

IKK α is involved in pro-inflammatory activity of extracellular nicotinamide phosphoribosyltransferase (eNAMPT) in bone marrow-derived macrophages.

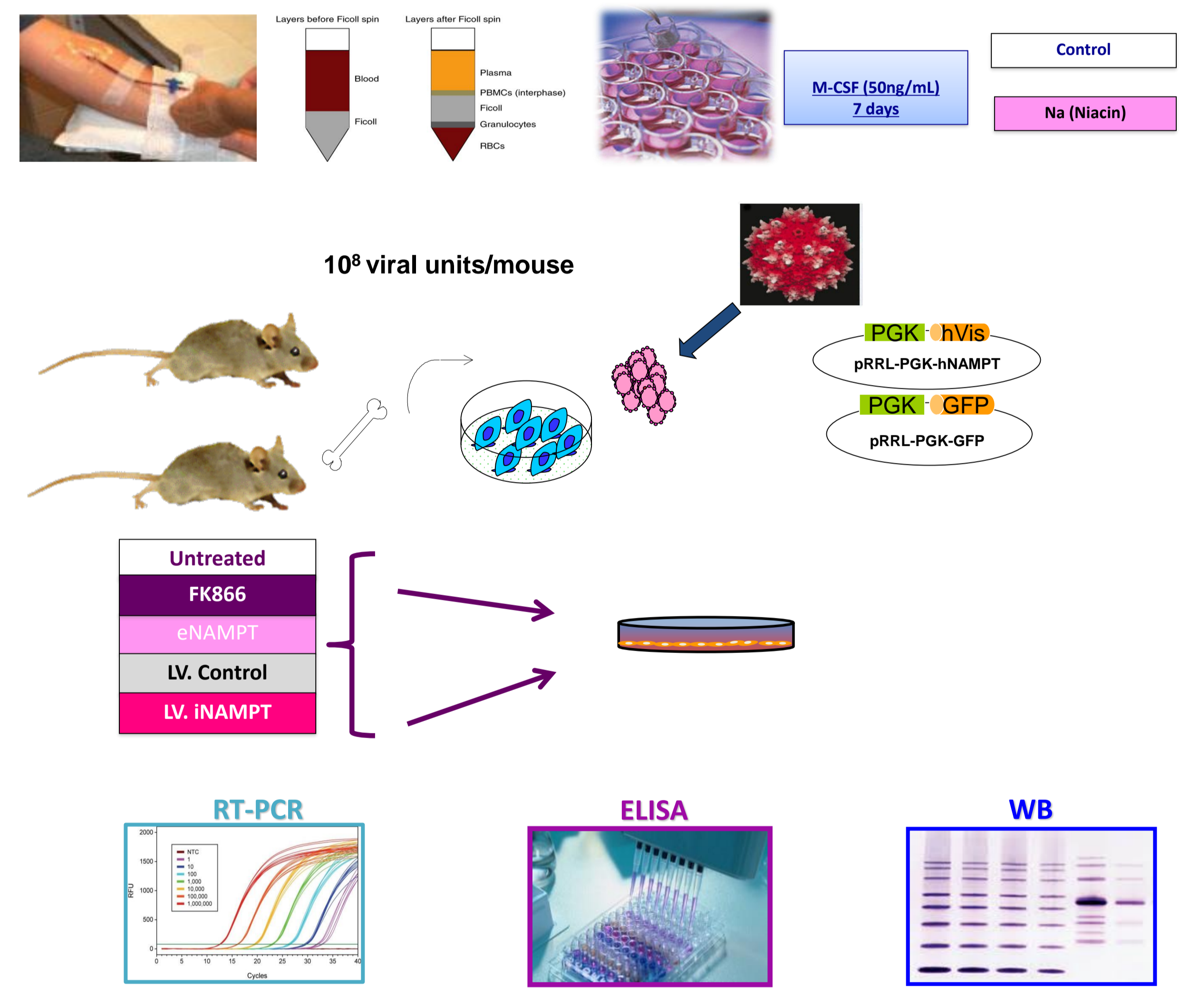
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37th SEF National Meeting (Barcelona, 2017)

INTRODUCTION

The IKK α , a subunit of the NF- κ B-activating IKK complex, has emerged as an important regulator of inflammatory gene expression. Although intracellular nicotinamide phosphoribosyltransferase (iNAMPT) is a key enzyme in controlling NAD⁺ metabolism, circulating eNAMPT has been associated with several metabolic and inflammatory disorders, including cancer and cardiovascular diseases. Herein, the potential role of IKK α and the underlying mechanisms by which eNAMPT could exert the metabolic and inflammatory dysfunctions were investigated.

MATERIAL / METHODS

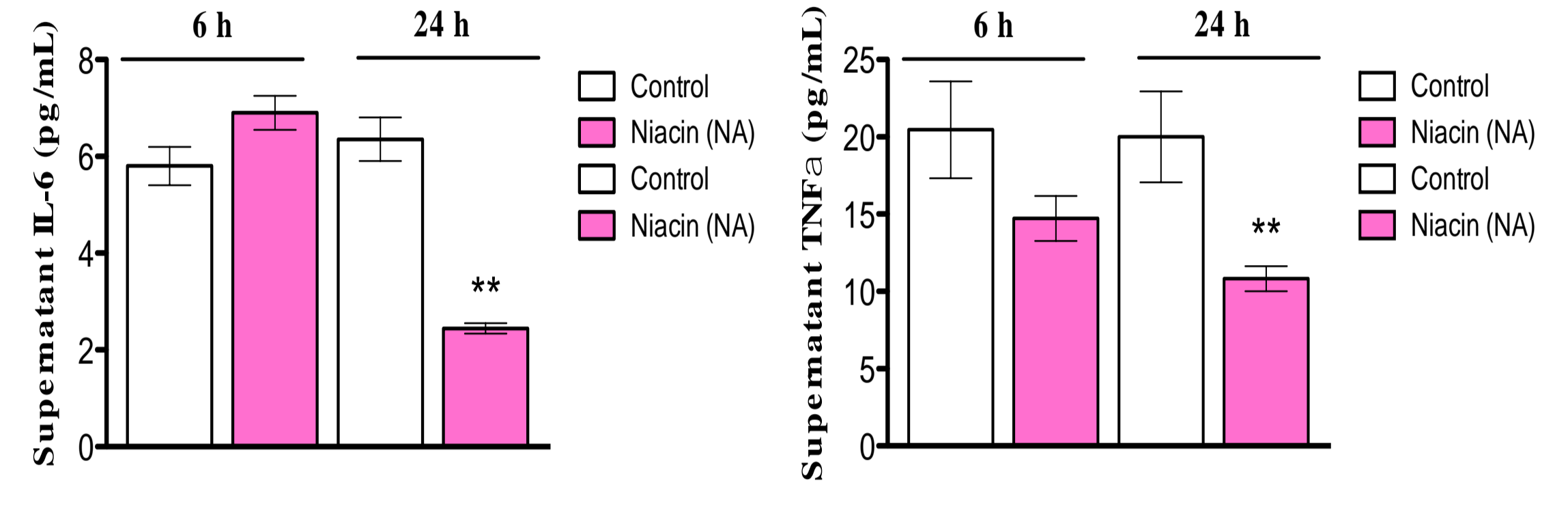


RESULTS

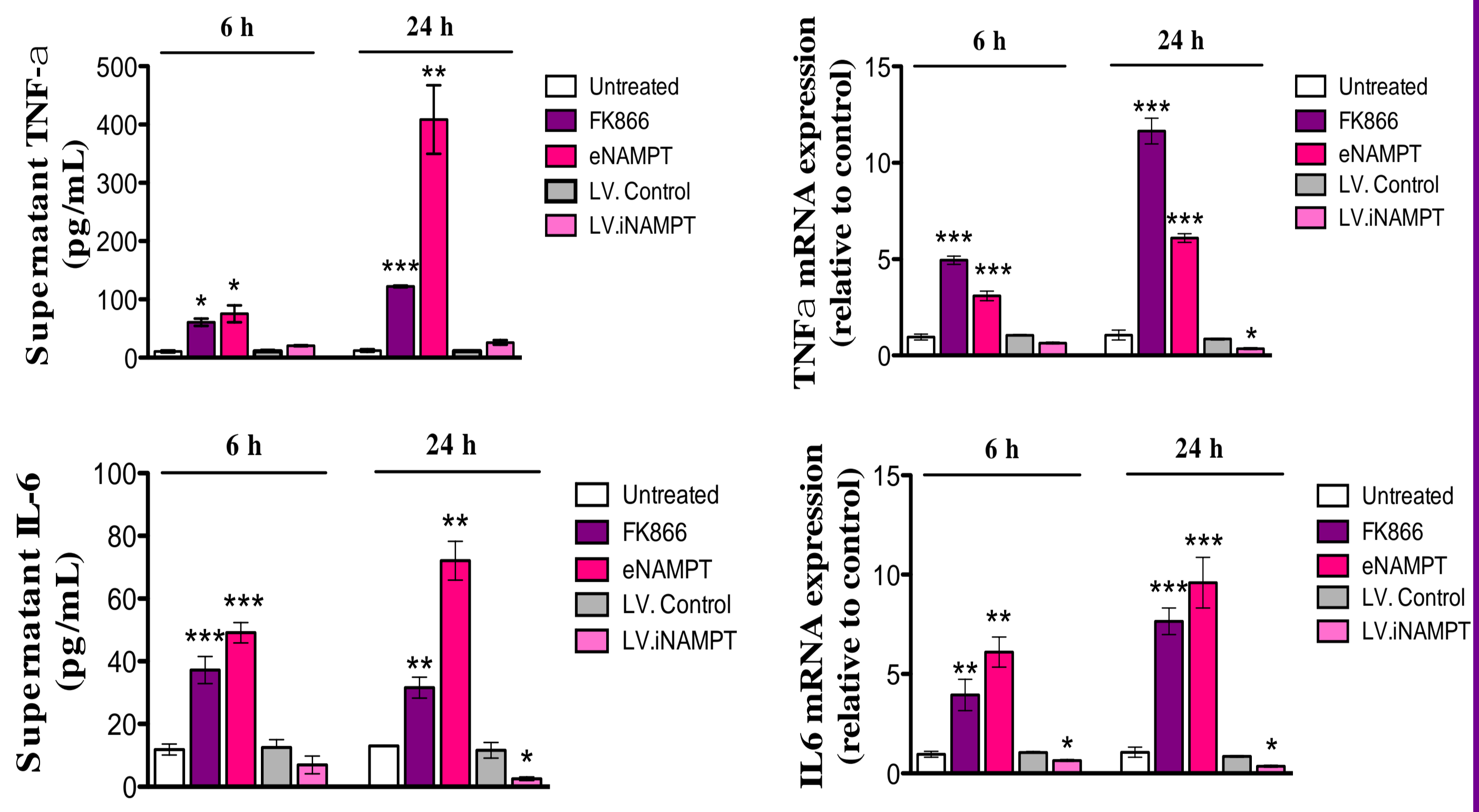
BMDMs pretreated with eNAMPT reduced pro-inflammatory TNF α , IL-1 β , and IL-6 gene, protein expression and cytokine release. Control BMDMs pretreated with eNAMPT were polarized towards M1 phenotype, whereas IKK α ^{-/-} BMDMs were remained unaltered. Finally, pre-incubation of BMDMs with LV.iNAMPT enhanced the pharmacological benefits of IKK α inhibition; increasing the expression of PPAR γ -related genes.

RESULTS

Niacin, the NAMPT's substrate, decreases proinflammatory cytokines in human primary monocytes



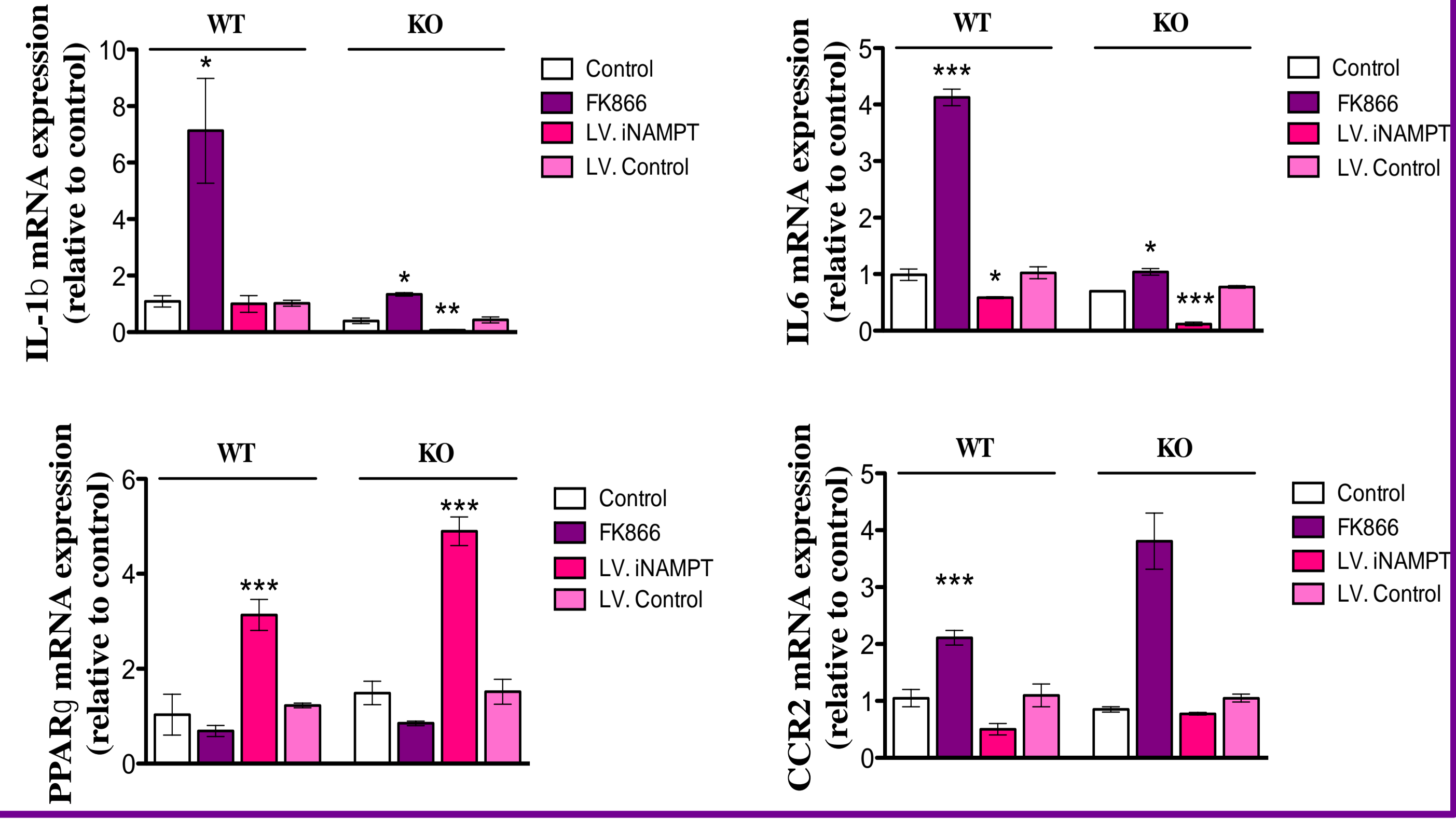
iNAMPT exerts an anti-inflammatory effect on primary human monocytes derived macrophages



eNAMPT unlike iNAMPT promotes the production of proinflammatory cytokines



iNAMPT enhance the effects of IKK α ^{-/-}



CONCLUSIONS

These findings provide evidence that NF- κ B play a role in pro-inflammatory activity of eNAMPT and reveal that targeting IKK α kinase activity represents a pharmacological approach.