**BACKGROUND.** Proteomic studies of the secretome of skeletal muscle cells will help to understand the processes that govern the synthesis and organization of skeletal muscle. In this systematic review, we have summarized recent mass-spectrometry based proteomics discoveries of the secretome of skeletal muscle cells in response to disease, exercise or metabolic stress.

**METHODS.** A literature search was performed according to the PRISMA guidelines in the Medline/Ovid and Scopus electronic databases and manual searching of relevant literature was also carried out. Only papers published in English from 2000 and reporting the analysis of the secretome of isolated skeletal muscle myoblasts or of skeletal muscle explants of all species by mass spectrometry were included.

**RESULTS.** According to the preliminary results, a total of 17 papers met the inclusion criteria for this review. Published research included comparative analysis of differently expressed proteins between healthy and unhealthy (Duchenne muscular dystrophy and insulin-resistant cells) muscle cells and comparison of the secretome of skeletal muscle cells during myogenesis and after insulin stimulation or exercising. The proteins were separated into several categories (extracellular matrix, growth factors and cytokines, enzymes, enzymatic inhibitors, cytoskeletons and miscellaneous proteins) and their differential secretion was compared and important differences were highlighted. In total, 644 proteins were listed in this systematic review as being present in the secretome of muscle cells. Among them, 11 proteins were differentially regulated by physical exercise (all up-regulated), 130 during myogenesis (90 up- and 40 down-regulated), 27 by insulin stimulation (14 up- and 13 down-regulated) and finally 174 proteins secreted by insulin-resistant muscle cells (26 up- and 148 down-regulated).

**CONCLUSIONS.** This systematic review of the secretome of skeletal muscle cells in health and diseases provides a comprehensive overview of the most regulated proteins in pathological or physiological conditions. These proteins may be therapeutic targets or biochemical markers of muscle diseases.