Reply to letter to the editor

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To the Editor: On behalf of the author group, we would hereby like to bring forward the following comments. In our recent study (5), we presented data of systemic insulin and amino acid (AA) concentrations, muscle protein synthesis (MPS), and selected signaling molecules known to influence the MPS response after a single bout of heavy resistance exercise followed by an intake of whey protein isolate, calcium caseinate [both adjusted to 0.30 g/kg lean body mass (LBM), ~17.5 g], or a noncaloric control drink. We appreciate Dr. Phillips’ interest in the study and the applied stable isotope-based methods.

We acknowledge the different molecular structure of micellar casein compared with caseinate as described by Dr. Phillips. However, we disagree with his interpretation that there are no differences in the AA concentration response to intake of whey and calcium caseinate (5) (see Fig. 4 in our paper). Especially in the total sum of essential AAs (see Fig. 4E) and total AAs (see Fig. 4F), time-dependent differences are evident. Actually, we believe that our AA concentrations following oral intake of 17.5 g of calcium caseinate better agree with previous data following intake of micellar casein (albeit a larger total amount, 43 g) (1) (see Fig. 2 and Table 2), 18.2 g of fluid nonfat milk protein made from skim milk powder [i.e., ~3.6 g whey (20%) and ~14.6 g micellar casein (80%)] (8) (see Fig. 2), 20 g of unspecified casein (7) (see Fig. 3), and 23.3 g of total milk proteins and 23.2 g of micellar casein (3) (see Fig. 3) than with the AA concentrations following intake of 21.9 g of micellar casein observed in the study by Tang et al. (6).

Following the intake of the specific casein types, all studies (1, 3, 5–8) show elevations in AA concentrations and insulin (except the study by Tang et al.) during the postintervention periods with durations ranging from 3 to 8 h. Regarding the insulin peak concentrations following the intake of whey, micellar casein, and calcium caseinate, we reported a peak after 30 min with a clear difference between whey and calcium caseinate (5), Boirie et al. (1) report a significantly increased value after 40 min with no differences between whey and native micellar casein; and Tipton et al. (7) report a peak value after 30 min (whey) and 45 min (casein) with difference between whey and casein. In contrast, Tang et al. (6) observed no increase in insulin at 60 min after intake of micellar casein, which, however, does not rule out the possibility that an insulin response may have occurred within the first 60 min.

From our point of view, the difference in digestion and absorption properties as interpreted by the AA and insulin responses between micellar casein and calcium caseinate might be of minor importance. However, we acknowledge that this has not been proved in a direct comparison. To our best conviction, the calcium caseinate digestion and absorption properties lie somewhere between those of whey and micellar casein but, in our view, close to micellar casein. Future work should address specific comparisons of milk in its natural form, micellar casein, and caseinate. On the basis of the present observations, we believe that it is justified with a comparison to milk in its native micellar form as part of our perspectives in our DISCUSSION and CONCLUSION. To support this perspective, MPS have been observed to be greater after milk ingestion compared with soy in relation to resistance exercise despite a higher total aminoacidemia following the isonitrogenous, isoenergetic, and macronutrient-matched soy intake (8).

With regard to the concern relating to the figure and table labeling, it is stated in our METHODS section that the type of casein used in the present study is calcium caseinate; furthermore, as pointed out in the letter from Dr. Phillips, the issue is already dealt with in the DISCUSSION. However, we do understand the arguments put forward, and for the sake of clarity we will be aware of Dr. Phillips’ advice regarding this semantic issue in future works.

Regarding the protein dose, we would suggest a dose of high-quality protein of no more than ~20 g, which recapitulates the conditions in our present study (0.30 g/kg LBM, ~17.5 g) (5); 20 g of whole egg protein, and 10 g of essential AA (corresponding to ~20 g high-quality protein) induce a maximal MPS as demonstrated in dose-response studies previously performed (2, 4). Thus, 40 g of protein, as put forward by Dr. Phillips, certainly seems to be too high. Theoretically, the dose-response relationship with MPS could be different following exercise and intake of milk, micellar casein, or caseinate.

As a final comment, Dr. Phillips points to the importance of including rest measurements. This point is well taken as a general critique of this type of study. However, in the project under discussion, the focus was clearly on potential differences between whey and calcium caseinate. Therefore, we wanted a relatively long postintervention time period, which unfortunately could not be combined with rest measurements using proper stable isotope techniques without a markedly longer experiment (i.e., at least 2–3 h longer). In our view, such long experiments potentially cause trouble with respect to subjects being fasted (except for the study intervention supplement). In fact, we believe this issue to be a general problem working with stable isotope-based methodology, which requires quite extensive protocols with regard to time and invasiveness. For example, in the study by Wilkinson et al. (8), no rest fractional synthesis rate measurements are presented, and in the study by Tang et al. (6), no baseline measurements are presented (i.e., without protein). However, we appreciate the studies and find the information important for development of nutritional advice, ideas, and methods.

Finally, we once again thank Dr. Phillips for drawing attention to questions and drawbacks in the study of protein...
administration in relation to exercise and MPS in humans. His comments certainly brought up some questions that should be addressed in future studies and are of great relevance for our understanding of protein metabolism in skeletal muscle.

DISCLOSURES
The authors declare no conflicts of interest, financial or otherwise.

REFERENCES