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The Short Review on Protein Markers in Sport and Fitness Exercises

by

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In this short review, we tried to elucidate a number of biological markers which, in our opinion, could be of potential use for the sport practice. Obviously, by suggesting this group we are fully aware of the subjectivity of our choice. It must also be stressed that a number of studies on the well-defined group of sportsmen have to be undertaken. Correlation between the levels of markers elucidated, as well as the data, have to be cross-correlated with the fitness level of the studied group. It has also been noticed, that to our knowledge, this is the first attempt ever to create the collection of markers potentially useful in sport practice..

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Introduction

The recent advance in biology, especially in such as fields as molecular biology lead to an outburst in the new fields of study, among them being proteomics and genomics. In generally accepted terms, proteomics is a branch of science referring to all the proteins expressed by a genome. In this understanding it involves the identification of protein spectrum in the body and determination of their role in physiological and pathophysiological functions. Together with proteomics development and the studies on biological (protein) markers, reflecting the physiological state of a living organism (human body) has also been spurred. The extensive studies have shown that protein or proteins can be used as specific markers of specific physiological, (i.e. normal and pathological) state of an organism. These observations stimulated the studies on usefulness of protein markers in monitoring the progress of fitness exercises on both competitive as well as recreational levels. The analysis of current literature on biological markers resulted in a vast number of papers focused on accurate assessment of a fitness stage prior to the competition or in recreation sports. However, at first glance the researcher may notice the lack of a defined path of research. Some of the studies take into considerations such categories as elderly, sedentary, wrestlers, swimmers or gymnasts, etc. In all these groups, completely different markers were studied. Such an approach makes the presented results inapplicable for daily practice, when preparing sportsman to a competition, or even when hoping to monitor the recreational progress. In this short review, we tried to elucidate a number of biological markers which, in our opinion, could be of potential use for the sport practice. Obviously, by suggesting this group we are fully aware of the subjectivity of our choice. It must also be stressed that a number of studies on the well-defined group of sportsmen have to be undertaken. Correlation between the levels of markers elucidated, as well as the data, have to be cross-correlated with the fitness level of the studied group. It has also been noticed, that to our knowledge, this is the first attempt ever to create the collection of markers potentially useful in sport practice.

Sport and exercises related protein markers

C-reactive protein (CRP): High level of CRP protein is associated with poor physical performance and muscle strength in older persons (Cesari, Penninx, Pahor, Lauretani, Corsi, Rhys Williams, Guralnik and Ferrucci, 2004). CRP level does not differ by gender when considering the mean fitness level. However, physical fitness is inversely related to CRP level in children and that this relationship is more pronounced in boys than in girls (Isasi, Deckelbaum, Tracy, Starc, Berglund, Shea and Corrigan, 2003) When considering CPR protein as an inflammatory marker some forms of physical activity are associated with a lower likelihood of elevation of the protein, although we cannot exclude the possibility that differences may be due to exercise intensity or duration (King, Carek, Mainous and Pearson, 2003). Physically active individuals with the metabolic syndrome, a condition that promotes atherosclerosis and increases the risk of cardiovascular mortality and morbidity, had 36% lower levels of CRP (Pitsavos, Panagiotakos, Chrysohoou, Kavouras and Stefanadis, 2005). Cardiorespiratory fitness levels are inversely associated with CRP levels in young adults independent of obesity, blood pressure, smoking and combined oral contraceptive use in women (Williams, Milne, Hancox and Poulton, 2005).

Serum amyloid-A (SAA): Physically active individuals with the metabolic syndrom, as defined above, had 19% lower levels of SAA compared to sedentary (Pitsavos, Panagiotakos, Chrysohoou, Kavouras and Stefanadis, 2005). It has also been shown that people devoted to high physical activity had 22% lower concentrations of amyloid-A as compared to those who were devoted to sedentary life (Panagiotakos, Pitsavos, Chrysohoou, Kavouras and Stefanadis, 2005).

Interleukin (IL-6): Interleukin (IL-6) is significantly correlated with physical performance. High levels of IL-6 is significantly associated with poor physical performance and muscle strength in older persons (Cesari, Penninx, Pahor, Lauretani, Corsi, Rhys Williams, Guralnik and Ferrucci, 2004). Individuals with the metabolic syndrome have 30% lower levels of IL-6 compared to sedentary (Pitsavos, Panagiotakos, Chrysohoou, Kavouras and Stefanadis, 2005). Adults devoted to high physical activity have 32% lower levels of interleukin-6 as compared to those who were devoted to sedentary life (Panagiotakos, Pitsavos, Chrysohoou, Kavouras and Stefanadis, 2005). It has been demonstrated that the IL-6R gene expression level in skeletal muscle are increased in response to acute exercise. It is a very conservative response which is not affected by either training status or intramuscular glycogen levels, as opposed to IL-6 protein expression (Keller, Steensberg, Hansen, Fischer, Plomgaard and Pedersen, 2005). The principal abnormal factors in overtraining are an increased production and/or intolerance to interleukin (IL)-6 during exercise. Strategies to attenuate the IL-6 response to exercise that may also reduce an athlete's susceptibility to overtraining are proposed (Robson, 2003).

Interleukin (IL-10)*, Interleukin (IL-1beta) and Interleukin (IL-6sR):* IL-10, IL-1beta, IL-6sR, and IL-1RA do not reflect the muscle strength in older persons

(Cesari, Penninx, Pahor, Lauretani, Corsi, Rhys Williams, Guralnik and Ferrucci, 2004). In the studies on muscle damage in athletes competing in a 160-km cycling race the seven plasma cytokines were measured (i.e. IL-6, IL-10, IL-8, IL-1ra, granulocyte colony-stimulating factor (G-CSF), monocyte chemotactic protein 1 (MCP-1), and macrophage inflammatory protein 1beta (MIP-1beta). No increases in IL-8 or MIP-1beta was observed (Nieman, Dumke, Henson, McAnulty, Gross and Lind, 2005).

Interleukin (IL-1beta): Delayed recovery of running performance after muscle-damaging downhill running is associated with increased brain IL-1beta concentration compared with uphill running (Carmichael, Davis, Murphy, Brown, Carson, Mayer and Ghaffar, 2006). It has been shown that increased brain IL-1beta plays an important role in fatigue after muscle-damaging exercise (Carmichael, Davis, Murphy, Brown, Carson, Mayer and Ghaffar, 2006). In the study on physiological changes after an extremely exhaustive military training, the levels of IL-6 were increased, while those of IL-1beta and IL-10 were unchanged (Gomez-Merino, Drogou, Chennaoui, Tiollier, Mathieu and Guezennec, 2005).

Interleukin (IL-2): It has been shown that after a competitive race of 16 male marathon runners, IL-2 concentration decreased by 32%. This fact was correlated with the induction of nitric oxide (NO) production (Suzuki, Yamada, Kurakake, Okamura, Yamaya, Liu, Kudoh, Kowatari, Nakaji and Sugawara, 2000).

Interleukin (IL-6sR): It has been shown that baseline serum levels of TNF-alpha and sIL-6R are significantly increased when comparing the runner's baseline serum with healthy controls. It has also been shown that the serum levels of both proteins after significant rise post exercise gradually return to baseline within 24 hrs. (Neidhart, Muller-Ladner, Frey, Bosserhoff, Colombani, Frey-Rindova, Hummel, Gay, Hauselmann and Gay, 2000). The obtained results suggest that circulating cytokines (e,g., IL-6sR) are related to both skeletal muscle mass and physical function. These findings provide further evidence to support the hypothesis that immune activation contributes to skeletal muscle atrophy and reduced functional capacity in heart failure patients (Toth, Ades, Tischler, Tracy and LeWinter, 2006).

Interleukin (IL-1RA): A high level of IL-1RA is significantly associated with poor physical performance and reduced muscle strength in older persons (Cesari, Penninx, Pahor, Lauretani, Corsi, Rhys Williams, Guralnik and Ferrucci, 2004). It has also been shown that during the wrestling season with intense exercise training the level of IL-1RA increased. In the postseason, the significant decrease was also observed (Nemet, Pontello, Rose-Gottron and Cooper, 2004). Our observations also demonstrated that triathletes differ from runners when considering the plasma level of interleukins (IL)-6, IL-1ra, and IL-10. Thus, triathletes due to a more intense training regimen, have higher levels of these proteins. On the other hand the level of the chemokine IL-8 increases solely in the runners. The differences between cytokine responses after a long distance triathlon and a 100-km run suggested that IL-6 and IL-8 could be employed as respective markers of the intensity of the muscular activity required for substrate availability and vascular inflammation. For the two groups, all parameters had returned to pre-race levels by seven days post-race (Gomez-Merino, Drogou, Chennaoui, Tiollier, Mathieu and Guezennec, 2005).

Tumor necrosis factor (TNF –alpha): It has been shown that physically active individuals with the metabolic syndrome have 15% lower levels of TNF-alpha compared to sedentary. Similar results were observed in the non-metabolic syndrome group (Pitsavos, Panagiotakos, Chrysohoou, Kavouras and Stefanadis, 2005). It has also been shown that exercise induce decreases of TNF-alpha (Drenth, Van Uum, Van Deuren, Pesman, Van der Ven-Jongekrijg and Van der Meer, 1995). Obese children had significantly higher concentrations of inflammatory parameters, such as TNF-alpha, than non-obese subjects. These data reveal that even in childhood, inflammatory parameters, are elevated in obesity and that physical fitness counteracts this association (Halle, Korsten-Reck, Wolfarth and Berg, 2004).

Cross-linked N-telopeptide (NTx): Urinary cross-linked N-telopeptide (NTx) can be used as bone resorption marker. It has also been shown that NTx was highest among rowers, and higher in rowers and runners than in swimmers or controls (O'Kane J, Hutchinson, Atley and Eyre, 2005). NTx also increases with age (Ryan and Elahi, 1998).

C-telopeptide of type II collagen (CTx-II): Urinary C-telopeptide of type II collagen (CTx-II) can be use as a cartilage degradation marker. It has been shown that CTx-II is significantly higher in runners than in swimmers (O'Kane J, Hutchinson, Atley and Eyre, 2005).

Apolipoprotein Al and apolipoprotein B100: The studies on apolipoprotein Al (Apo-Al), and apolipoprotein B100 show a lack of significant differences between wrestlers and male students, and between female students and sedentary females. These results indicate that medium and high level of exercises did not cause significant differences in lipid and lipoprotein levels. However, the differences are sex pronounced (Kishali, Imamoglu, Kaldirimci, Akyol and Yildirim, 2005), (Panagiotakos, Pitsavos, Chrysohoou, Skoumas, Zeimbekis, Papaioannou and Stefanadis, 2003). The experimental data demonstrate that an intervention based on a low-fat diet and intensive physical exercise is capable of improving apolipoprotein levels, associated with retardation of progression of coronary artery disease (Niebauer, Hambrecht, Velich, Marburger, Hauer, Kreuzer, Zimmermann, von Hodenberg, Schlierf, Schuler and Kubler, 1996). After training, we observed an 36% increase in apo A-I (Tikkanen, Hamalainen and Harkonen, 1999).

Plasma atrial natriuretic peptide (ANP): Atrial natriuretic factor (ANF) is a peptite within the plasma which causes pulmonary vasodilation. The animal model study shows that increase in proteinuria, plasma atrial natriuretic peptide, and serum leptin levels observed in rats with heart failure were suppressed by low-intensity exercise training (Emter, McCune, Sparagna, Radin and Moore, 2005). It has also been shown that absolute increase in ANP during exercise was higher in trained subjects than in untrained subjects and was positively correlated to ANP at rest (Bentzen, Pedersen, Nyvad and Pedersen 2002). Plasma levels of ANP increased in both groups (athletes and untrained) after It has also been shown that short-term exercise results in a significant increase in atrial natriuretic factor in minimally trained but not in well trained men (Rogers, Tyce, Bailey and Bove 1991). Some researchere shows that haemodynamic changes associated with endurance training are reflected in plasma ANF levels during exercise, but not at rest (Vollmer-Larsen, Vollmer-Larsen, Larsen, Breum, Larsen and Keller 1989).

Serum leptin: The increases in proteinuria, plasma atrial natriuretic peptide, and serum leptin levels observed in rats with HF were suppressed by low-intensity exercise training (Emter, McCune, Sparagna, Radin and Moore 2005).

Serotonin: The results of [35S]GTPgammaS binding assays showed that h5-HT 1B/1D receptors were desensitized after the training program, although serum serotonin (5-HT) was unchanged. These data suggest the existence of a control on T cells mediated through h5-HT 1B/1D receptors leading cytokine production modulation after a physical training (Chennaoui, Drogou, Gomez-Merino and Guezennec 2005). In the studies employing high performance liquid chromatography of blood sample of trained and untrained individuals have been shown that basal serum serotonin levels are increased by exercise training (Soares, Naffah-Mazzacoratti and Cavalheiro 1994). It has also been shown that the severe overtraining state could have been related to decreased serotonin reuptake in the brain and signs of major depression (Uusitalo, Valkonen-Korhonen, Helenius, Vanninen, Bergstrom and Kuikka 2004). In the studies on brain serotonin (5-HT) transporter binding i.e., 5-HT reuptake in severely overtrained athletes and their controls at the baseline and after a one-year recovery period

5-HT reuptake did not correlate with the depression scores either in the whole group or in the OA. These findings does not support the idea of long-term changes in 5-HT neurotransmission in overtraining state, in this case serotonin reuptake in midbrain, the regulating area of brain serotonin neurotransmission (Uusitalo, Vanninen, Valkonen-Korhonen and Kuikka 2006).

Tryptophan, branched-chain amino acids (BCAA): The major symptoms of overtraining including decreased exercise performance, altered mood states, and depleted muscle glycogen stores closely resemble the effects of brain serotonin, the level of which is dependent on the plasma ratio of tryptophan to branched-chain amino acids (BCAA). Plasma free or total tryptophan, BCAA, and the tryptophan/BCAA ratio were not significantly altered throughout this study (highly-trained endurance runners underwent performance training). These results lead to the conclusion that plasma tryptophan and BCAA levels, are not sauitable marker of increase of training volume (Tanaka, West, Duncan and Bassett 1997).

Oxidized low-density lipoprotein (Ox-LDL): Analytical results indicated that the plasma Ox-LDL level remained unchanged after 8 weeks of exercise training. Importantly, resting and exercise-induced Ox-LDL-potentiated platelet activation was decreased by exercise training. However, this was reversed by detraining to the pre training level (Wang and Chow 2004). The findings suggest that long duration exercise of non-exhaustive intensity decreases the concentration Ox-LDL simultaneously with an increase in serum antioxidant potential in healthy trained men (Vuorimaa, Ahotupa, Irjala and Vasankari 2005).

Antibodies against oxidized LDL (AuAb-ox-LDL): Active sportsmen showed significantly less AuAb-ox-LDL than healthy sedentary males. However, AuAb-ox-LDL levels were not statistically different between the groups of active and previously active sporting men (Garcia-Unzueta, Gutierrez-Sanchez, de Mier, Amado and Berrazueta 2003).

Low-density lipoprotein LDL: It has been shown that 8 weeks of exercise training decreased the plasma LDL level (Wang and Chow 2004) with no statistically significant differences observed for the other lipids and lipoproteins. The studies also showed that low-density lipoprotein (LDL) was significantly higher in postmenopausal inactive athletes than premenopausal active athletes (Chen and Yang 2004).

Low-density lipoprotein cholesterol LDL-C: The current studies indicate lack of significant differences in LDL-C values between wrestlers and male students, and between female students and sedentary females. However, LDL-C values were found to be lower in females than males (Kishali, Imamoglu, Kaldirimci, Akyol and Yildirim 2005). It has also been shown that level of LDL-cholesterol was significantly decreased in walkers group in comparison with control subjects (Haluzik, Haluzikova, Brandejsky, Nedvidkova, Boudova, Barackova and Vilikus 1999). The level of LDL-C after anaerobic swim shows not to be significantly higher as compared with the rest level (Ohkuwa and Itoh 1993).

Insuline like growth factor (IGF-I): Serum GH/IGF-I levels decrease significantly after a 2-day rest in gymnasts, to a nadir as low as those of the control subjects level (Adiyaman, Ocal, Berberoglu, Evliyaoglu, Aycan, Cetinkaya, Bulca, Ersoz and Akar 2004). It has been shown that prolonged work producing losses in body mass lowers total IGF-I, free IGF-I and nonternary IGF-I (Nindl, Castellani, Young, Patton, Khosravi, Diamandi and Montain 2003). The studies on overnight responses show the lack of differences for total or free IGF-I. This suggest resistance exercise influence the level of the circulating IGF-I not by means of alteration of the amount of IGF-I but rather of the manner in which IGF-I is partitioned among its family of binding proteins (Nindl, Kraemer, Marx, Arciero, Dohi, Kellogg and Loomis 2001). Intense physical training results in a marked influence on the IGF system and its binding proteins with generally more extensive changes seen in the untrained individuals (Rosendal, Langberg, Flyvbjerg, Frystyk, Orskov and Kjaer 2002).

high-density lipoprotein cholesterol (HDL-C): No significant differences were found in HDL-C between wrestlers and male students, and between female students and sedentary females. HDL-C values of female students and sedentary females were significantly higher when compared with the same values of wrestlers and male. However, LDL-C values were found to be lower in females than males (Kishali, Imamoglu, Kaldirimci, Akyol and Yildirim 2005). A study also shows that HDL-C and glycerol concentrations were significantly enhanced following anaerobic swim test (Ohkuwa and Itoh 1993).

Serum growth hormone (GH): The studies on the level of serum growth hormone were performed on seventeen female rhythmic gymnasts, aged 11.4 +/- 0.9 years, who had 10 h per week intense exercise for at least 4 months. The group was followed up to 4 years. The results shows that intense exercise induces an acute rise in GH levels, but this acute elevation rapidly normalizes after a 2-day rest (Adiyaman, Ocal, Berberoglu, Evliyaoglu, Aycan, Cetinkaya, Bulca, Ersoz and Akar 2004). The marked differences in the dynamics of changes in the serum GH concentrations during exercise period between the groups of various level of physical activity despite the lack of the significant differences in basal level and maximal level of serum GH concentration at the end of exercise were also observed. Untrained subjects showed faster increase in serum GH concentration than trained subjects, but in trained subjects the restoration of the basal values in the recovery period was faster. These results indicate that the level of physical activities in young, healthy male subjects has no influence on GH response to acute physical exercise (Hadzovic, Nakas-Icindic, Kucukalic-Selimovic, Avdagic and Zaciragic 2004).

***5'AMP activated protein kinse (AMPK)*:** As for now the metabolic role of 5'AMP-activated protein kinase (AMPK) in regulation of skeletal muscle metabolism in humans is unresolved. The assumptions have been made that exercise in the glycogen-depleted state elicits an enhanced uptake of circulating fuels that might be associated with elevated muscle AMPK activation (Wojtaszewski, MacDonald, Nielsen, Hellsten, Hardie, Kemp, Kiens and Richter 2003). Some study also demonstrate that protein content and basal AMPK activity in human skeletal muscle are highly susceptible to endurance exercise training (Frosig, Jorgensen, Hardie, Richter and Wojtaszewski 2004). It has also been shown that AMPK regulates several metabolic pathways during acute exercise and modifies the expression of many genes involved in the adaptive changes to exercise training (Musi, Yu and Goodyear 2003).

Uncoupling protein (UCP3): There is very strong evidence that UCP3 is negatively related to mechanical energy efficiency, suggesting that the down-regulation of UCP3 with training increases mechanical energy efficiency. Taken together, although the exact function of UCP3 is still unknown, exercise and training studies clearly show that under certain circumstances UCP3 is strongly related to human energy metabolism, possibly as a secondary effect of its (yet) unknown primary function (Schrauwen and Hesselink 2003).

Natural IgM (nIgM): The animal studies shows that physically active rats have higher serum nIgM after 7 days of running nIgM also remains elevated over 56 days of running. Because nIgM is important in multiple aspects of the immune response, an elevation in this innate humoral component may contribute to improved immunity in physically active organisms (Elphick, Greenwood, Campisi and Fleshner 2003). It has also been shown that acute exercise following heavy training did not alter pokeweed-stimulated IgM synthesis (Verde, Thomas, Moore, Shek and Shephard 1992).

Intestinal IgA and IgM: Marathon runners maintain or enhance their intestinal IgA and IgM-production. This might reflect a stress-induced hormonal influence on the homing of primed B cells to the mucosa, or perhaps an immune response to elevated influx of stimulatory luminal antigens (Nilssen, Oktedalen, Lygren, Opstad and Brandtzaeg 1998).

Carboxy-terminal peptide of type II collagen (CPII) and telopeptide fragments of degraded type I collagen (CTx1): Two markers of collagen metabolism, CPII and CTx1 are potential serum indicators of the exercise effects on the developing skeletal system in horses (Billinghurst, Brama, van Weeren, Knowlton and McIlwraith 2003). Currently no extensive human studies on this subject are reported.

Cartilage proteoglycan (aggrecan), stromelysin-1, tissue inhibitor of metalloproteinases-1 (TIMP-1) and procollagen II C-propeptide: All markers except stromelysin shows lower concentrations in athletes at rest compared to the reference group. The increase in markers after exercise may reflect an effect of mechanical loading in combination with a possible high turnover rate of body cartilage matrix in these individuals (Roos, Dahlberg, Hoerrner, Lark, Thonar, Shinmei, Lindqvist and Lohmander 1995).

GLUT-4 glucose transfer protein: GLUT-4 protein concentration, irrespective of age increase after short period exercises. These data suggest that older human skeletal muscle retains the ability to rapidly increase muscle GLUT-4 and improve insulin action with endurance training (Cox, Cortright, Dohm and Houmard 1999). Some studies indicates also that a 14-day 50% reduction in exercise frequency maintains the improvements in GLUT-4 protein concentration (Houmard, Tyndall, Midyette, Hickey, Dolan, Gavigan, Weidner and Dohm 1996).

IGF-binding protein: Endurance training in middle-aged men increases the activity of the GH/IGF-I system and improved glucoregulation both at rest and during high-intensity endurance exercise (Manetta, Brun, Maimoun, Callis, Prefaut and Mercier 2002). It has been shown that circulating IGF-I is correlated with fitness, but results of prospective exercise training studies have been inconsistent, showing both increases and decreases in IGF-I. Exercise-associated mechanisms may inhibit increases in IGF-I early in the course of a training protocol, even in overfed subjects (Nemet, Connolly, Pontello-Pescatello, Rose-Gottron, Larson, Galassetti and Cooper 2004).

Salivary cortisol C and DHEA*:* The studies on salivary cortisol (C) and DHEA concentrations performed on 9 elite swimmers (4 female and 5 male) over a 37-week period show the lack of equivalent relationship for C. Thus, the C is not a good predictor of swimming performance. However, C may be considered useful markers for dry-land training stress (Chatard, Atlaoui, Lac, Duclos, Hooper and Mackinnon 2002) for individual females. DHEA is found to be an useful markers for dry-land training stress (Chatard, Atlaoui, Lac, Duclos, Hooper and Mackinnon 2002).

Luteinizing hormone (LH): It has been shown that decline in overnight testosterone concentrations after acute heavy-resistance exercise is accompanied by a blunted LH production rate and elevated C concentrations (Nindl, Kraemer, Deaver, Peters, Marx, Heckman and Loomis 2001).

Neuropeptide Y: In the elderly group plasma neuropeptide Y did not increase during exercise and showed a tendency to fall below basal level 5 min post-exercise (Winther Jensen, Espersen, Kanstrup and Christensen 1992).

adrenocorticotropin (ACTH): The experimental group demonstrated a significant reduction in the ACTH response to the work rate. On the other hand the control group demonstrated an unchanged response) over the course of the study. These results suggest that the ACTH response to an absolute submaximal work rate is blunted after training (Buono, Yeager and Sucec 1987).

creatine kinase (CK): The level of creatine kinase (CK) was measured in a group of recreationally trained men participating in a 12-week resistance training. The training sessions consist of 4 training periods (t1, t2, t3, and t4). The data analysis shows that CK increased only after t3 (Fatouros, Destouni, Margonis, Jamurtas, Vrettou, Kouretas, Mastorakos, Mitrakou, Taxildaris, Kanavakis and Papassotiriou 2006).

Discussion and Conclusions

The presented list of protein markers comprises roughly of 37 markers, which in our opinion may be of use for profiling the changes in physical fitness on both recreational as well as competitive level. As mentioned in the introduction one may, at first glance, notice the enormous functional spread of the markers. Generally, the protein markers can be divided into two main groups. The first group comprises the markers of high concentration associated with low physical fitness. The second group consists of markers appearing in low concentration reflecting low physical fitness. The first group consists among others of CRP protein which high level is associated with low physical performance. However, the CRP level does not differ by gender when considering the mean fitness level. Another member of this group are some of interleukins. The reader may easily notice that high levels of IL-6 is significantly associated with poor physical performance and muscle strength in older persons and IL-1RA is significantly associated with poor physical performance and muscle strength in older persons. However, the researchers also show that some of the interleukin are training season depended and the fore mentioned correlation does not hold in some cases. It has been shown that during the wrestling season with intense exercise training the level of IL-1ra increases.

Another group comprises the markers which concentration decreases which the increase of the level of physical fitness. This group may be represented by, for example, tumor necrosis factor (TNF) or amyloid-A. The level of these both markers decreases circa 20% when comparing physically active and sedentary individuals.

It also appears that some of the markers are sport specific. Such an example is urinary C-telopeptide of type II collagen and its level is significantly higher in swimmers than in runners.

The analysis of the presented data leads to the following conclusions. The approach undertaken by many of the research is rather chaotic not taking into account the previously presented data. This may be caused by the complexity of the problem. It seems that most of the researchers are searching for " a holly grail" among the protein markers. Such an approach is obviously very tempting but one has to be rather naïve thinking to be able to find a single marker reflecting the level of physical performance. In our opinion a different approach should be taken. The current progress in proteomics allows analysis of human proteome on a large scale - up to 2000 protein in one run. Taking into consideration the complexity of the problem one may expect not a single marker but a group of marker to reflect the fitness level. The extensive statistical analysis of the changes of markers level correlated with basic physiological studies may be the only way of approaching this problem.

References

Adiyaman, P., G. Ocal, M. Berberoglu, O. Evliyaoglu, Z. Aycan, E. Cetinkaya, Y. Bulca, G. Ersoz and N. Akar (2004). "Alterations in serum growth hormone (GH)/GH dependent ternary complex components (IGF-I, IGFBP-3, ALS, IGF-I/IGFBP-3 molar ratio) and the influence of these alterations on growth pattern in female rhythmic gymnasts." J Pediatr Endocrinol Metab 17(6): 895-903.

Bentzen, H., R. S. Pedersen, O. Nyvad and E. B. Pedersen (2002). "Influence of training habits on exercise-induced changes in plasma atrial and brain natriuretic peptide and urinary excretion of aquaporin-2 in healthy man." Scand J Clin Lab Invest 62(7): 541-51.

Billinghurst, R. C., P. A. Brama, P. R. van Weeren, M. S. Knowlton and C. W. McIlwraith (2003). "Significant exercise-related changes in the serum levels of two biomarkers of collagen metabolism in young horses." Osteoarthritis Cartilage 11(10): 760-9.

Buono, M. J., J. E. Yeager and A. A. Sucec (1987). "Effect of aerobic training on the plasma ACTH response to exercise." J Appl Physiol 63(6): 2499-501.

Carmichael, M. D., J. M. Davis, E. A. Murphy, A. S. Brown, J. A. Carson, E. P. Mayer and A. Ghaffar (2006). "Role of brain IL-1beta on fatigue after exercise-induced muscle damage." Am J Physiol Regul Integr Comp Physiol 291(5): R1344-8.

Cesari, M., B. W. Penninx, M. Pahor, F. Lauretani, A. M. Corsi, G. Rhys Williams, J. M. Guralnik and L. Ferrucci (2004). "Inflammatory markers and physical performance in older persons: the InCHIANTI study." J Gerontol A Biol Sci Med Sci 59(3): 242-8.

Chatard, J. C., D. Atlaoui, G. Lac, M. Duclos, S. Hooper and L. Mackinnon (2002). "Cortisol, DHEA, performance and training in elite swimmers." Int J Sports Med 23(7): 510-5.

Chen, K. T. and R. S. Yang (2004). "Effects of exercise on lipid metabolism and musculoskeletal fitness in female athletes." World J Gastroenterol 10(1): 122-6.

Chennaoui, M., C. Drogou, D. Gomez-Merino and C. Y. Guezennec (2005). "Effects of an intense training on functional activity of 5-HT(1B) receptors in human peripheral blood lymphocytes." Neurosci Lett 382(1-2): 1-4.

Cox, J. H., R. N. Cortright, G. L. Dohm and J. A. Houmard (1999). "Effect of aging on response to exercise training in humans: skeletal muscle GLUT-4 and insulin sensitivity." J Appl Physiol 86(6): 2019-25.

Drenth, J. P., S. H. Van Uum, M. Van Deuren, G. J. Pesman, J. Van der Ven-Jongekrijg and J. W. Van der Meer (1995). "Endurance run increases circulating IL-6 and IL-1ra but downregulates ex vivo TNF-alpha and IL-1 beta production." J Appl Physiol 79(5): 1497-503.

Elphick, G. F., B. N. Greenwood, J. Campisi and M. Fleshner (2003). "Increased serum nIgM in voluntarily physically active rats: a potential role for B-1 cells." J Appl Physiol 94(2): 660-7.

Emter, C. A., S. A. McCune, G. C. Sparagna, M. J. Radin and R. L. Moore (2005). "Low-intensity exercise training delays onset of decompensated heart failure in spontaneously hypertensive heart failure rats." Am J Physiol Heart Circ Physiol 289(5): H2030-8.

Fatouros, I. G., A. Destouni, K. Margonis, A. Z. Jamurtas, C. Vrettou, D. Kouretas, G. Mastorakos, A. Mitrakou, K. Taxildaris, E. Kanavakis and I. Papassotiriou (2006). "Cell-free plasma DNA as a novel marker of aseptic inflammation severity related to exercise overtraining." Clin Chem 52(9): 1820-4.

Frosig, C., S. B. Jorgensen, D. G. Hardie, E. A. Richter and J. F. Wojtaszewski (2004). "5'-AMP-activated protein kinase activity and protein expression are regulated by endurance training in human skeletal muscle." Am J Physiol Endocrinol Metab 286(3): E411-7.

Garcia-Unzueta, M. T., J. B. Gutierrez-Sanchez, I. de Mier, J. A. Amado and J. R. Berrazueta (2003). "Autoantibodies against oxidized LDL and serum total antioxidant status in active cyclists and ex-cyclists." Horm Metab Res 35(9): 541-5.

Gomez-Merino, D., C. Drogou, M. Chennaoui, E. Tiollier, J. Mathieu and C. Y. Guezennec (2005). "Effects of combined stress during intense training on cellular immunity, hormones and respiratory infections." Neuroimmunomodulation 12(3): 164-72.

Hadzovic, A., E. Nakas-Icindic, E. Kucukalic-Selimovic, N. Avdagic and A. Zaciragic (2004). "The level of physical activity and the growth hormone (GH) response to acute physical exercise." Bosn J Basic Med Sci 4(3): 47-9.

Halle, M., U. Korsten-Reck, B. Wolfarth and A. Berg (2004). "Low-grade systemic inflammation in overweight children: impact of physical fitness." Exerc Immunol Rev 10: 66-74.

Haluzik, M., D. Haluzikova, P. Brandejsky, J. Nedvidkova, L. Boudova, M. Barackova and Z. Vilikus (1999). "[Effect of aerobic training in top athletes on serum leptin: comparison with healthy non-athletes]." Vnitr Lek 45(1): 51-4.

Houmard, J. A., G. L. Tyndall, J. B. Midyette, M. S. Hickey, P. L. Dolan, K. E. Gavigan, M. L. Weidner and G. L. Dohm (1996). "Effect of reduced training and training cessation on insulin action and muscle GLUT-4." J Appl Physiol 81(3): 1162-8.

Isasi, C. R., R. J. Deckelbaum, R. P. Tracy, T. J. Starc, L. Berglund, S. Shea and B. Corrigan (2003). "Physical fitness and C-reactive protein level in children and young adults: the Columbia University BioMarkers Study DHEA: the last elixir DHEA and sport." Pediatrics 111(2): 332-8.

Keller, C., A. Steensberg, A. K. Hansen, C. P. Fischer, P. Plomgaard and B. K. Pedersen (2005). "Effect of exercise, training, and glycogen availability on IL-6 receptor expression in human skeletal muscle." J Appl Physiol 99(6): 2075-9.

King, D. E., P. Carek, A. G. Mainous, 3rd and W. S. Pearson (2003). "Inflammatory markers and exercise: differences related to exercise type." Med Sci Sports Exerc 35(4): 575-81.

Kishali, N. F., O. Imamoglu, M. Kaldirimci, P. Akyol and K. Yildirim (2005). "Comparison of lipid and lipoprotein values in men and women differing in training status." Int J Neurosci 115(9): 1247-57.

Manetta, J., J. F. Brun, L. Maimoun, A. Callis, C. Prefaut and J. Mercier (2002). "Effect of training on the GH/IGF-I axis during exercise in middle-aged men: relationship to glucose homeostasis." Am J Physiol Endocrinol Metab 283(5): E929-36.

Musi, N., H. Yu and L. J. Goodyear (2003). "AMP-activated protein kinase regulation and action in skeletal muscle during exercise." Biochem Soc Trans 31(Pt 1): 191-5.

Neidhart, M., U. Muller-Ladner, W. Frey, A. K. Bosserhoff, P. C. Colombani, P. Frey-Rindova, K. M. Hummel, R. E. Gay, H. Hauselmann and S. Gay (2000). "Increased serum levels of non-collagenous matrix proteins (cartilage oligomeric matrix protein and melanoma inhibitory activity) in marathon runners." Osteoarthritis Cartilage 8(3): 222-9.

Nemet, D., P. H. Connolly, A. M. Pontello-Pescatello, C. Rose-Gottron, J. K. Larson, P. Galassetti and D. M. Cooper (2004). "Negative energy balance plays a major role in the IGF-I response to exercise training." J Appl Physiol 96(1): 276-82.

Nemet, D., A. M. Pontello, C. Rose-Gottron and D. M. Cooper (2004). "Cytokines and growth factors during and after a wrestling season in adolescent boys." Med Sci Sports Exerc 36(5): 794-800.

Niebauer, J., R. Hambrecht, T. Velich, C. Marburger, K. Hauer, J. Kreuzer, R. Zimmermann, E. von Hodenberg, G. Schlierf, G. Schuler and W. Kubler (1996). "Predictive value of lipid profile for salutary coronary angiographic changes in patients on a low-fat diet and physical exercise program." Am J Cardiol 78(2): 163-7.

Nieman, D. C., C. L. Dumke, D. A. Henson, S. R. McAnulty, S. J. Gross and R. H. Lind (2005). "Muscle damage is linked to cytokine changes following a 160-km race." Brain Behav Immun 19(5): 398-403.

Nilssen, D. E., O. Oktedalen, I. Lygren, P. K. Opstad and P. Brandtzaeg (1998). "Intestinal IgA- and IgM-producing cells are not decreased in marathon runners." Int J Sports Med 19(6): 425-31.

Nindl, B. C., J. W. Castellani, A. J. Young, J. F. Patton, M. J. Khosravi, A. Diamandi and S. J. Montain (2003). "Differential responses of IGF-I molecular complexes to military operational field training." J Appl Physiol 95(3): 1083-9.

Nindl, B. C., W. J. Kraemer, D. R. Deaver, J. L. Peters, J. O. Marx, J. T. Heckman and G. A. Loomis (2001). "LH secretion and testosterone concentrations are blunted after resistance exercise in men." J Appl Physiol 91(3): 1251-8.

Nindl, B. C., W. J. Kraemer, J. O. Marx, P. J. Arciero, K. Dohi, M. D. Kellogg and G. A. Loomis (2001). "Overnight responses of the circulating IGF-I system after acute, heavy-resistance exercise." J Appl Physiol 90(4): 1319-26.

O'Kane J, W., E. Hutchinson, L. M. Atley and D. R. Eyre (2005). "Sport-related differences in biomarkers of bone resorption and cartilage degradation in endurance athletes." Osteoarthritis Cartilage 23: 23.

Ohkuwa, T. and H. Itoh (1993). "High density lipoprotein cholesterol following anaerobic swimming in trained swimmers." J Sports Med Phys Fitness 33(2): 200-2.

Panagiotakos, D. B., C. Pitsavos, C. Chrysohoou, S. Kavouras and C. Stefanadis (2005). "The associations between leisure-time physical activity and inflammatory and coagulation markers related to cardiovascular disease: the ATTICA Study." Prev Med 40(4): 432-7.

Panagiotakos, D. B., C. Pitsavos, C. Chrysohoou, J. Skoumas, A. Zeimbekis, I. Papaioannou and C. Stefanadis (2003). "Effect of leisure time physical activity on blood lipid levels: the ATTICA study." Coron Artery Dis 14(8): 533-9.

Pitsavos, C., D. B. Panagiotakos, C. Chrysohoou, S. Kavouras and C. Stefanadis (2005). "The associations between physical activity, inflammation, and coagulation markers, in people with metabolic syndrome: the ATTICA study." Eur J Cardiovasc Prev Rehabil 12(2): 151-8.

Robson, P. (2003). "Elucidating the unexplained underperformance syndrome in endurance athletes : the interleukin-6 hypothesis." Sports Med 33(10): 771-81.

Rogers, P. J., G. M. Tyce, K. R. Bailey and A. A. Bove (1991). "Exercise-induced increases in atrial natriuretic factor are attenuated by endurance training." J Am Coll Cardiol 18(5): 1236-41.

Roos, H., L. Dahlberg, L. A. Hoerrner, M. W. Lark, E. J. Thonar, M. Shinmei, U. Lindqvist and L. S. Lohmander (1995). "Markers of cartilage matrix metabolism in human joint fluid and serum: the effect of exercise." Osteoarthritis Cartilage 3(1): 7-14.

Rosendal, L., H. Langberg, A. Flyvbjerg, J. Frystyk, H. Orskov and M. Kjaer (2002). "Physical capacity influences the response of insulin-like growth factor and its binding proteins to training." J Appl Physiol 93(5): 1669-75.

Ryan, A. S. and D. Elahi (1998). "Loss of bone mineral density in women athletes during aging." Calcif Tissue Int 63(4): 287-92.

Schrauwen, P. and M. Hesselink (2003). "Uncoupling protein 3 and physical activity: the role of uncoupling protein 3 in energy metabolism revisited." Proc Nutr Soc 62(3): 635-43.

Soares, J., M. G. Naffah-Mazzacoratti and E. A. Cavalheiro (1994). "Increased serotonin levels in physically trained men." Braz J Med Biol Res 27(7): 1635-8.

Suzuki, K., M. Yamada, S. Kurakake, N. Okamura, K. Yamaya, Q. Liu, S. Kudoh, K. Kowatari, S. Nakaji and K. Sugawara (2000). "Circulating cytokines and hormones with immunosuppressive but neutrophil-priming potentials rise after endurance exercise in humans." Eur J Appl Physiol 81(4): 281-7.

Tanaka, H., K. A. West, G. E. Duncan and D. R. Bassett, Jr. (1997). "Changes in plasma tryptophan/branched chain amino acid ratio in responses to training volume variation." Int J Sports Med 18(4): 270-5.

Tikkanen, H. O., E. Hamalainen and M. Harkonen (1999). "Significance of skeletal muscle properties on fitness, long-term physical training and serum lipids." Atherosclerosis 142(2): 367-78.

Toth, M. J., P. A. Ades, M. D. Tischler, R. P. Tracy and M. M. LeWinter (2006). "Immune activation is associated with reduced skeletal muscle mass and physical function in chronic heart failure." Int J Cardiol 109(2): 179-87.

Uusitalo, A. L., M. Valkonen-Korhonen, P. Helenius, E. Vanninen, K. A. Bergstrom and J. T. Kuikka (2004). "Abnormal serotonin reuptake in an overtrained, insomnic and depressed team athlete." Int J Sports Med 25(2): 150-3.

Uusitalo, A. L., E. Vanninen, M. Valkonen-Korhonen and J. T. Kuikka (2006). "Brain serotonin reuptake did not change during one year in overtrained athletes." Int J Sports Med 27(9): 702-8.

Verde, T. J., S. G. Thomas, R. W. Moore, P. Shek and R. J. Shephard (1992). "Immune responses and increased training of the elite athlete." J Appl Physiol 73(4): 1494-9.

Vollmer-Larsen, B., A. Vollmer-Larsen, O. G. Larsen, L. Breum, J. Larsen and N. Keller (1989). "Atrial natriuretic factor during exercise in male endurance athletes: effect of training." Clin Physiol 9(5): 449-56.

Vuorimaa, T., M. Ahotupa, K. Irjala and T. Vasankari (2005). "Acute prolonged exercise reduces moderately oxidized LDL in healthy men." Int J Sports Med 26(6): 420-5.

Wang, J. S. and S. E. Chow (2004). "Effects of exercise training and detraining on oxidized low-density lipoprotein-potentiated platelet function in men." Arch Phys Med Rehabil 85(9): 1531-7.

Williams, M. J., B. J. Milne, R. J. Hancox and R. Poulton (2005). "C-reactive protein and cardiorespiratory fitness in young adults." Eur J Cardiovasc Prev Rehabil 12(3): 216-20.

Winther Jensen, E., K. Espersen, I. L. Kanstrup and N. J. Christensen (1992). "Age-related changes of exercise-induced plasma catecholamines and neuropeptide Y responses in normal human subjects." Acta Physiol Scand 144(2): 129-33.

Wojtaszewski, J. F., C. MacDonald, J. N. Nielsen, Y. Hellsten, D. G. Hardie, B. E. Kemp, B. Kiens and E. A. Richter (2003). "Regulation of 5'AMP-activated protein kinase activity and substrate utilization in exercising human skeletal muscle." Am J Physiol Endocrinol Metab 284(4): E813-22.

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