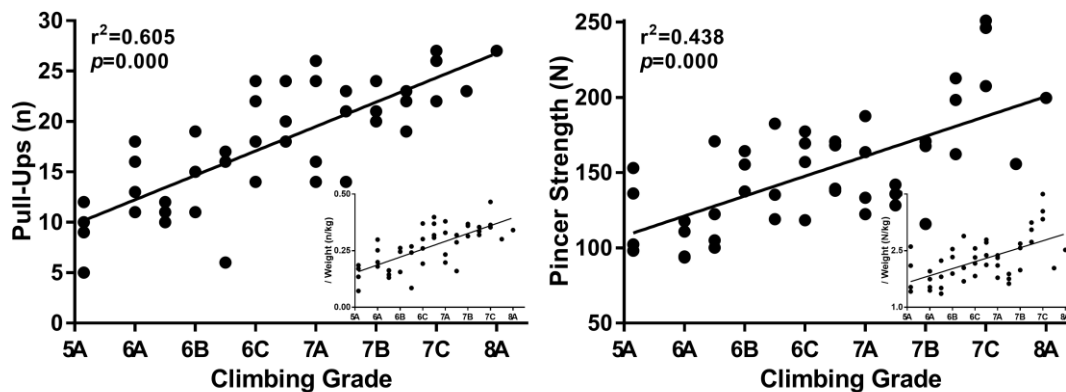


Figure 8 – From Kemi Lab (MacKenzie et al, International Journal of Sports Physiology and Performance 2020): These plots show that upper-body and shoulder endurance and power (measured by maximum pull-ups in this case) and finger strength (measured by peak force during finger pincer movement) correlate well with climbing performance.