Oxygen release from hemoglobin has limited effects on mitochondrial respiration measured from red blood cells. Reply to the Comment on "Increased retention of functional mitochondria in mature sickle red blood cells is associated with increased sickling tendency, hemolysis and oxidative stress"

## Authors

Antoine Stier,<sup>1,2</sup> Sofia Esperti,<sup>3,4,5</sup> Elie Nader,<sup>3,4</sup> Damien Roussel<sup>6</sup> and Philippe Connes<sup>3,4</sup>

<sup>1</sup>Université de Strasbourg, CNRS, Institut Pluridisciplinaire Hubert Curien, UMR7178, Strasbourg, France; <sup>2</sup>Department of Biology, University of Turku, Turku, Finland; <sup>3</sup>Laboratoire interuniversitaire de Biologie de la Motricité (LIBM) EA7424, Team «Vascular Biology and Red Blood Cell» Université Claude Bernard Lyon 1, Université de Lyon, Lyon, France; <sup>4</sup>Laboratoire d'Excellence du Globule Rouge (Labex GR-Ex), PRES Sorbonne, Paris, France; <sup>5</sup>Erytech Pharma, Lyon, France and <sup>6</sup>Laboratoire d'Ecologie des Hydrosystèmes Naturels et Anthropisés, CNRS UMR 5023, Université Claude Bernard Lyon 1, Université de Lyon, Lyon, France

## Correspondence:

A. STIER - antoine.stier@iphc.cnrs.frP. CONNES - philippe.connes@univ-lyon1.fr

https://doi.org/10.3324/haematol.2024.286361

Received: August 5, 2024. Accepted: August 8, 2024. Early view: August 15, 2024.

©2025 Ferrata Storti Foundation Published under a CC BY-NC license © © ©

## Electronic Supplementary Material of Stier et al. 2024, Haematologica:

## 'Oxygen release from hemoglobin has limited effects on mitochondrial respiration measured from red blood cells'

**Table S1**: Data of Fig. 1 from Japanese quail (*Coturnix japonica*) on non-mitochondrial oxygen consumption (JO<sub>2</sub>) by red-blood cells in response to variation in PO<sub>2</sub> in-vitro. The variation in PO<sub>2</sub> was achieved by letting the cells consume more or less oxygen before adding antimycin A to inhibit mitochondrial respiration.

**Table S2**: Data of Fig. 2A on oxygen consumption  $(JO_2)$  by red blood cells of both Japanese quail and human with sickle cell disease in response to a standard high-resolution respirometry protocol. JO2 data were already published in Stier et al. 2022 and Esperti et al. 2023, and are here plotted along the respective PO<sub>2</sub> at which they have been measured *invitro* 

**Table S3**: Data of Fig. 2B on hemoglobin-O2 dissociation curves extracted from the literature for birds (Powell 2015) and human (Abdu et al. 2008). Slopes of the  $PO_2 - \%$  Hb saturation for the range of  $PO_2$  encountered in Stier et al. 2022 and Esperti et al. 2023 (highlighted in blue and green respectively) have been calculated.

**Table S4**: Calculations and Data of Fig. 2C on the contribution of  $O_2$  release by hemoglobin to  $JO_2$  in Japanese quail red blood cells assessed *in-vitro* using high-resolution respirometry

**Table S5**: Calculations and Data of Fig. 2D on the contribution of  $O_2$  release by hemoglobin to  $JO_2$  in human sickle red blood cells assessed *in-vitro* using high-resolution respirometry