

## Palmitate induces CD11b expression in monocytes independent of altered redox state

C. Pararasa, C. J. Bailey and H. R. Griffiths

*Life and Health Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, UK*

Ageing has been associated with increased oxidative stress<sup>(1)</sup> and elevated risk of developing CVD<sup>(2)</sup> and insulin resistance<sup>(3)</sup>. Studies in middle-aged individuals suggest that elevated serum saturated fatty acids are indicative of greater CVD and type-2 diabetes risk<sup>(4)</sup>. Furthermore, serum SFA levels increase with age, whereas levels of the cellular antioxidant glutathione decline<sup>(5)</sup>. Whether age-associated changes to SFA levels contribute to or arise from an ageing metabolic phenotype, altered redox state and/or vascular inflammation is unknown.

This work has determined the effect of the SFA, palmitate, on intracellular redox status and expression of the integrin CD11b in THP-1 monocytes, a cell surface marker that mediates monocyte interaction with the endothelium.

THP-1 cells were incubated with 50, 150 and 300  $\mu\text{M}$  palmitate conjugated to albumin and albumin-vehicle control as previously described<sup>(6)</sup>. This was not associated with a significant loss of viability. The total intracellular level of glutathione (GSH+GSSG) was measured using a DTNB-dependent recycling assay and corrected for protein content determined by BCA assay<sup>(7)</sup>. Monocyte CD11b expression was determined using flow cytometry<sup>(8)</sup>.

Palmitate treatment (24 h) depleted total glutathione (GSH) levels in THP-1 monocytes: this was significant at 50  $\mu\text{M}$ , but at higher concentrations of palmitate, the GSH levels were not significantly different to control values (Fig. 1). CD11b expression increased dose dependently with increasing palmitate concentration, confirming previous observations<sup>(6)</sup>.

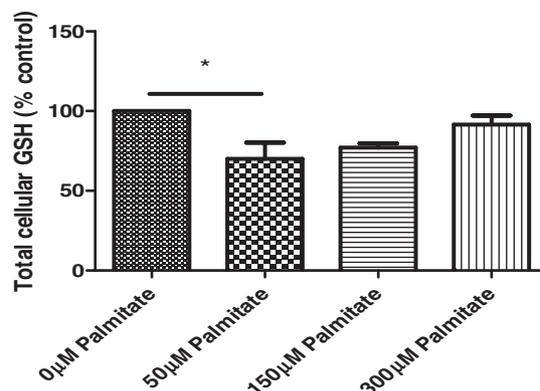


Fig. 1. Monocyte incubation with palmitate for 24 h depletes cellular glutathione. \* $P < 0.05$  v. control.

The change to cellular glutathione levels indicates that the incubation of monocytes with 50  $\mu\text{M}$  palmitate induces a redox shift after 24 h that is not evident at higher palmitate concentrations. However, the redox shift did not correlate with the enhanced CD11b expression observed with increasing palmitate concentrations.

Together, these data suggest that palmitate may mediate the increased CD11b expression leading to a pro-inflammatory monocyte phenotype typically seen in older adults and manifest as an increased binding of monocytes to endothelium. However, CD11b expression changes are not associated with a redox shift, suggesting that the two phenomena are unrelated.

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