Skeletal muscle wasting in hypoxia; a matter of altitude

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To the editor: D'Hulst and Deldicque (1) argue that the severity of muscle atrophy incurred at high altitude is dependent on the combined effect of duration and degree of hypoxia exposure, or 'hypoxic dose' (1). We do see a limitation of this concept, as it implies that someone residing in Leuven (altitude: 28 m) for ten years would be subjected to a 'hypoxic dose' of 2454 km·h and incur 5% atrophy. While the authors wrote that 'it is unknown which parameter, altitude or time spent at altitude, is most decisive in the overall metric of hypoxic dose', our illustration suggests that altitude is the prime determinant. This is further supported by the cut-off point at 4000 m in a plot of the degree of atrophy *vs.* altitude (using the data in Table 1), whereas there was no clear relationship with duration of altitude residence. This cut-off point is likely related to the shape of the hemoglobin dissociation curve, where the oxygen tension at 4000 m is such that physiologically significant arterial hemoglobin desaturation occurs (2). We acknowledge that one cannot entirely dismiss the importance of duration of hypoxic exposure, simply because skeletal muscle atrophy can only be noticed some time after net protein breakdown is initiated. However, muscle atrophy will not continue indefinitely, but will reach a new steady state (how can otherwise Tibetans still have muscle?). Finally, other adaptations than atrophy, such as an increase in hematocrit and capillarization, serve to attenuate muscle tissue hypoxia and atrophy (3) during residence at altitude.

1. D'Hulst G, and Deldicque L. Human skeletal muscle wasting in hypoxia: a matter of hypoxic dose? J Appl Physiol (1985) in press, 2017.
2. Wagner PD, Wagner HE, Groves BM, Cymerman A and Houston CS. Hemoglobin P(50) during a simulated ascent of Mt. Everest, Operation Everest II. High Alt Med Biol. 8(1):32-42, 2007.
3. Wüst RCI, Jaspers RT, van Heijst AF, Hopman MT, Hoofd LJ, van der Laarse WJ, and Degens H. Region-specific adaptations in determinants of rat skeletal muscle oxygenation to chronic hypoxia. Am J Physiol Heart Circ Physiol 297: H364-374, 2009.