

## DESCRIPTION FOR THE GENERAL PUBLIC

Proper dietary supplementation may have a significant effect on health, the sense of well-being, and also functional and physical capacity of the organism. However, influences of many commercially available supplements on human body have not been verified in a reliable study, without that using of such preparations cannot be recommended.

One of the supplements with a wide spectrum of effects is beta-hydroxy-beta-methylbutyrate (HMB). Effectiveness of this compound is frequently reported in different groups, for example in athletes, malnourished subjects, the elderly, trauma patients, and those suffering from many diseases. Moreover, HMB may support cancer or sarcopenia therapies. It may also stimulate the activity of the immune system and bone tissue metabolism. However, mechanisms of action or actual effects of HMB on human body have not been fully clarified. Furthermore, we may expect that the HMB supply should be precisely calculated with respect to lean body mass. The effectiveness of this preparation may also depend on additional stimuli, including malnutrition or exercise. These aspects have never been tested.

We assume that HMB supplementation acts through activation of protein kinase pathways and hormones concentrations, which determine the synthesis of muscle proteins and anabolic processes in the body. We also hypothesize that HMB stimulates metabolic rates and changes utilization and availability of energy substrates. HMB can therefore stimulate lean body mass and increase exercise capacity, and reduce body fat. Moreover, we hypothesize that the effect of HMB intake depends on the type of exercise stimulus and the greatest benefits can be when additional physical activity is included during supplementation.

The objective of this project is thus to evaluate molecular and physiological mechanisms of HMB supplementation on the human body, taking into account that the effect of HMB may be dependent on additional factors, particularly functional physical exercise or low muscle mass.

This project will be performed with the participation of two men groups: a group of trained subjects, regularly practicing sports (S group) and an inactive group showing features of malnutrition (W group). Participants will be supplemented with beta-hydroxy-beta-methylbutyrate free acid (HMB-FA) or placebo (at a dose adjusted for lean body mass) for 21 days. Supplementation will be conducted twice - period I: during normal physical activity (S group) / lifestyle (W group); period II: with additional functional physical activity (S and W groups).

The research procedures will include analysis of protein kinases activity. We selected kinases which determine the effectiveness of muscle protein synthesis (*Akt/PBK/mTOR/p70<sup>S6K</sup>* and *MAPK/ERK*). In order to evaluate an anabolic status, organism homeostasis, and metabolism of energy substrates, concentration of hormones (*testosterone, IGF-1, growth hormone, cortisol*), alternative energy sources (*ketone bodies, free fatty acids* and the *index evaluating lipolysis efficiency*), gasometric and electrolytes indices, urea, creatinine, glucose, lactate and bilirubin, as well as activity of intramuscular enzymes (*creatine kinase* and *lactate dehydrogenase*) will be analyzed in blood. Daily energy expenditure, resting and exercise metabolic rates, aerobic capacity, and utilization of energy substrates will be measured. Additionally body composition, nutrient intake and physical activity will be also assessed.

It needs to be stressed that studies planned in this project are necessary in the context of scientific evaluation as well as the practical knowledge on actual impact of HMB on the human body. The obtained results will allow to describe metabolic and physiological response to HMB supplementation. It seems particularly significant, since HMB intake may in many cases contribute to healthy aging, improving nutritional status and therapy of many diseases. It may also support people working under particularly difficult conditions or stimulate training process efficiency in athletes. This interdisciplinary project is of considerable importance for broadening basic scientific knowledge, as well as for numerous practical problems related to health and quality of life.