PROJECT REVIEW

"Circulating myomiRs as markers of myogenic precursor abundance"

Dr. P. Costelli (University of Turin, Italy)

Skeletal muscle size is dynamic and responsive several stimuli, among which exercise. However, while resistance exercise results in hypertrophy and increased force generation, endurance exercise leads to increased expression of the peroxisome proliferator-activated receptor (PPAR)-γ coactivator-1α (PGC-1α) and increased number of mitochondria, with little changes in the skeletal muscle mass. Both types of exercise stimulate the proliferation of satellite cells, muscle-specific stem cells that will subsequently differentiate and fuse with existing myofibers. Finally, exercise also increases circulating microRNAs (miRs), short noncoding RNAs that post-transcriptionally modulate gene expression. Some miRs (myomiRs: miR-1, miR-133a, miR-133b, miR-206) are abundant in the skeletal muscle and appear modulated in muscle atrophy, hypertrophy and myogenesis.

Autologous transplantation of myogenic stem cells has been proposed as the next generation doping strategy. The number of myogenic precursors may be increased both 'artificially' by autologous implantation, or physiologically, by regular exercise. However, while all myogenic precursors are increased by the implantation, exercise mainly leads to satellite cell accumulation.

The target of the study is to define if autologous myogenic stem cell implantation may effectively impinge on muscle mass and function and to clarify if circulating myomiR levels can be useful as biomarkers of myogenic stem cell abundance and type. The study will be developed by using transgenic mice hyperexpressing PGC-1α specifically in the skeletal muscle. These mice mimic the condition of endurance-trained subjects, being characterized by high exercise performance. Briefly, circulating myomiRs will be evaluated in these mice, and correlated with the abundance and type of myogenic stem cells. Subsequently, myogenic stem cells isolated from wild-type and transgenic animals will be implanted into wild-type recipients, to test the effectiveness of the procedure in improving muscle mass/function. The results obtained with the transgenic mice will be validated on human volunteers.