



Myeloperoxidase and protein-radicalization are linked to insulin resistance in the obese adipose tissue



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Introduction

Our B6 mouse model of diet-induced obesity showed adipose tissue macrophages (ATM) forming typical crown-like structures in the adipose tissue (AT). These ATM from obese mice express 15-times more myeloperoxidase (MPO) mRNA than those from control mice. MPO protein, but not mRNA, was also found inside adipocytes in the obese AT. Treatment with the nitron spin trap 5,5-dimethyl-1-pyrroline N-oxide (DMPO) improved insulin sensitivity in obese mice.

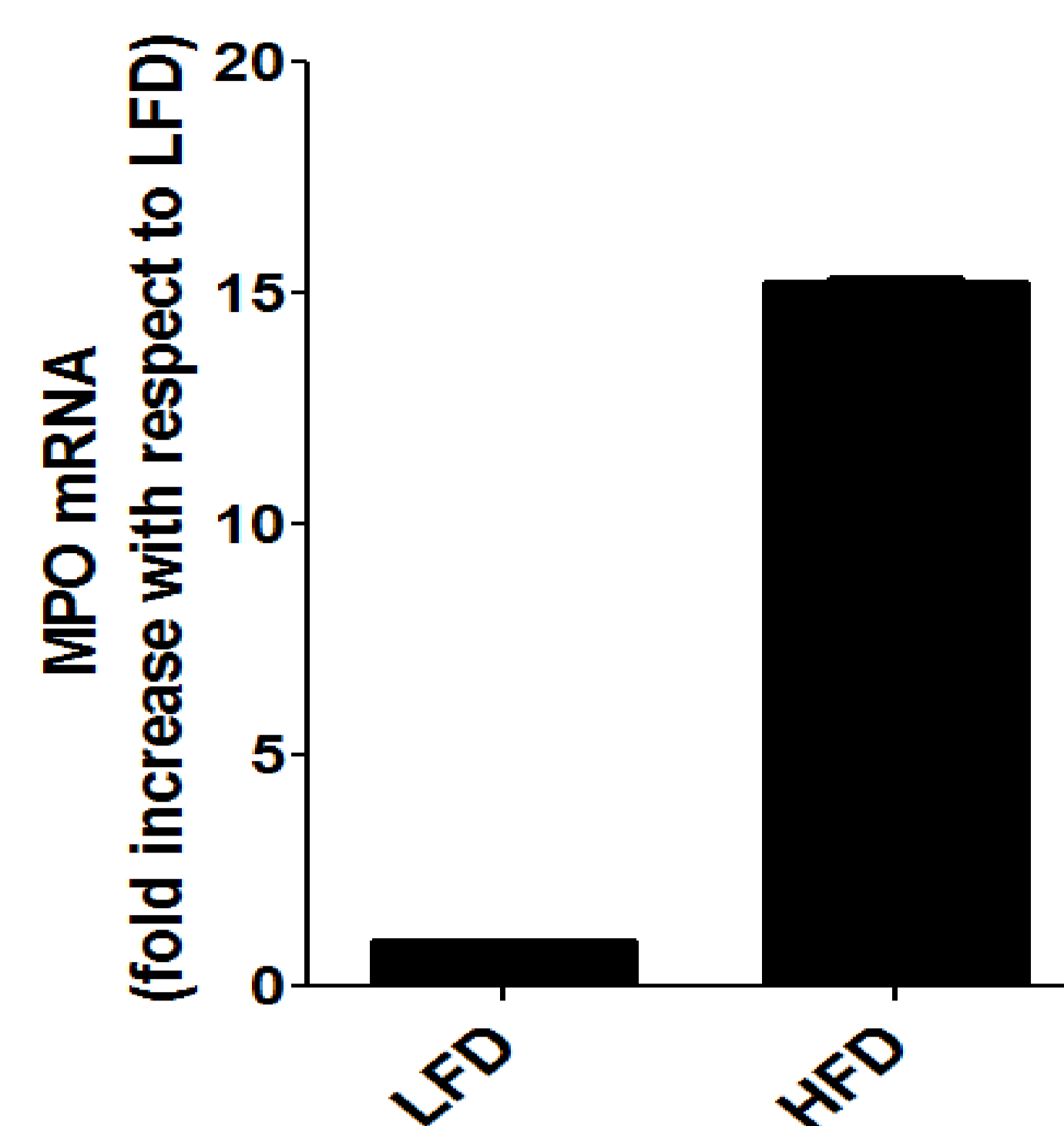
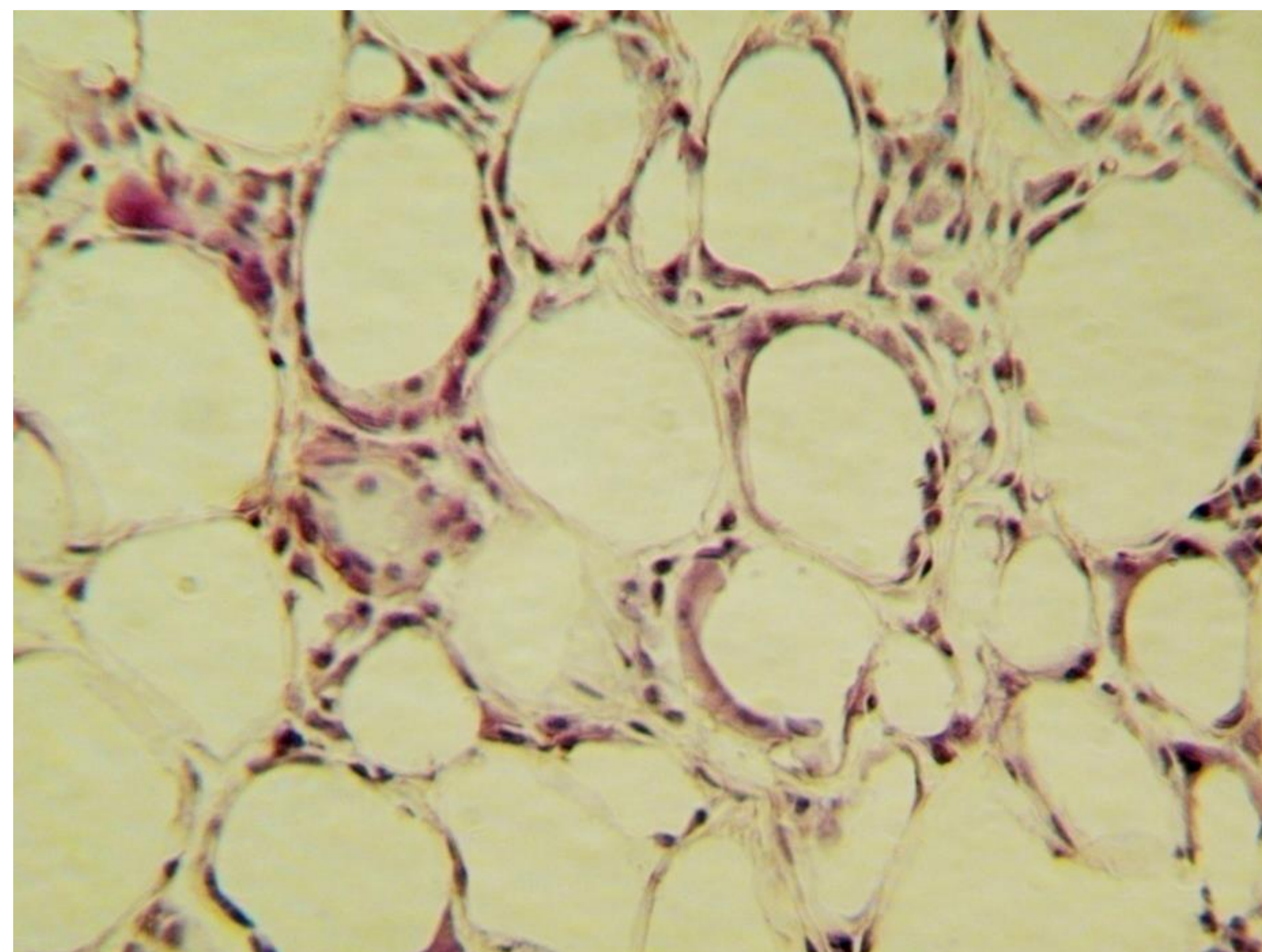


Figure 1. A) Adipose tissue macrophages (ATM) forming typical crown-like structures in the adipose tissue (AT). B) The ATM of obese mice expresses 15 times more MPO than control mice

Hypothesis

HOCl produced by MPO inside adipocytes interferes with insulin signaling in the AT. This may be caused by HOCl-induced radicalization and oxidation of specific proteins involved in insulin-triggered signaling.

Experimental Procedures

We differentiated human adipocytes and loaded them with human MPO.

Results

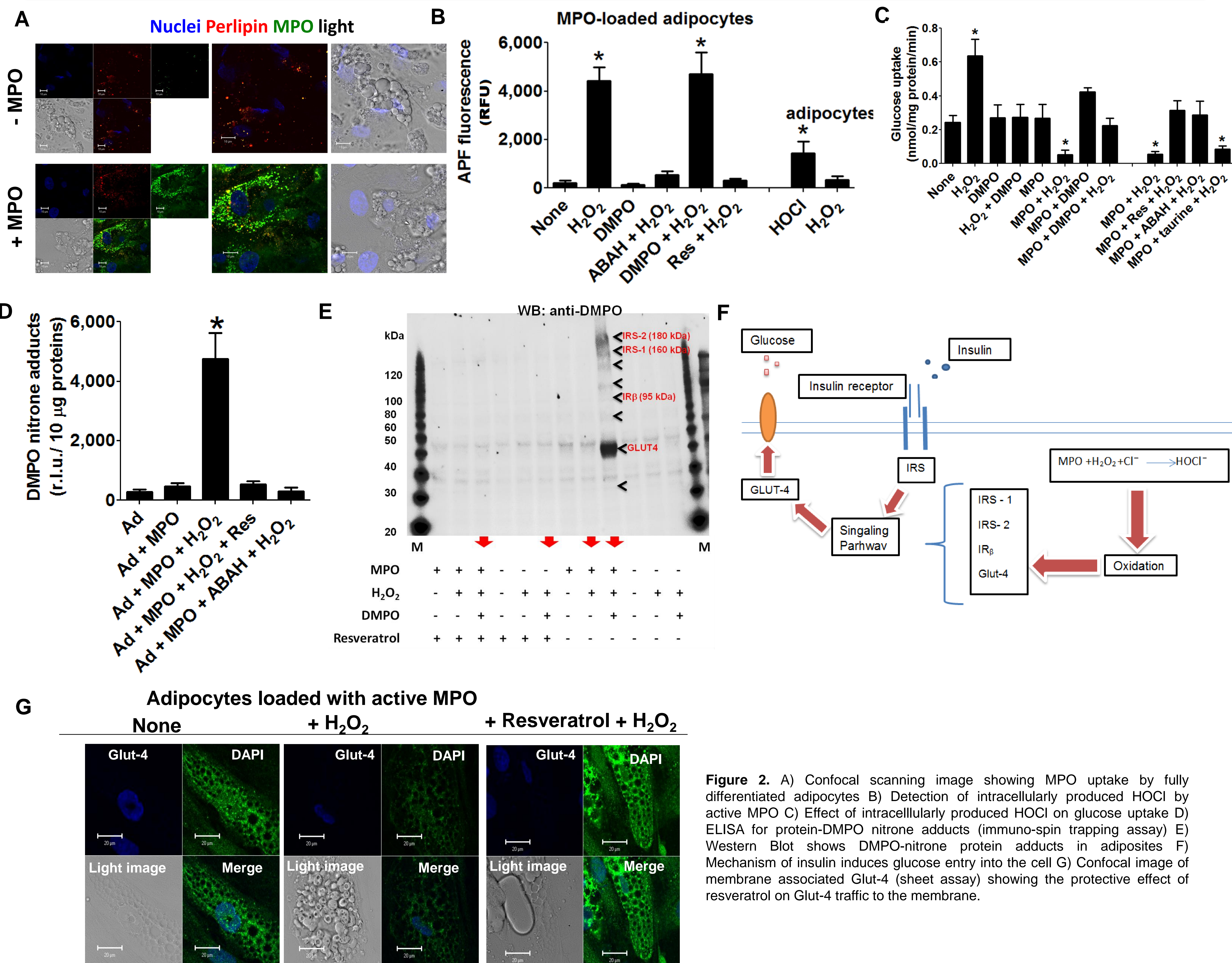


Figure 2. A) Confocal scanning image showing MPO uptake by fully differentiated adipocytes B) Detection of intracellularly produced HOCl by active MPO C) Effect of intracellularly produced HOCl on glucose uptake D) ELISA for protein-DMPO nitron adducts (immuno-spin trapping assay) E) Western Blot shows DMPO-nitron protein adducts in adipocytes F) Mechanism of insulin induces glucose entry into the cell G) Confocal image of membrane associated Glut-4 (sheet assay) showing the protective effect of resveratrol on Glut-4 traffic to the membrane.

Conclusion

Scavenging HOCl produced inside adipocytes with resveratrol or preventing protein oxidation with spin traps can protect insulin signaling in adipocytes.