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MEETING ABSTRACT

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Nitric oxide inhibits adipogenesis by *S*-nitrosation of CCAAT/enhancer-binding protein β

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Background: Within the last decades the prevalence of adipositas, obesity and associated diseases has been escalating world-wide highlighting the need for development of effective therapeutic concepts. 3T3-L1 adipocytes share many similarities with primary fat cells and represent a reliable *in vitro* model of adipogenesis. The aim of the present study was to investigate the effect of nitric oxide on adipocyte differentiation.

Methods: Adipogenesis was experimentally induced with a mixture of insulin, dexamethasone, and 3-isobutyl-1-methylxanthine in the absence and presence of increasing concentrations of *S*-nitroso-glutathione (GSNO) and diethylenetriamine NONOate (DETA/NO). After 7 days cells were harvested and analyzed for protein and triglyceride content as well as for mRNA and protein expression of early and late transcription factors and markers of terminal differentiation. *S*-Nitrosation and transcriptional activity of CCAAT/enhancer-binding protein β (C/EBPβ) were measured by biotin switch assay and dual luciferase reporter assays, respectively.

Results: GSNO exerted a prominent anti-adipogenic effect evident as reduced cellular triglyceride and protein content as well as decreased mRNA and protein expression of late transcription factors (*e.g.* peroxisome proliferator-activated receptor γ) and markers of terminal differentiation (*e.g.* leptin). By contrast, GSNO did not affect mRNA and protein expression of C/EBPβ, which represents a pivotal early transcription factor of adipogenesis. Differentiation was also inhibited by the NO donor DETA/NO. Biotin switch experiments showed significantly increased *S*-nitrosation of C/EBPβ variants liver-enriched transcriptional activator protein*, liver-enriched transcriptional activator protein, and liver-enriched inhibitory protein. Moreover, transcriptional activity of C/EBPβ was significantly reduced by the NO donor.

Discussion: Our data demonstrate that posttranslational *S*-nitrosative modification of C/EBPβ accounts for the anti-adipogenic effect of NO, suggesting that *S*-nitrosation represents an important physiological concept to control fat cell maturation.

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