Manipulating β-adrenergic signaling in skeletal muscle: implications for exercise and muscle wasting disorders

Gordon S. Lynch, Department of Physiology, University of Melbourne, Australia

Muscle wasting is an urgent and unmet health risk that is commonly associated with ageing and with conditions as diverse as cachexia caused by cancer, renal, respiratory and cardiac insufficiency; disuse from inactivity/nerve injury/unloading; sepsis, burns, and metabolic disorders; HIV-AIDS; and neuromuscular diseases of genetic origin. Manipulation of the β-adrenoceptor (β-AR) signalling pathway could be utilized to combat muscle wasting. Several β_2-AR agonists (β-agonists) readily promote muscle anabolism, and related compounds have been used clinically for other indications with positive outcomes. However, the indisputable capacity of β-agonists to promote muscle growth has not been clinically deployed because of concerns over potential adverse cardiac effects with chronic use. While some effects of β-agonist administration on skeletal muscle are desirable, especially for many wasting disorders, there are pitfalls associated with off-target and/or undesirable outcomes relevant to exercise and fatigue. If beneficial clinical implementation of effective treatments for muscle wasting is to occur, developing interventions that eliminate unwanted effects of β-AR signaling must be viewed as an utmost priority.