**Dear Editor,**

I would like to request you to consider the attached manuscript entitled " Creatine enhances protein deposition and improves mitochondrial quality in myotubes at fasting state by serving as an energy substrate" for publication in the skeletal muscle.

While many studies have been conducted to investigate the role of creatine on muscle energy homeostasis by forming phosphorylated creatine to serve as an energy buffer for ATP replenishment, we found few studies to deal with the effect of creatine on muscle protein metabolism. In mammals, the fast-twitch glycolytic fibres are more susceptible to age-related atrophy than slow-twitch oxidative fibres. In the present study, we employed a chicken model, of which the breast muscle primarily comprises of the fast-twitch glycolytic fibres. We investigated the role of Cr on muscle protein metabolism and mitochondrial function in *in vitro* cultured chicken myotubes at fasting condition. The results indicated that Cr supplementation alleviated myotube atrophy mainly by inhibiting ubiquitin proteasome pathway. Cr enhances ATP production, suppresses ROS accumulation, and improves mitochondrial quality. In the present of glucose, however, the beneficial effects of Cr were diminished, suggesting that Cr mainly play a role of energy source at fasting state. The result highlights the potential clinical application for the modulation of muscle atrophy at fasting state.

I believe that the findings of this study are relevant to the scope of your journal and will be interesting to its readership. This manuscript has not been published elsewhere and that it is not currently being considered by another journal. There are no conflicts of interest to declare.

Thank you very much for your considering our manuscript for potential publication. I'm looking forward to hearing from you.

**Sincerely yours,**

**Dr. Hai Lin**

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