The Role of TNFAIP1 in Regulation of LPS-induced Pathway

THANARUT TANGKHAM, XIAOREN TANG, YUN MA, BUSHRA ALIAHDALI, SEAN LEE, MINGFANG SU, SERGE DIBART

Background :

Porphyromonas gingivalis /lipopolysaccharide (P.g/LPS) induces inflammatory diseases via TNF-α-mediated transcription factors. Our recent data showed that TNFAIP1 (TNF-α induced protein 1) is related to TNF-α in response to LPS. However, The involvement of TNFAIP1 in the LPS-induced pathway is largely unknown.

Aim :

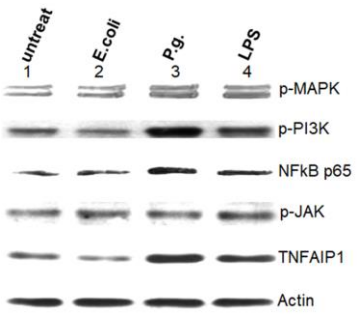
To determine transcriptional regulation of TNFAIP1 gene

Materials and Methods :

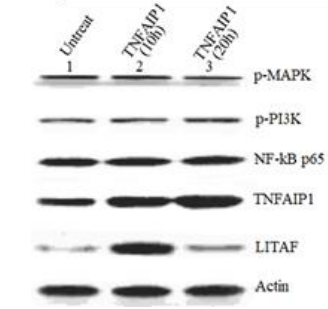
- human macrophage THP-1 cells, mouse macrophage RAW264.7 cells
- Cloning of human or mouse TNFAIP1 cDNA and TNFAIP1 promoter DNA into plasmid of pcDNA3 and pGL3-basic
- Western blot to determine LPS stimulated downstream pathway
- ELISA to quantify TNF-α/Caspase1
- Protein Array to determine apoptotic gene expression

Results :

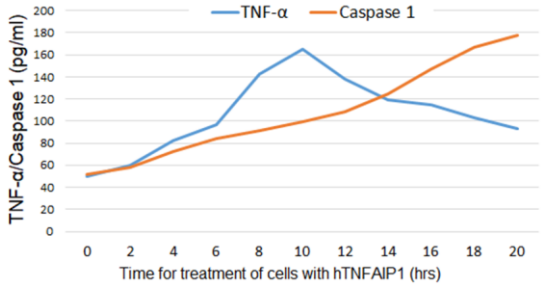
1. Increasing NFκB (p65), TNFAIP1, MAP kinase, and PI3K by P.g/LPS stimulation



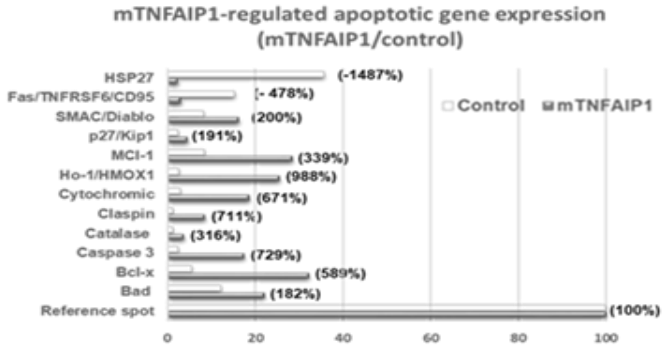
2. The overexpression of humanTNFAIP1 did not activate MAP kinase, PI3K, and NF-kB, except LITAF.



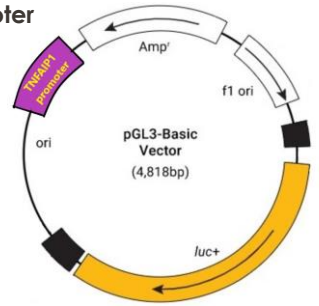
3. TNF-α production rose to the top (10 hrs), gradually drop to 20 hrs, while Caspase 1 increased.



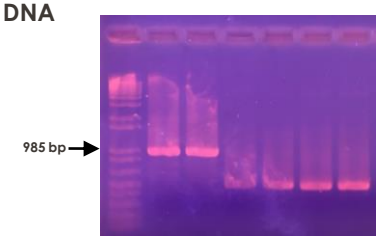
4. Overexpression of mouse TNFAIP1 cDNA caused increasing Bad, Bcl-x, Caspase 3, Catalase, Claspin, Cytochromic, Ho-1/HMOX1/HSP32, MCI-1, P27/Kip1, SMAC, reducing Fas/TNFRSF6/CD and HSP27



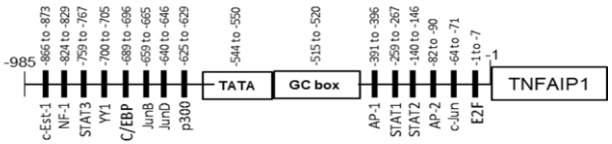
5. The recombinant plasmid DNA of TNFAIP1 promoter



6. Confirmation of the cloned TNFAIP1 promoter DNA



7. The proposed interaction of TNFAIP1 promoter with transcription factors



Conclusion:

- MAP kinase or PI3K as upstream factor and LITAF as downstream factor in TNFAIP1-dependent pathway
- Overexpression of TNFAIP1 induces apoptotic proteins

Future research plan:

- Further analysis of TNFAIP1 promoter activity;
  To determine factors that control TNFAIP1 promoter activity as possible targets for inhibition of P.g/LPS-induced inflammatory diseases

BU Henry M. Goldman School of Dental Medicine