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**Title:** Muscle remodelling is blunted in hypoxemic COPD patients after pulmonary rehabilitation

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**Body:** Pulmonary rehabilitation in COPD patients aims at increasing exercise tolerance, partly through improving muscle function. The influence of chronic hypoxia on the training-induced muscle adaptations has not been specifically investigated. We studied muscle adaptations and exercise capacity following 2 months of endurance and resistance exercises in 8 COPD patients with long term oxygen therapy (hypoxic group) and 15 without arterial oxygen desaturation (normoxic group). Biopsies of the vastus lateralis were analyzed before and after training for fiber size, citrate synthase activity, and markers of protein synthesis/degradation. At baseline both groups did not differ in pulmonary function, fat free mass, or exercise capacity. Maximal workload and walking distance improved in both groups but to a greater extent in the hypoxic group (27.5 versus 10.5%,  $p=0.06$ ; 23.7% versus 6.9%,  $p=0.01$ , respectively). Fiber cross sectional area and citrate synthase activity increased significantly in the normoxic group only (both  $p<0.05$ ). Levels of phosphorylated AKT, p70S6K and GSK3b tended to increase with training in the normoxic group in favour of an upregulation of anabolism while decreased significantly in the hypoxic group ( $p=0.01$ ). mRNA levels of anabolic genes (IGF1, MGF) and catabolic genes (MurF-1, Atrogin, Foxo-1 and -3, Myostatin) did not change with training in both groups. We conclude that in COPD patients with chronic hypoxemia, pulmonary rehabilitation improved exercise capacity while the markers of muscle remodelling remained unchanged. It deserves to be studied whether changes in genes expression occurred earlier during rehabilitation in these patients.