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**Genetic prescription for health: The impact of exercise and inflammation on immunogenetics**

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ABSTRACT

While inflammation is a central part of our immune defense, excessive inflammation in acute and chronic situations (sepsis; inflammaging) can be very harmful and life shortening. Exercise has been shown to induce and modify gene expression in different tissues. Among the genes strongly activated by exercise, inflammation-related genes are of prime importance. We try to give an overview about the effect of exercise on the activation of genes and pathways involved in inflammation. Activation of inflammatory genes can readily be observed in the muscle, where exercise begins. Other organs can also be influenced by exercise, such as brain, liver and heart, but a mirror of inflammatory regulations by exercise can be found in peripheral blood. The majority of investigations, including ours, thus, have used peripheral blood for analysis. With the advent of microarray technology enormous amounts of data on gene expression following exercise have been generated and a large part of these is related to inflammation. Altogether, it seems that exercise induces both, pro-inflammatory genes (including asthma related genes) but also prominent anti-inflammatory genes. There are differences in gene regulation due to type and duration of exercise, sex and age of the subjects, and the technologies used for analysis. Observations of exercise activity in athletes with solid transplants who are under immunosuppressive medication shows that the vast part of the inflammatory reaction and its anti-inflammatory counter reaction are absent in these patients in spite of performance comparable to healthy subjects. We also present results from a recent study which includes ex vivo stimulation by endotoxin (LPS). They show that exercise can also modify the reaction of peripheral blood cells to TLRs mediated pathogen activation. In special, activation of TNIP3, a negative regulator of TLRs signaling and down-regulation of IFN- $\beta$ 1 through exercise could be observed in these cultures but not in unstimulated cultures. A hypothesis of the interaction of exercise with TLRs signaling will be presented.

