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LA MEDICINA DEL DEPORTE Y LA GENÉTICA - UN ÁREA DE INVESTIGACIÓN DIFÍCIL

SPORT MEDICINE AND GENETICS – A CHALLENGING RESEARCH AEREA

EDITORIAL

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As all other medical specialities in the beginning of the 21st century sports medicine and exercise physiology are entering the challenging research area of molecular biology, genomics and proteomics. Detailed knowledge in this area will influence all fields of research and practical applications, which sports medicine has to fulfil, with special emphasis to keep athletes healthy and to increase their performance, to foster regular physical activity as preventive measures, to shorten the come-back-time of athletes and patients in the frame of treatment and rehabilitation and to fight against doping and gendoping. Out of a plethora of research, three areas will be addressed in the following paragraphs.

One important application of genetic research is the development of genetic performance-test, to predict (talent-diagnosis) and/or influence the performance of athletes with individualised training programmes, which are also applicable in the prevention and rehabilitation, in a way to identify those persons, who are most likely to benefit medically from individualised exercise-prescriptions. Genetic testing can be also applied for pre-participation risk screening for example to prevent sudden death during sport or to lower the incidence of repeated injuries and overstrain in the musculoskeletal system. In the past years an increasing number of "interesting genes" like ACTN3, ACE, PPAR…. e.g. were found and a lot of studies were published about the association of different polymorphisms of these genes to differentiate performance characteristics. However, a lot of conflicting results were evaluated, showing that there is no "black and white" because of a lot of interrelations between the genes and the genes and environment underlying the polygenic approach of the physical performance. Therefore, recent studies try to include more polymorphisms of different genes, relating them to the physical performance. In a study, A.G. Williams, *et al*[1]. tried to identify associations between 23 genetic polymorphisms and human endurance phenotypes, using probability calculations. The authors found only a 0,0005 % chance of a single individual in the world having the "preferable" profile of all investigated 23 polymorphisms. In another trial, Ahmetof I.I[2]. analysed eight genetic polymorphisms (NFATC4 Gly160, PPARGC1A Gly482, PPARGC1B 203Pro, PPP3R1 5I, TFAM 12Thr, VEGF rs2010963 C, UCP2 55Val, UCP3 rs1800849 T) in 1580 Russian athletes and 1057 controls. 66,7% of highly endurance trained athletes were carriers of 8-12 endurance-related alleles, compared with only 18,1% of such persons in the control-group. In a recent publication J.R. Ruiz[3] analysed seven genetic polymorphisms (ACE, ACTN3, AMPD1, CKMM, HFE, GDF8, PPARGC1A) in 46 world class endurance athletes and 123 controls (all Spanish caucasians). They found a probability of a Spanish individual possessing a theoretical optimal polygenic profile for these candidate gene polymorphisms of about 0,074% chance. In addition, only three of the best Spanish endurance athletes had the best possible score for up to six genes and none of them were found to have the optimal profile. Therefore, future studies have to clarify, which yet undiscovered polymorphisms as well as several factors independent of genetic endovement may explain, why some athletes have performance advantages and which combinations of gene-polymorphisms may be able to compensate missing "optimal polymorphism" in a so-called "optimal profile" which – from a future data-based knowledge must not be the real "optimal profile".

Similar mechanisms may be underlying the occurrence of so-called chronic diseases, like type II diabetes, cardiovascular diseases, colon cancer, breast cancer, over-weight and obesity, dementia and depression. Most of these diseases are not independent of each other, although they are often diagnosed and treated individually. To understand the underlying mechanisms of this diseases network, it is necessary to find out detailed pattern of various cellular responses influenced by specific genes and specific polymorphisms. Such a genetic network based thinking is more and more introduced into the research about the pathogenesis of chronic diseases, turning the research from the disease to the "diseasome" (A. Brand, *et al*.[4]). For example, Pedersen, *et al*[5]. are investigating the existence of a so-called "diseasome of physical inactivity" to understand, why the before mentioned diseases appear in clusters, although there is a highly difference in terms of genotypical presentation, symptoms and treatment. In contrast, regular exercise and physical activity counteracts these effects because of inducing an anti-inflammatory response, which in part is mediated by muscle-derived cytokines, called myokines, like IL-6 and others. It is suggested, that these myokines may play important roles in the protection against diseases associated with low grade inflammation.

Another field of interest is the therapeutic use of growth factors in the musculoskeletal system after sports-related injuries. These growth factors act as signalling agents for cells and become a more and more popular mean to influence the human body and its tissues (Bachl, *et al*.)[6]. Global statistics figure out, that there are over 100 million musculoskeletal (tendon, muscle, bone) injuries annually which cause a significant loss of performance capability in sport and daily life and decreased the functional capacity in the workplace. That means that musculo-skeletal injuries have also a negative impact on the ability and desire of the patients to undertake physical activities. In addition, these injuries may cause long-term pain and discomfort since many of them are difficult to treat. Growth factors compile a number of secreted and cell-surface proteins, which are able to modulate the growth of target-cells affecting different processes as migration, chemotaxis, celldivision, matrix-production and the coordination of tissue differentiation. For example FGF (fibroblast growth factor), VEGF (vascular endothelial-growth factor), TGF – ß (transforming growth factor), Myostatin, LIF (leukaemia inhibitory factor) and MGF (mechanical growth factor) are involved into the skeletal muscle adaption and repair, which can be important to treat muscle atrophy after severe injuries and operations, and/or bedrest or patients with sarcopenia. A lot of these growth factors play also an important role with regard to bone formation and repair as well as ligament and tendon-repair. Summarizing the worldwide research in that area, it is becoming apparent, that the repair and the modelling of muscular skeletal tissues involve a network of signalling pathways that results from the expression of several genes. That means, that more than one growth factor may be expressed and in addition in different time courses which may depend on the tissue and severity of injuries. There are existing also some studies, exhibiting improved healing of patients treating them with autologous PRP (plateled-rich plasma) (Foster TE)[7] which contains several kinds of growth factors in high concentration. Future research has to figure out the time course in which these growth factors are expressed in different tissues and also the necessary concentrations to ensure an optimal therapeutic effect with and without physical exercise. Although some of these growth factors show a high promise for future clinical use, it has pointed out very clearly that there is also the possibility that those growth factors which enhance skeletal muscle strength may be used illegally for performance enhancement.

Summarising these areas, it can be clearly understood, that a lot of future research has to be done, to understand the molecular mechanism induced by physical activity and – on the other hand – sedentary lifestyle and thereout to use the knowledge for preventive and rehabilitative measures in the future.

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