COPD is defined by its effects on the lung, however skeletal muscle atrophy and a slow-to-fast fibre shift are common clinical observations, associated with reduced survival and exercise intolerance in patients; making the molecular pathways which regulate these processes of interest. MicroRNAs (miRNAs) are small non-coding RNAs that can reduce mRNA half-life and inhibit protein translation, and we have previously shown that the expression of muscle-specific miRNAs, miR-1 and miR-499 are altered in the quadriceps of COPD patients compared to controls. To further investigate the relationship between miRNAs and muscle disease in COPD, we have now conducted a TaqMan miRNA array. The key finding of this study is that a low fat-free mass index (LFFMI) in COPD patients, is associated with a marked reduction in a number of stem-cell associated miRNAs derived from a miRNA cluster on chromosome-19 (e.g. miR-519a). There was also a reduction in the number of regenerating muscle fibres in LFFMI patients, implying some degree of satellite cells dysfunction. Circulating levels of miR-519a were also reduced in LFFMI patients relative to patients with a normal FMMI (NFFMI), and both plasma and muscle levels of miR-519a were correlated with FFMI in a larger validation cohort. Together these data suggest that loss of muscle mass in COPD is associated with a reduction in stem-cell associated miRNAs and a reduced regenerative capacity.