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## Role of P38MAPK in palmitate-induced inflammation in C2C12 muscle cells

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### Introduction:

Obesity is frequently associated with insulin resistance (IR). The decrease in insulin response in skeletal muscle could be related to the inflammation process. The increase in adipose tissue proinflammatory factors secreted during obesity and the lipotoxic compound accumulation in skeletal muscle, could at least in part explain the skeletal muscle inflammation. The SFA palmitate (PAL, C16:0) is now recognized as an inducer of inflammation in muscle cells. The secretion of inflammatory cytokines by muscle cells such as interleukine-6 (IL-6) and tumor necrosis factor-alpha (TNF- $\alpha$ ) was observed after 16hour incubation with 500 $\mu$ M of palmitate. It also induced mRNA expression of cyclooxygenase-2 (COX-2) (Coll et al. 2010). PAL-induced inflammation has been demonstrated to be reversed by MUFA oleate (C18:1) (Coll et al. 2008) and n-3 polyunsaturated fatty acids (n-3PUFA) are also expected to reverse it, as they are widely described to have anti-inflammatory properties (Wall et al. 2010), especially eicosapentaenoic acid (EPA, C20:5 n-3) and docosahexaenoic acid (DHA, C22:6 n-3). Their precursor, alpha-linolenic acid (ALA, C18:3) has not been extensively studied and further work is needed to understand its potential role in obesity and inflammation. The causes and consequences of inflammation in muscle cells are poorly understood and p38 mitogen-activated protein kinase (p38MAPK) might be involved in this process.

### Objectives:

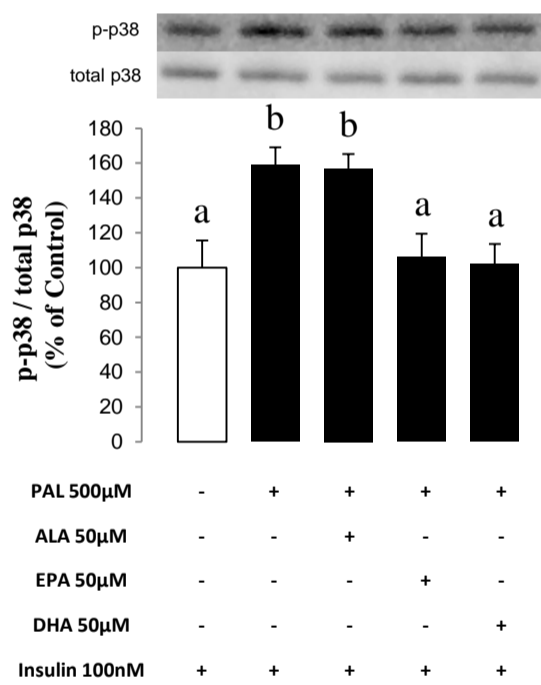
The aim of the study was to investigate the n-3PUFA effects on PAL-induced inflammation and the potential link between inflammation, p38 mitogen-activated protein kinase (p38MAPK) activation and IR in C2C12 myotubes. As PAL also induces insulin resistance (IR) in muscle (Chavez et al. 2003), we also tried to determine whether inflammation and p38MAPK signaling pathway are involved in palmitate-induced IR.

### Materials & Methods:

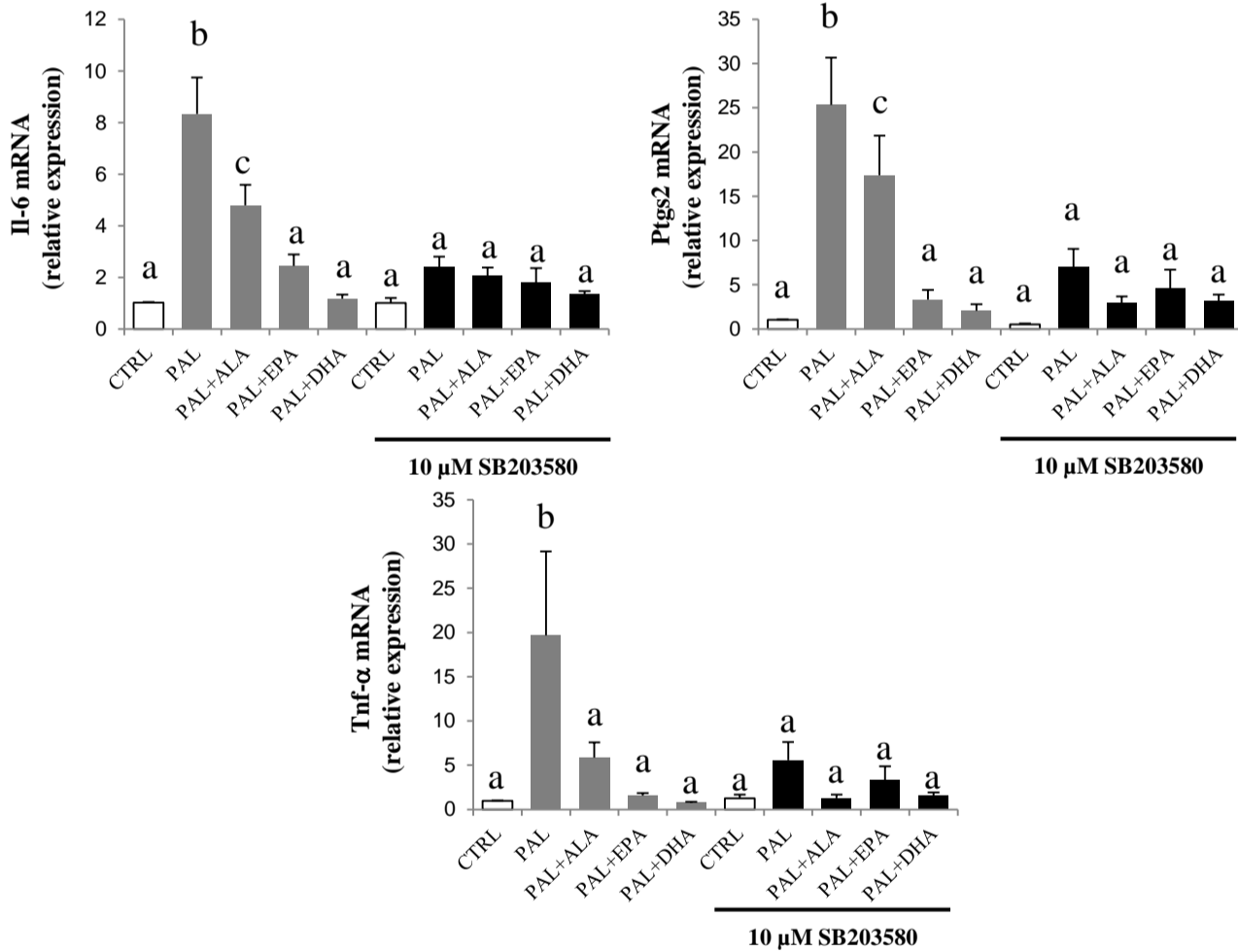
After 16 hours incubation with 500 $\mu$ M PAL without or with 10 $\mu$ M of SB203580, a specific inhibitor of p38MAPK, and 50 $\mu$ M of alpha linolenic acid (ALA), eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA), myotubes were harvested and submitted to mRNA quantification or immunoblotting.

### Results:

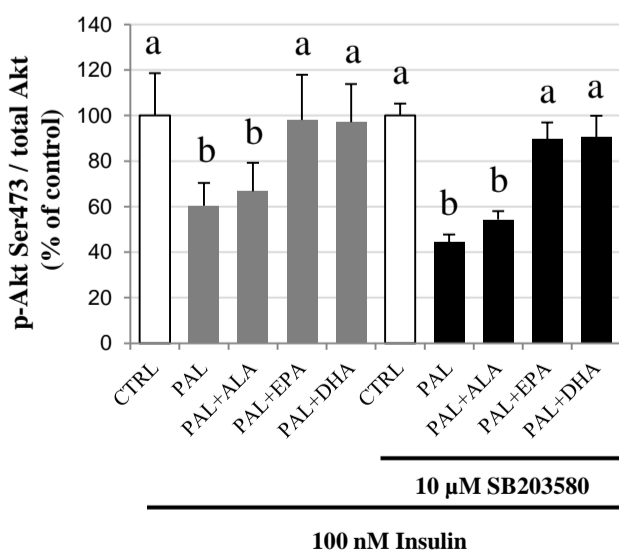
**Figure 1. : PAL-induced p38MAPK was reversed by EPA and DHA supplementation.**



**Figure 2. : mRNA levels of inflammation markers were reduced by n-3 PUFA and restored to the control with SB203580.**



**Figure 3. : p38MAPK inhibition had no beneficial effect on PAL-induced IR.**



### Conclusion and perspectives:

Our results suggested that p38MAPK activation by PAL is crucial to induce inflammation in C212 muscle cells, but is not involved in PAL-induced IR. Among n-3PUFA, only EPA and DHA reduced p38MAPK activation and improved IR. Additional studies are currently performed to explore the involvement of nuclear factor kappa B signalling in these effects.