

The Impact of Lipopolysaccharide on Mitochondrial Efficiency in Brown Adipocytes

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BACKGROUND

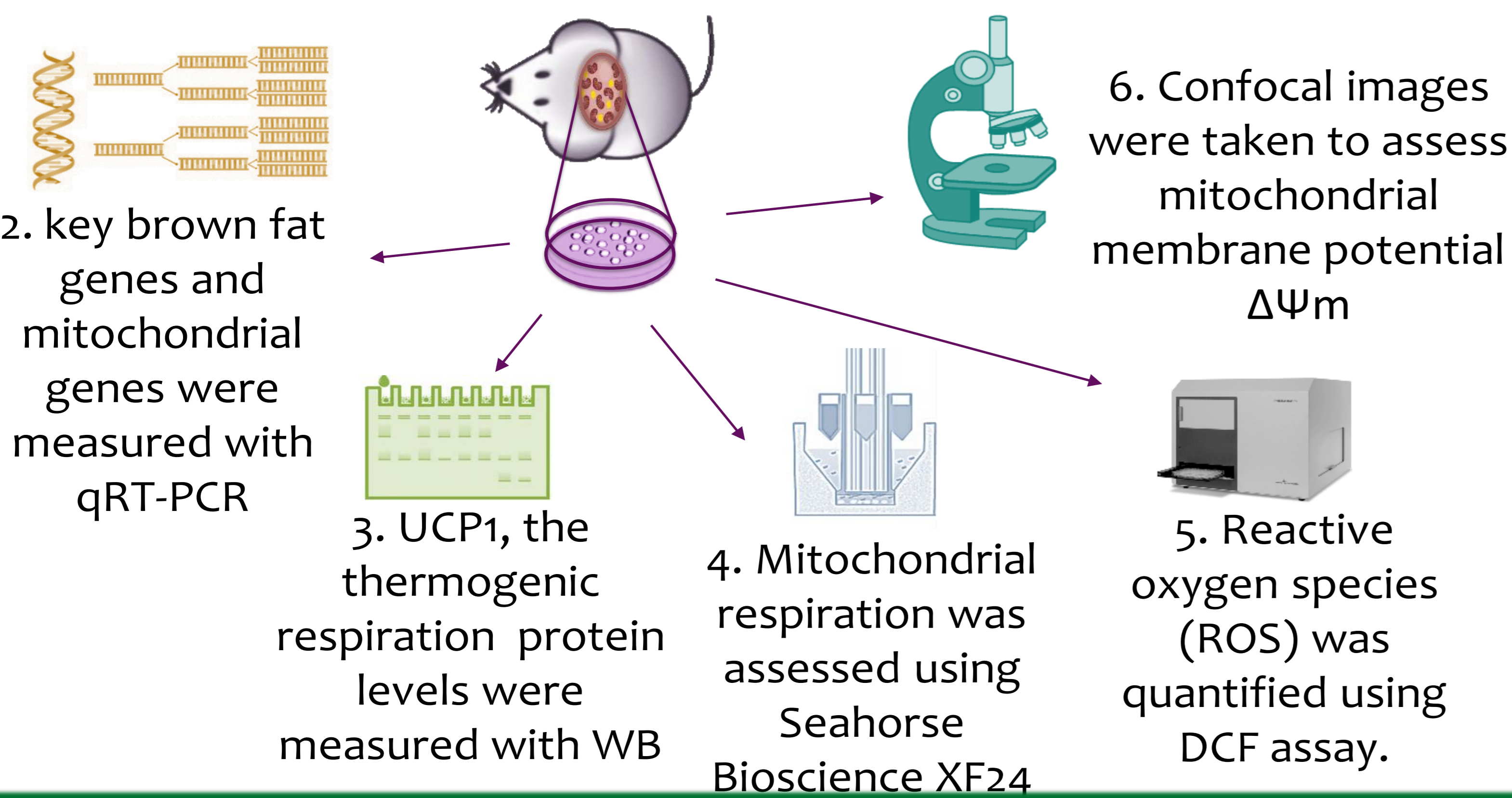
The presence of brown adipose tissue (BAT) in adult humans opens new avenues for research to ameliorate obesity consequences including metabolic and cardiovascular disease because of its special feature to expend rather than store energy.

Lipopolysaccharide (LPS) is known to be elevated in obesity and initiate an inflammatory state, but its effect has not been fully explored in BAT. β_3 adrenergic receptor ligands such as CL 316,243 (CL) induce BAT activity through stimulation of UCP1. The interaction between the LPS receptor TLR4 and β_3 adrenergic receptors has not been well studied in BAT.

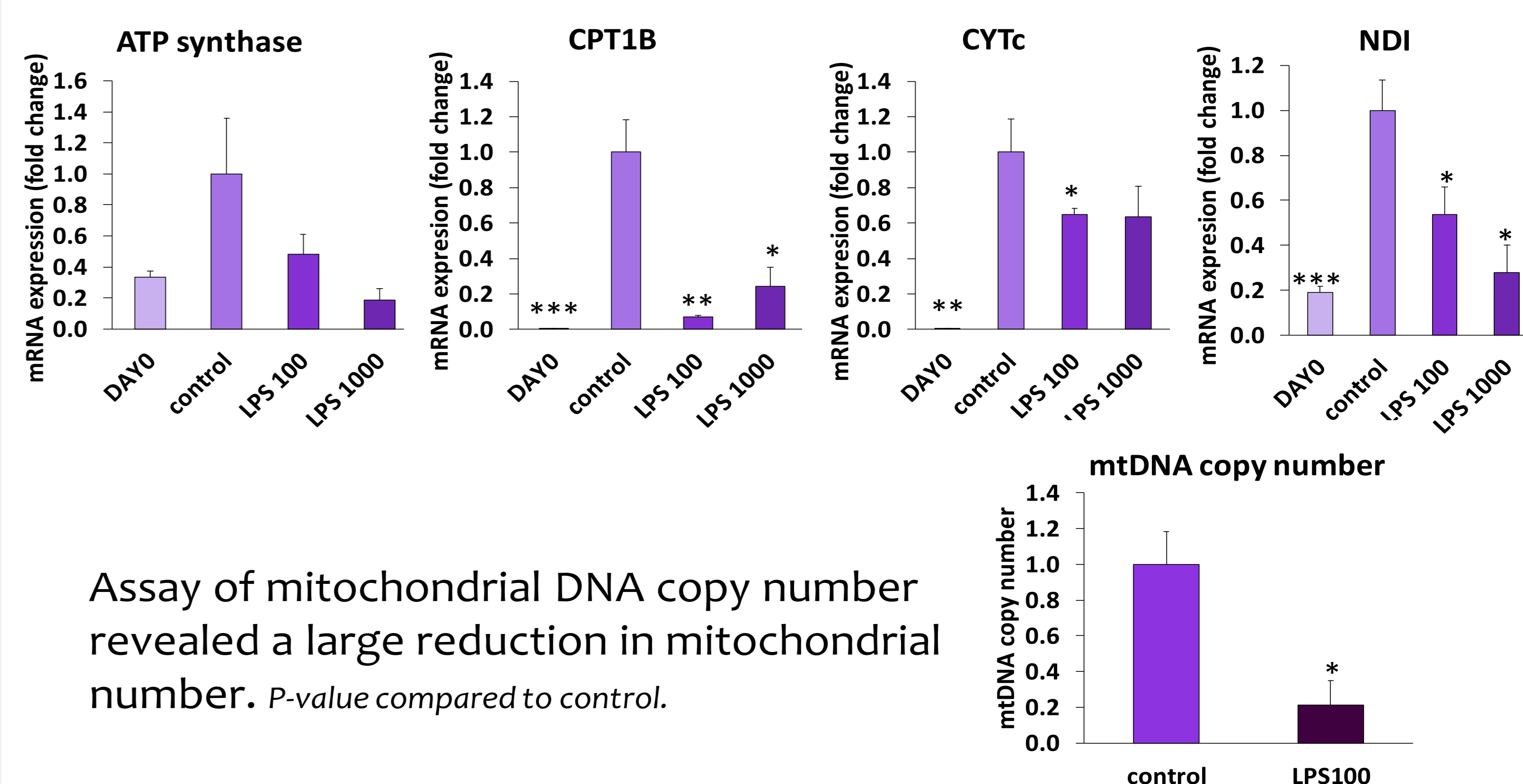
Therefore, the objective of this study is to investigate the effect of LPS on the CL response and examine how LPS may alter mitochondrial function in BAT.

METHODS

1. Immortalized brown adipocytes were differentiated with or without LPS (100ng/ml or 1000ng/ml) and treated with or without CL.



key mitochondrial genes (ATPase8, CPT1B, CytC, ND1) were reduced by LPS treatment. *P*-value compared to control.

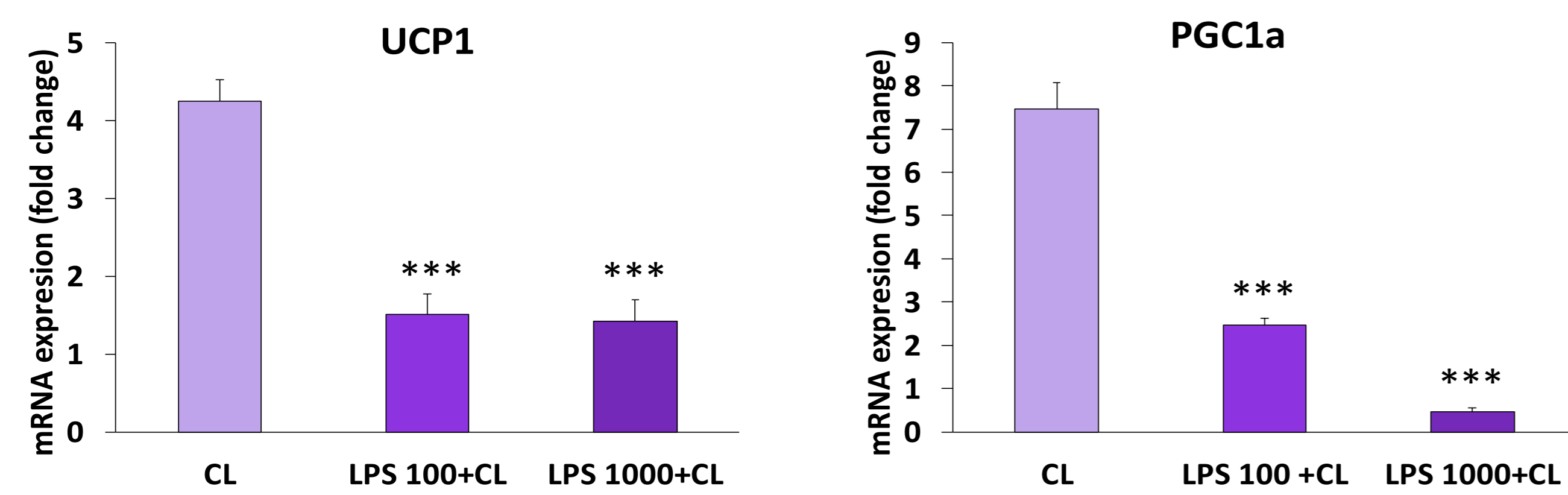
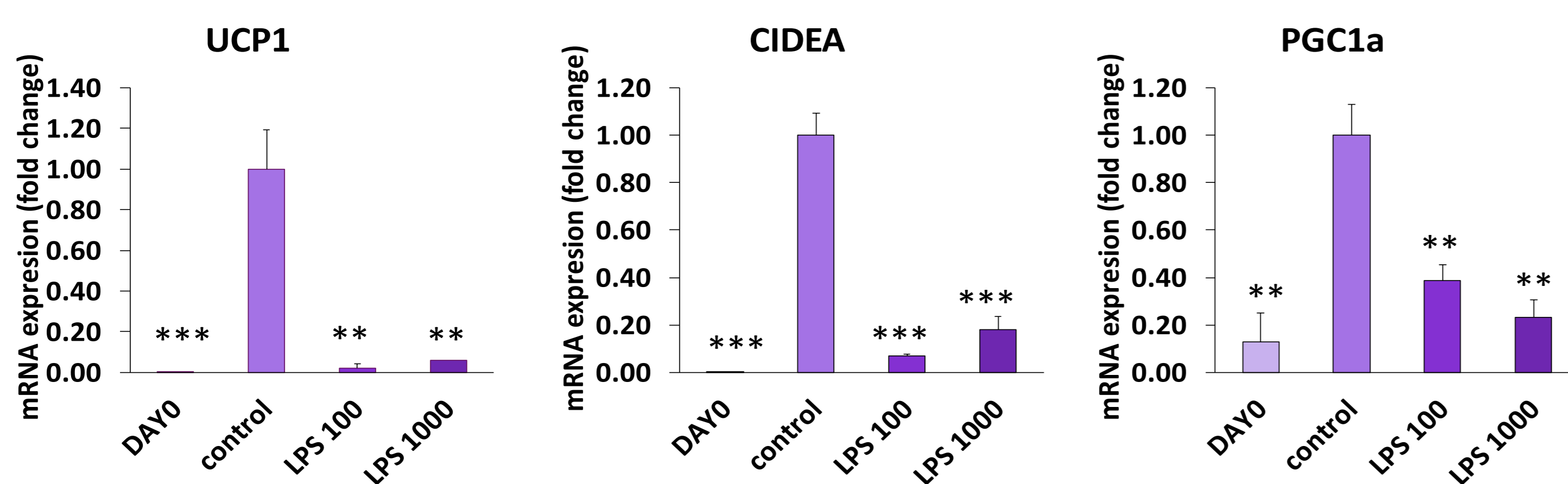


Assay of mitochondrial DNA copy number revealed a large reduction in mitochondrial number. *P*-value compared to control.

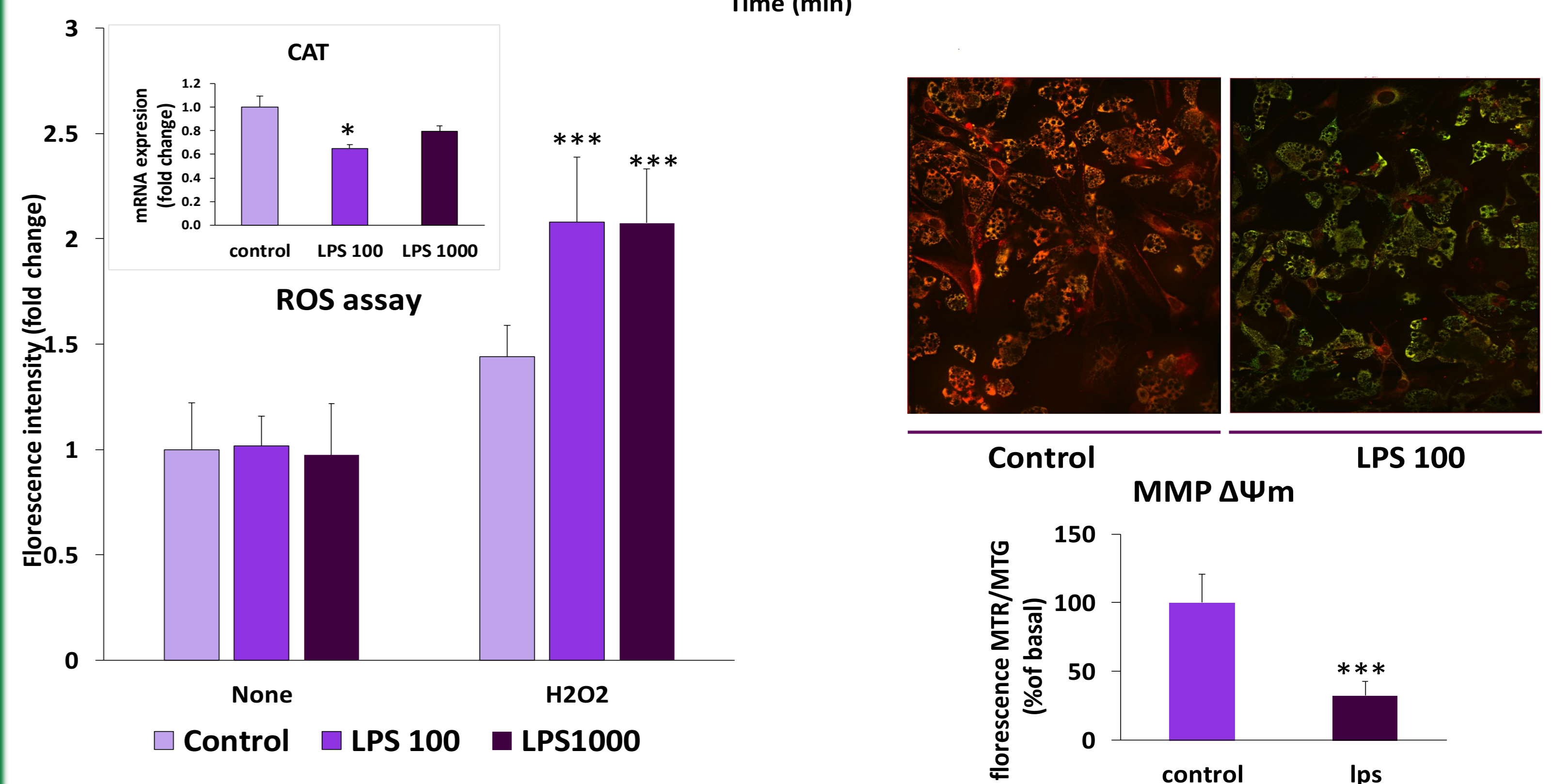
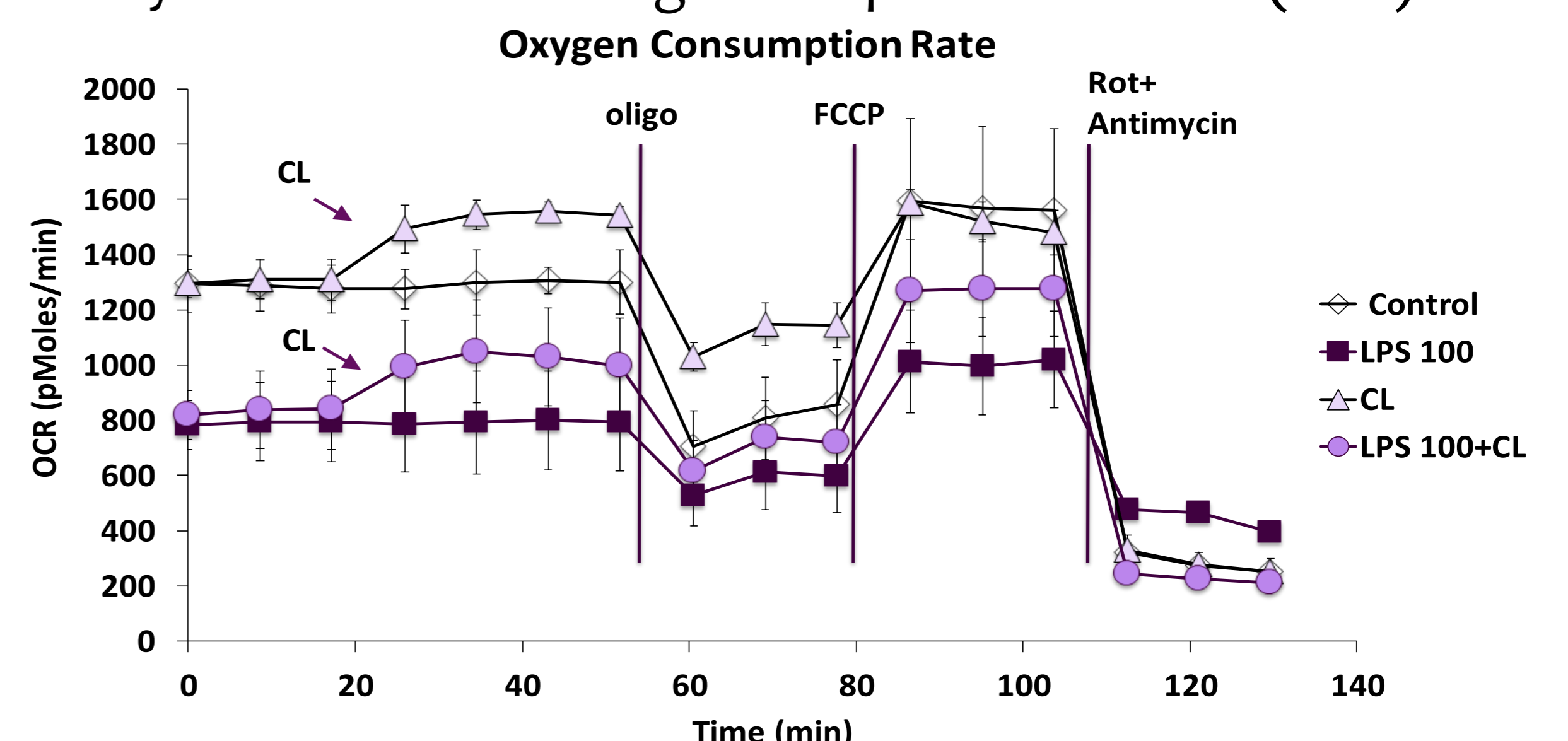
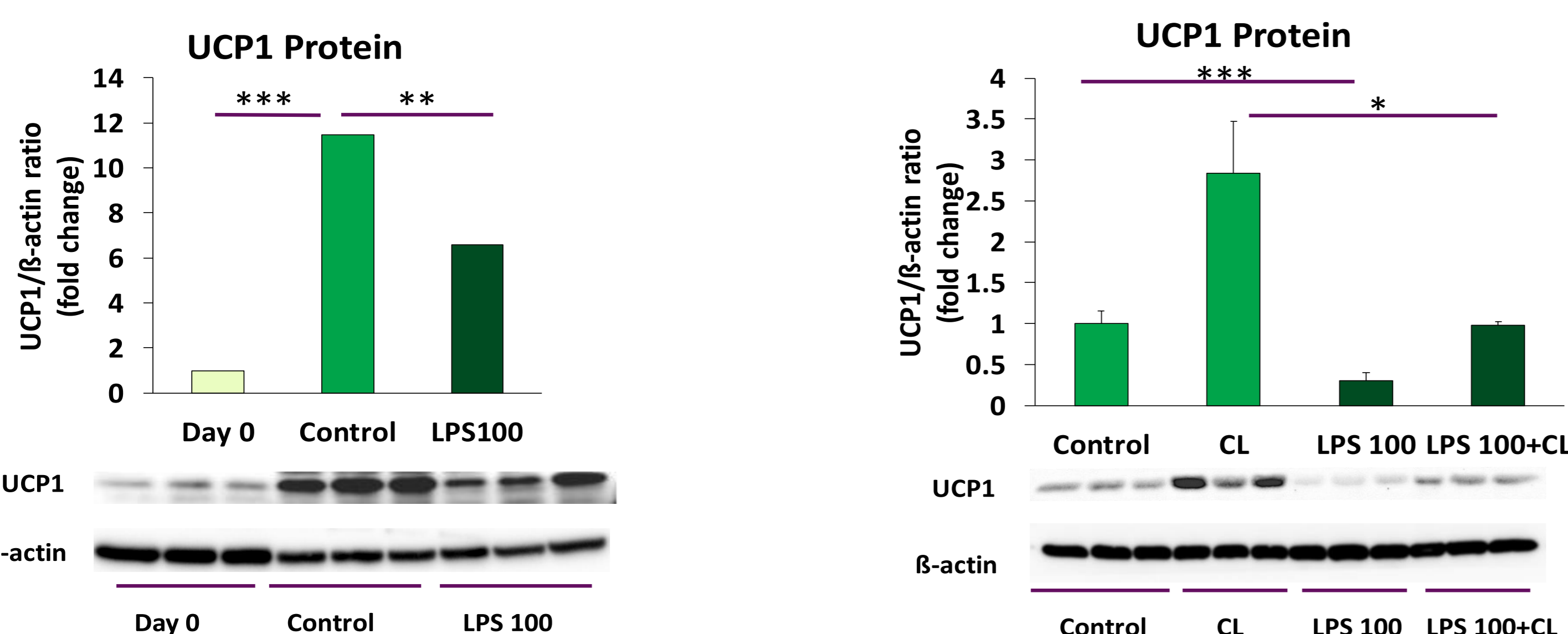
This implicates LPS in acting to impair mitochondrial function and is supported by a reduced O_2 consumption rate in LPS treated cells as well as loss of mitochondrial membrane potential $\Delta\Psi_m$. Also, LPS increased susceptibility to hydrogen peroxide (oxidative agent) which was accompanied by reduced catalase gene expression levels (CAT).

RESULTS

LPS significantly decreased key brown fat genes (CIDEA, UCP1, PGC-1 α). Furthermore, LPS-treated cells showed significantly lower UCP1, PGC1 α gene induction in response to CL. *P*-value compared to control or CL.



UCP1 protein also decreased in LPS-treated cells and was less induced in response to CL. *P*-value compared to control or CL.



CONCLUSIONS

These findings suggest that systemic LPS poses a risk to damaging mitochondrial function in BAT. As such, this current data indicates that blocking LPS-TLR4 signalling has potential to enhance BAT activity and mitigate inflammation to counteract obesity and type 2 diabetes

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CARA