Myokines and metabolic regulation

M.A. Febbraio[1] and B.K. Pedersen,[2] [1]Cellular & Molecular Metabolism Laboratory, Division of Metabolism & Obesity, Baker IDI Heart & Diabetes Institute, 75 Commercial Rd, Melbourne, VIC 3004, Australia. and [2]Centre of Inflammation and Metabolism, Rigshospitalet - Section 7641, Blegdamsvej 9, DK-2100, Copenhagen, Denmark.

Regular physical activity is known to have multiple health benefits. Of note, exercise is associated with increased insulin stimulated glucose uptake in the immediate post exercise period, while chronic physical activity enhances insulin sensitivity. However, the precise mechanisms by which physical activity confers protection against metabolic disease are not fully understood. Approximately five years ago, we identified skeletal muscle as a cytokine-producing organ demonstrating that the metabolic and physiologic effects of exercise also may be mediated by muscle derived humoral factors (Pedersen & Febbraio, 2008). We have identified that both interleukin-6 and brain derived neurotrophic factor are "myokines" that are up-regulated by muscle contraction and released from contracting skeletal muscle where they play important roles in lipid and glucose metabolism in other metabolically active tissues such as liver and adipose tissue. These discoveries were made serendipitously, but it is likely that contracting skeletal muscle produces many myokines that positively act on the metabolism of other organs, presenting novel targeted therapeutics for the treatment of obesity related type 2 diabetes. We are currently using the well established quantitative method, namely Stable Isotope Labelling by Amino Acids in Cell Culture (SILAC) which allows the direct and unbiased quantification of protein expression/secretion to identify novel myokines. SILAC utilizes the capability of the cells to be grown in defined media, containing “normal” amino acid or a stable isotope-labelled “heavy” versions of the same amino acid thereby encoding the entire proteome of a given cellular population. Using triple encoding SILAC in combination with highly advanced mass spectrometry we are currently identifying the proteins secreted by the myoblast C2C12 cells during contraction. The identification of novel myokines that play a biological role in energy metabolism may aid in the development of identifying new drug targets to treat obesity related disorders.

Pedersen BK & Febbraio MA. (2008) *Physiological Reviews,* **88**, 1379-1406. doi:10.1152/physrev.90100.2007.