Response to the letter to the Editor: **Spirulina supplementation improves oxygen uptake in arm cycling exercise**

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Dear Editor in Chief,

We are pleased that our recent publication has been of interest to the wider research community, and we particularly welcome and thank Engan et al. for their constructive comments in their letter to the Editor. Their comments highlight an interesting insight into a potential additional mechanism of action when interpreting the increases in haemoglobin (Hb) after the supplementation of spirulina (SP). Indeed, we acknowledge the comments regarding SP as a potential source of available dietary nitrate for humans due to its assimilation of nitrate when growing/forming, and as such, according to Engan et al's recent work, may also potentially facilitate the contraction of the spleen resulting in an elevation of Hb (Engan et al. 2020).

Although we do not dispute this suggestion, to the best of our knowledge, at the time of publication, nutritional and compositional analysis of SP in previous research had not reported or considered nitrate concentrations within the algae (Andrade, 2018; Lafarga et al. 2020). At the time of our study design and hypothesis generation, we directed its potential mechanistic analysis in line with previous research which purported good assimilation of iron from SP supplementation and therefore increases in Hb. Multiple clinical studies had demonstrated increases in Hb in anaemic individuals with varying daily doses and length of supplementation periods. Moreover, Kelkar et al. (2008) also demonstrated that after just two-weeks of 4g/day SP supplementation, Hb in healthy elite marathon runners prior to a race significantly increased. A further positive haemopoietic system trend was also noted by Milasius et al. (2009) following a two-week supplementation of just 2.25g/day in '*high performance sportsmen'*. With both authors further supporting the notion of good bodily assimilation of iron from SP, whilst also suggesting that SP can combat against the adverse effects from oxidative stress that may occur in erythrocyte membranes (Kelkar et al. 2008). Both studies consequently interested us and helped to develop our rationale to see whether an even shorter intervention

with a higher daily dosage would provide similar results in healthy males, in which it did. Whilst we acknowledge the potential short comings of not measuring serum iron and ferritin levels, it was beyond the available resources we had at the time. We agree that the findings of Engan et al. (2020) will be an important mechanism to measure in future studies when trying to elucidate a specific potential mechanism following an elevation in Hb in healthy participants during short SP supplement interventions.

To conclude, we must highlight that research into SP supplementation and its potential ergogenic aid capabilities in humans is quite novel and limited thus far, with the majority of research focussing on antioxidant capabilities and with little true mechanistic data. We thank Engan and colleagues for shedding light on an alternative speculated mechanism of action but at this time further research is warranted to support this notion in SP supplementation. Indeed, previous research has also not considered this as a potential mechanistic avenue, given the recentness of the authors novel publication on this very topic (Engan et al. 2020). We are most pleased it has stimulated discussion and we welcome and encourage other researchers to investigate SP further as there are clearly many potential avenues to consider.

Yours sincerely,
Tom Gurney & Dr Owen Spendiff

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