ADIPONECTIN SECRETED BY TUBULAR RENAL CELLS MEDIATES THE CELLULAR INFLAMMATORY DAMAGE LPS-INDUCED IN AN AUTOCRINE DEPENDENT-MANNER

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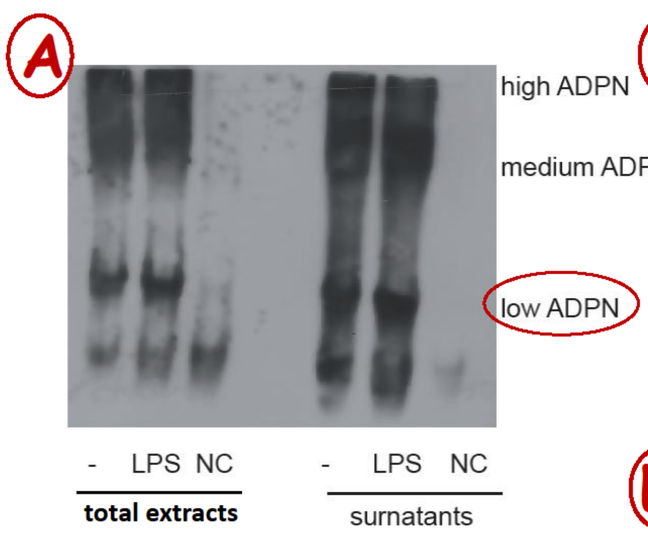
BACKGROUND AND AIM

The pathogenic role of Adiponectin (ADPN) in kidney failure is not yet elucidated, since in vitro and in vivo studies demonstrated that ADPN exerts both anti-inflammatory and pro-inflammatory effects and that ADPN deficiency may worsens or protects against kidney injury. Recently we reported that in proximal tubular renal cells, HK-2, the expression and secretion levels of ADPN increased upon LPS-exposure. Therefore in this study we investigated the role of ADPN secreted by HK-2 cells in the inflammatory damage LPS-induced and the molecular mechanisms by which the adipokine exerts its effects.

MATERIALS AND METHODS

Immortalized human proximal tubular renal cells, HK-2; Real-time RT-PCR assays, Western Blot Analysis, RNA interference (RNAi), Transient transfection assay, Immunoprecipitation studies, Statistical analysis.



RESULTS

Firstly, we demonstrated that all isoforms of ADPN were increased in LPS treated-cells, especially low-molecular weight form (A). Next we observed that LPS short-treatment enhanced ADPN protein expression levels (B) activating signaling pathways downstream of AdipoR1, pAMPK, pERK, pJNK (C) and promoting the up-regulation of TNFa, IL-6 and MCP-1 mRNA expression (D). The addition of a ADPN-targeting RNAi (E) reduced the phosphorylation status of AMPK/ERK/JNK and the mRNA levels of the above reported cytokines. We found that LPS promoted the nuclear translocation of NFkB (F) together with the kinases upstream regulator of NFkB activation (G) and pcFos/pcJun (AP-1) (H), both induced by the activated JNK-pathway, and involved in the TNF-α activation, which nuclear up-regulation was abrogated in the presence of ADPN RNAi. Using HK-2 cells transfected with wt-TNFa gene-promoter, we demonstrated that LPS induced the TNFa promoter activity and that the pretreatment with the inhibitors of NFkB pathway and AP-1 transcription capacity, abrogated the TNF-α-promoter activity (I).

CONCLUSIONS

Collectively our results suggest that the ADPN produced by HK-2 cells during LPS-exposure could mediate the inflammatory damage in an autocrine-dependent-manner

REFERENCES

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