

## High-Resolution Respirometry in skeletal muscle fibres

# Metabolic basis to Sherpa altitude adaptation

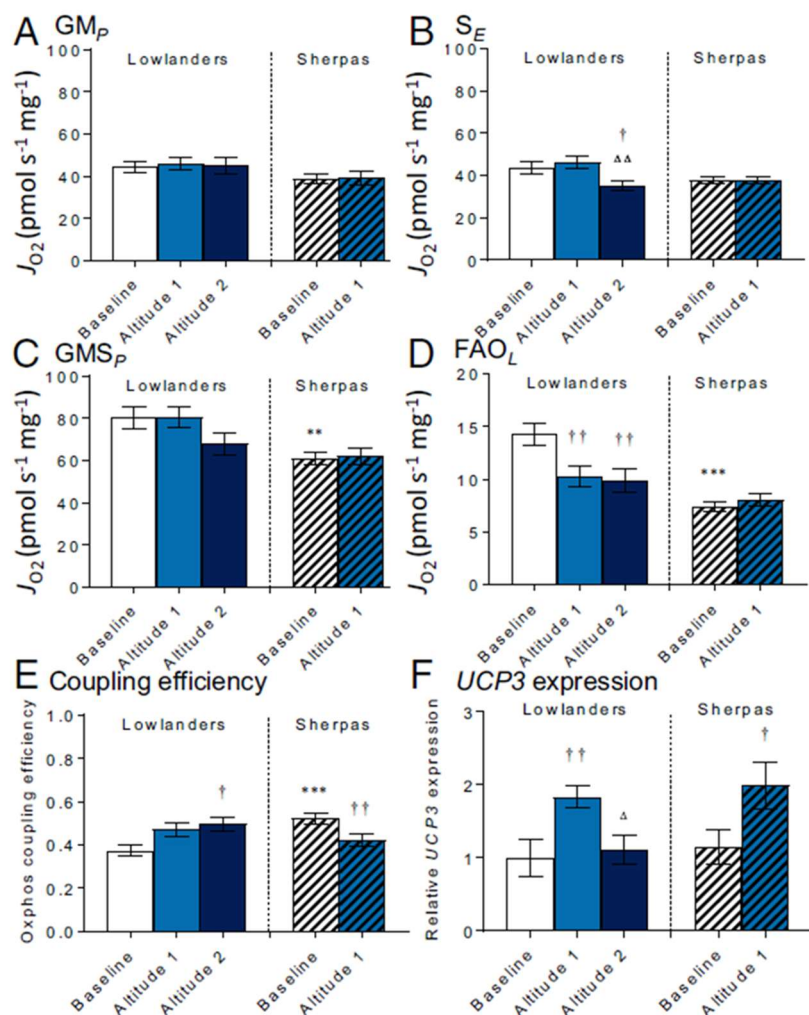
James A. Horscroft<sup>a</sup>, Aleksandra O. Kotwica<sup>a</sup>, Verena Laner<sup>b</sup>, James A. West<sup>c,d</sup>, Philip J. Hennis<sup>e</sup>, Denny Z. H. Levett<sup>e</sup>, David J. Howard<sup>e</sup>, Bernadette O. Fernandez<sup>f</sup>, Sarah L. Burgess<sup>a</sup>, Zsuzsanna Ament<sup>c,d</sup>, Edward T. Gilbert-Kawai<sup>e</sup>, André Vercueil<sup>e</sup>, Blaine D. Landis<sup>g</sup>, Kay Mitchell<sup>e</sup>, Monty G. Mythen<sup>e</sup>, Cristina Branco<sup>a</sup>, Randall S. Johnson<sup>a</sup>, Martin Feelisch<sup>f,h</sup>, Hugh E. Montgomery<sup>e</sup>, Julian L. Griffin<sup>c,d</sup>, Michael P. W. Grocott<sup>e,f,h,i</sup>, Erich Gnaiger<sup>b,j</sup>, Daniel S. Martin<sup>e</sup>, and Andrew J. Murray<sup>a,1</sup>

## Enhanced efficiency of O<sub>2</sub> utilization, improved muscle energetics, protection against oxidative stress and lower capacity for fatty acid oxidation are the hallmarks of the Sherpas

### Mitochondrial oxygen consumption, efficiency, and uncoupling protein expression.

N-OXPHOS (GM<sub>P</sub>) (A), S-ETS capacity (S<sub>E</sub>) (B), and NS-OXPHOS capacity (GMS<sub>P</sub>) (C) in permeabilized muscle fibers from Lowlanders and Sherpas. Octanoyl carnitine and malate-supported LEAK (FAO<sub>L</sub>) (D) and OXPHOS coupling efficiency (E). (F) Muscle UCP3 expression relative to Lowlanders at baseline. Mean ± SEM (*n* = 7–11).

\*\**P* ≤ 0.01, \*\*\**P* ≤ 0.001 in Lowlander vs. Sherpas at baseline. †*P* ≤ 0.05, ††*P* ≤ 0.01 at baseline vs. altitude within cohort. Δ*P* ≤ 0.05, ΔΔ*P* ≤ 0.01 at altitude 1 vs. altitude 2 within cohort. G, glutamate; J<sub>O<sub>2</sub></sub>, oxygen flux; M, malate, S, succinate.



Reference: Horscroft JA, Kotwica AO, Laner V, West JA, Hennis PJ, Levett DZH, Howard DJ, Fernandez BO, Burgess SL, Ament Z, Gilbert-Kawai ET, Vercueil A, Landis BD, Mitchell K, Mythen MG, Branco C, Johnson RS, Feelisch M, Montgomery HE, Griffin JL, Grocott MPW, Gnaiger E, Martin DS, Murray AJ (2017) Metabolic basis to Sherpa altitude adaptation. Proc Natl Acad Sci U S A 114:6382–7.