TO THE EDITOR: We thank Snijders et al. (5) for raising important questions worthy of further discussion. In our study, 14 days of bed rest induced robust myofiber atrophy and muscle weakness that was accompanied by a reduction in satellite cell content (1). Individual changes in satellite cell quantity were significantly correlated with the decline in myofiber cross-sectional area after bed rest. A key concern raised was the decrement in satellite cell content and the potential influence of functional testing that occurred before the pre-bed rest (BR) muscle biopsy. Snijders and colleagues propose that satellite cell content reported pre-BR may be elevated because of an expansion from the stimulus of the functional testing, facilitating the observation of a decline in satellite content post-BR (5). Although our reported basal (pre-BR) satellite cell content (0.13-0.16 satellite cells/fiber) (1) is higher than that reported in a recent review of satellite cell literature (4), it is well within published ranges, including those from the Parise lab (0.15–0.20 satellite cells/fiber) (3). These debates underscore the relative heterogeneity in basal satellite cell content among adults and emphasize the need for further study.

We agree that functional testing may have influenced satellite cell content because of biopsy timing. However, we provide data showing negligible satellite cell activation pre-BR. As a proxy of activation, MyoD+ satellite cells were quantified pre-BR and demonstrated substantially fewer “activated” satellite cells (1). Comparatively, MyoD+ satellite cells were observed ~40× less frequently than Pax7+ and CD56+ satellite cells pre-BR, providing support for minimal influence of the pre-BR functional testing on satellite cell activation and expansion (1). The relatively infrequent occurrence of MyoD+ satellite cells can make their quantification problematic but serves to highlight the likely quiescent state of the collective satellite cell pool pre-BR. These data are supported by a recent manuscript showing the limited abundance of activated satellite cells in the basal state (2). Although our MyoD data argue against satellite cell expansion, we cannot discount a potential effect of the functional testing. Although the magnitude of the change in satellite cell quantity may then be slightly overestimated, the overall conclusions are likely unchanged.

We agree with Snijders et al. that the timing of muscle biopsies in relation to interventions and subject testing is of utmost importance when appraising satellite cell number/activation status. Subjects in the current study underwent a barrage of functional and metabolic assessments as inpatients over a period of 25 days, including the 14-day bed rest period (1). Although care was taken to minimize the influence of various testing protocols on outcome measures, we also had to be respectful of the significant time commitment undertaken by our study participants. In conclusion, there remains considerable work to uncover the contribution of satellite cells to disuse-induced muscle adaptation.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
Author contributions: E.A.-L., D.P.-J., and C.S.F. edited and revised manuscript; E.A.-L., D.P.-J., and C.S.F. approved final version of manuscript; C.S.F. drafted manuscript.

REFERENCES