

## ABSTRACT

### **Title: Select DNA Replication and Repair Genes are Transcriptionally Modified by Acute Exercise in Hypoxia**

**Authors:** Gareth W. Davison FACSM, Conor McClean.

**Institution:** Ulster University, Jordanstown, Co. Antrim, Northern Ireland, BT37 OQB, UK.

DNA replication and repair in eukaryote cells are critical processes that ensures the correct transfer of DNA material through mitosis. Errors in the replication and repair of DNA during and following cell division may lead to genome instability. **PURPOSE:** To investigate the regulation of select gene transcripts aligned to DNA replication and repair following exercise in hypoxia. **METHODS:** Twenty-four ( $n=24$ ) apparently healthy male participants were recruited (age  $28 \pm 5$  years; mass  $74 \pm 8$  kg; stature  $177 \pm 6$  cm;  $\dot{V}O_{2\max}$  hypoxia  $45 \pm 2$  ml·kg<sup>-1</sup>·min<sup>-1</sup>; normoxia  $60 \pm 9$  ml·kg<sup>-1</sup>·min<sup>-1</sup>), and completed 1 hr of exercise at a workload corresponding to 75% of pre-determined  $\dot{V}O_{2\max}$  in hypoxia ( $F_{iO_2} = 0.16\%$ ), and repeated in normoxia ( $F_{iO_2} = 0.21\%$ ). RNA was extracted from whole blood. Two-colour oligonucleotide microarrays [for DNA primase subunit 1 - *PRIM1*; Chromatin assembly factor 1 subunit B - *CHAF1B*; and Werner syndrome RecQ like helicase - *WRN*] were processed on an Agilent DNA microarray scanner, while mRNA analysis was conducted using GeneSpring software incorporating checks for data normalisation, quality control, filtering grouping (by experimental condition) and statistical analysis (paired t-test with Benjamini & Hochberg False Discovery Rate corrections for multiple comparisons). **RESULTS:** Exercise performed in hypoxia *per se* downregulated *PRIM1* and *CHAF1B* ( $p=0.03$  and  $p=0.01$  respectively vs. pre-exercise), with no change observed in normoxia ( $p>0.05$ ). Compared with normoxia, *CHAF1B* and *WRN* were differentially downregulated following exercise in hypoxia ( $p=0.05$  and  $p=0.05$  respectively vs. pre-exercise). **CONCLUSION:** Acute exercise in moderate hypoxia interferes with gene transcription aligned to blood cell DNA

replication and repair. Further work is necessary to ascertain the consequence of these select modifications on genome stability.