



2019 台灣胸腔暨重症加護醫學會

2019 Taiwan Society of Pulmonary and Critical Care Medicine

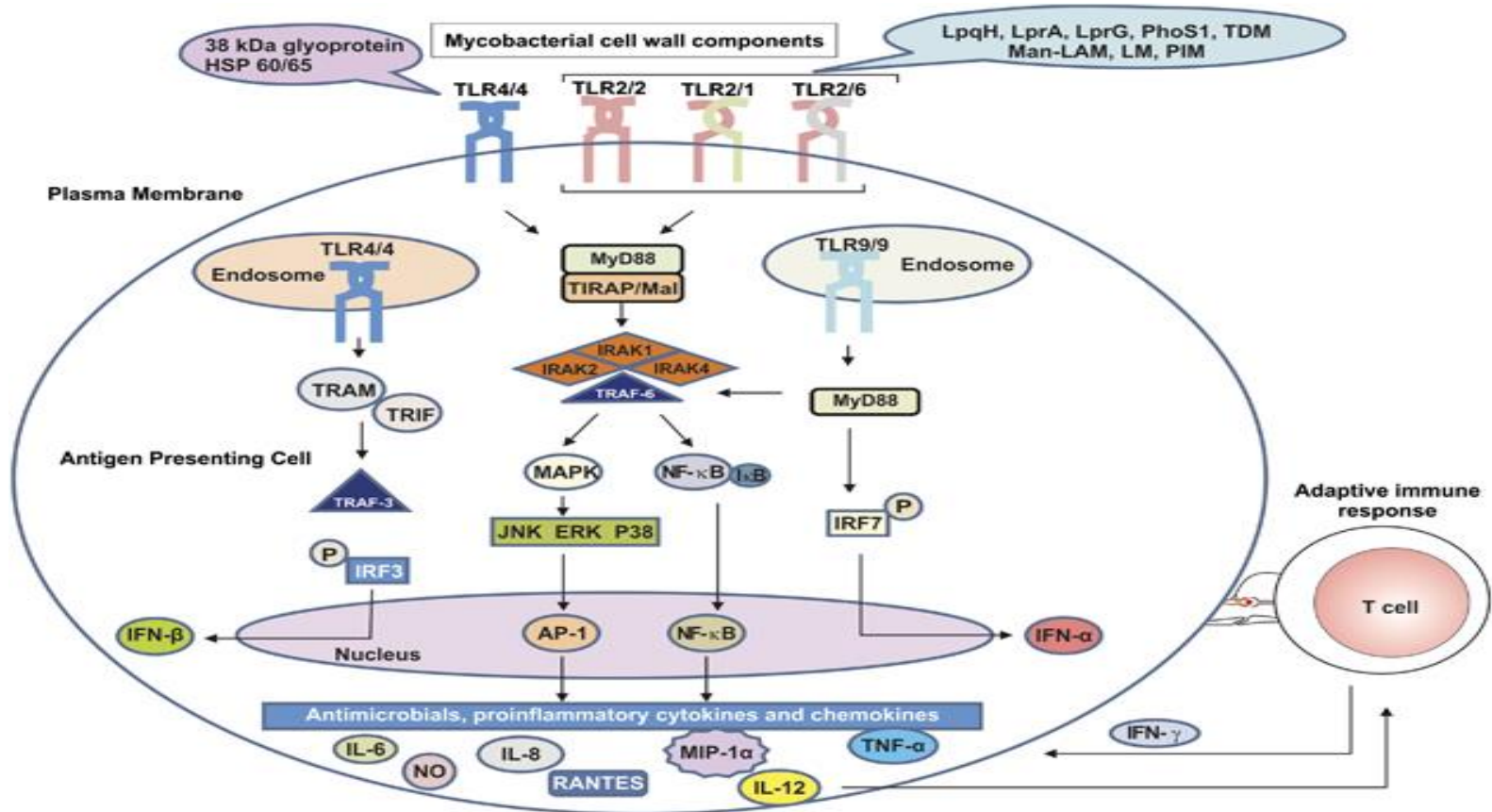
Induction of TREM-1 expression by ESAT6 protein of *Mycobacterium tuberculosis*- a mouse model study

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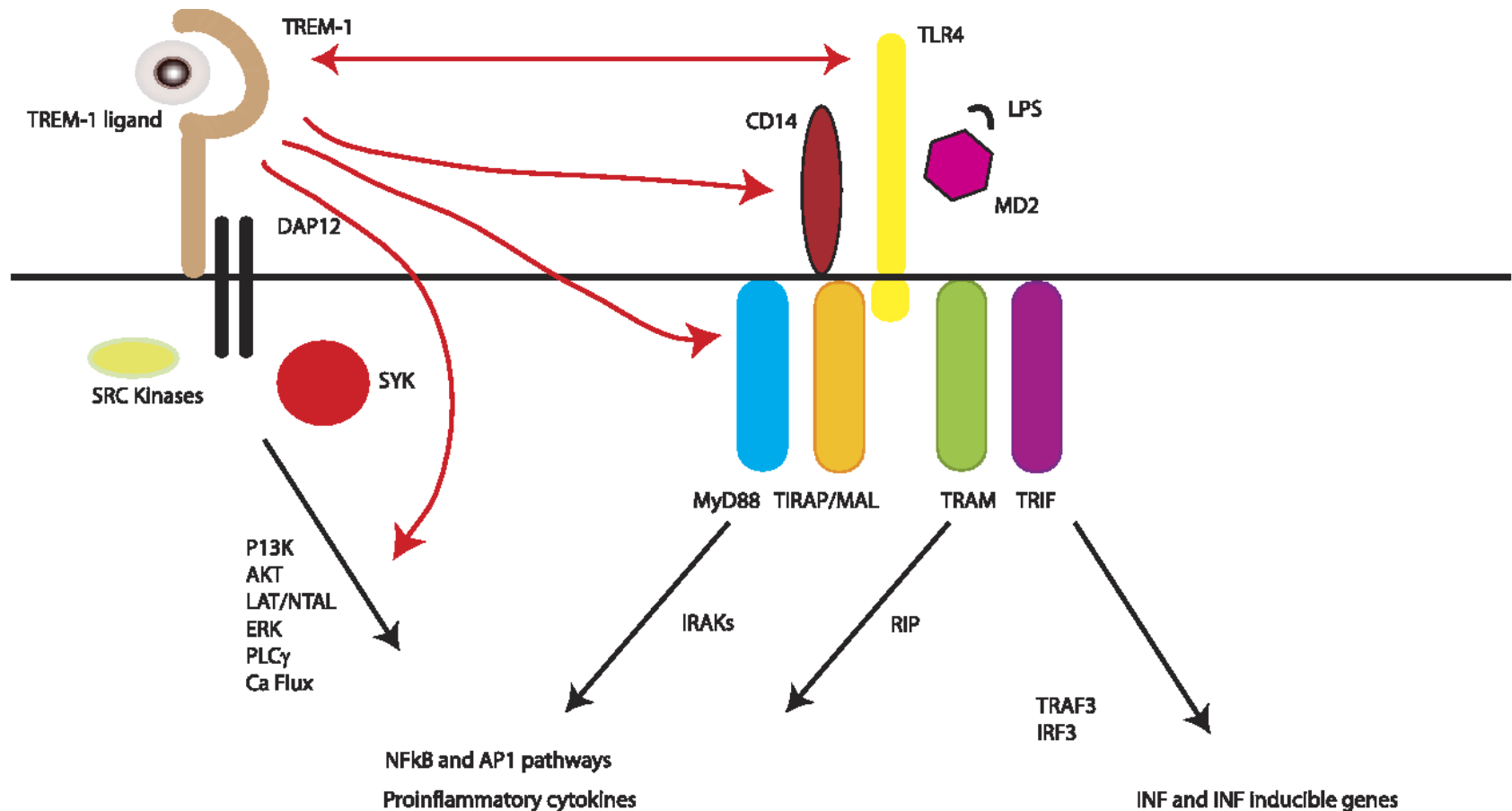
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MTB vs. TLRs

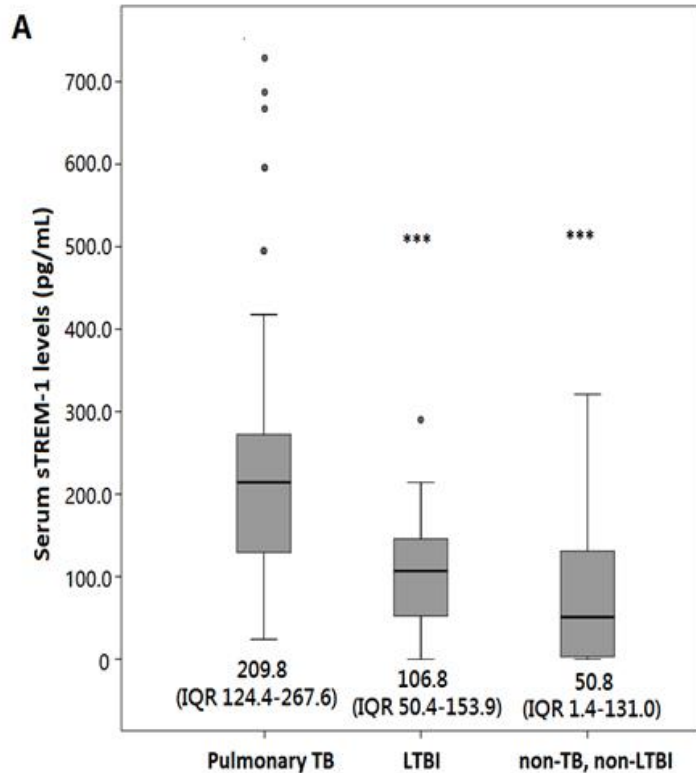


Triggering receptor expressed on myeloid cells-1 (TREM-1)

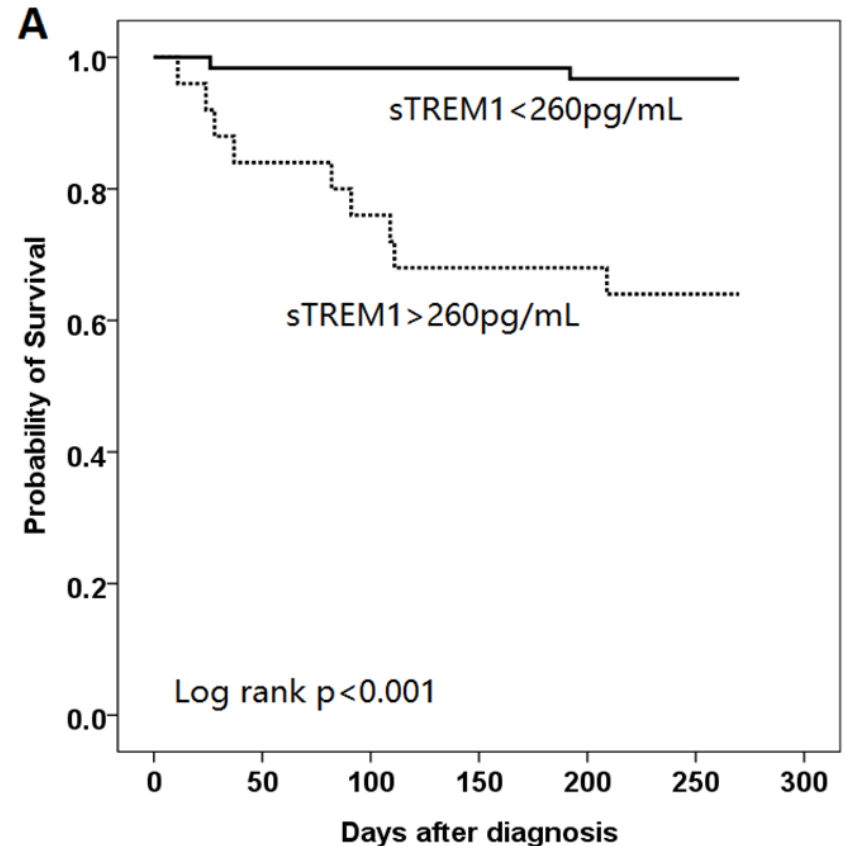


1. Simplified overview of triggering receptors expressed on myeloid cells-1 (TREM-1)/DAP12 and Toll-like receptor 4 (TLR4) signaling events. TREM

sTREM-1 levels in active TB

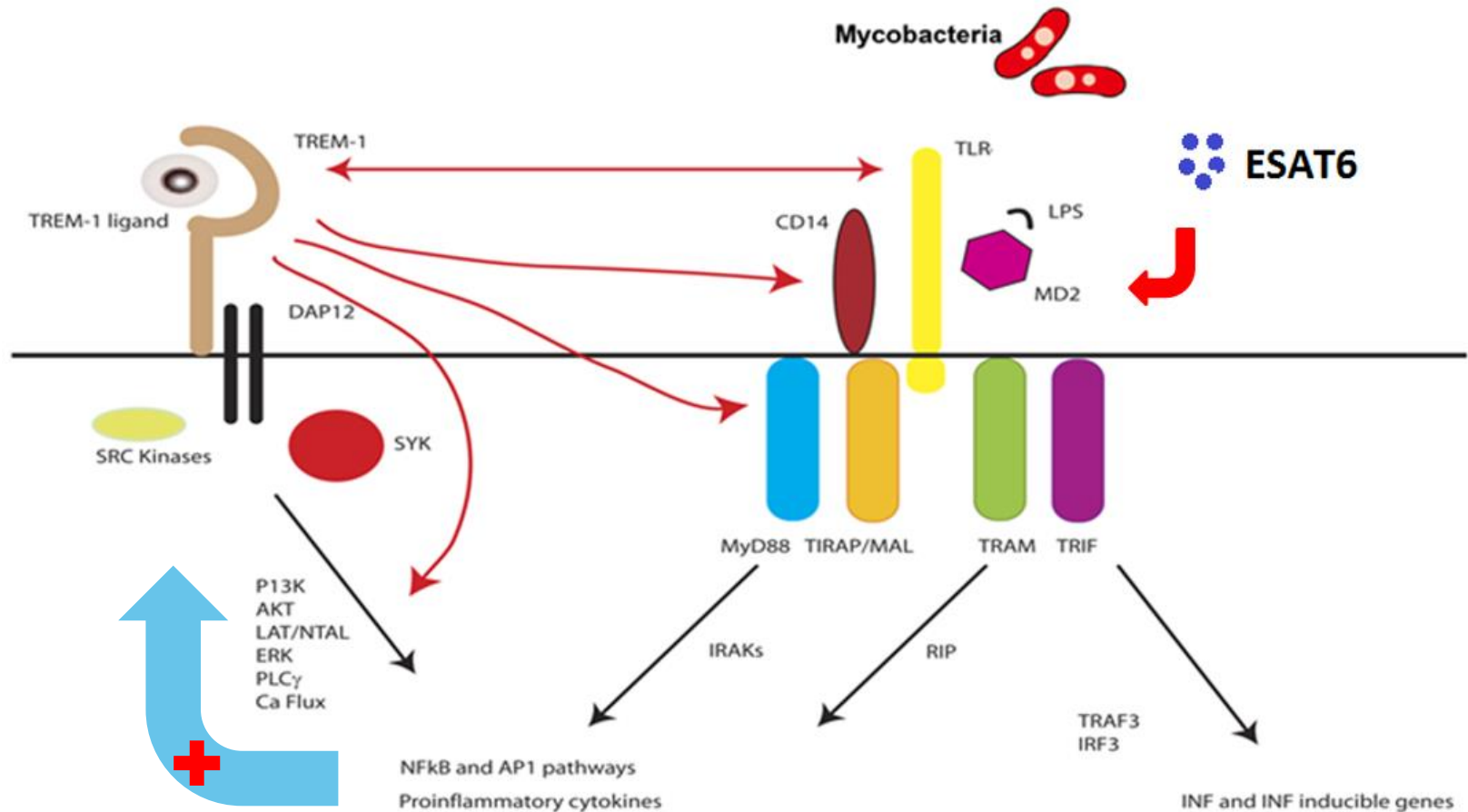


Increased sTREM-1 in ATB patients



sTREM-1 predicts outcomes of ATB patients

Our Hypothesis

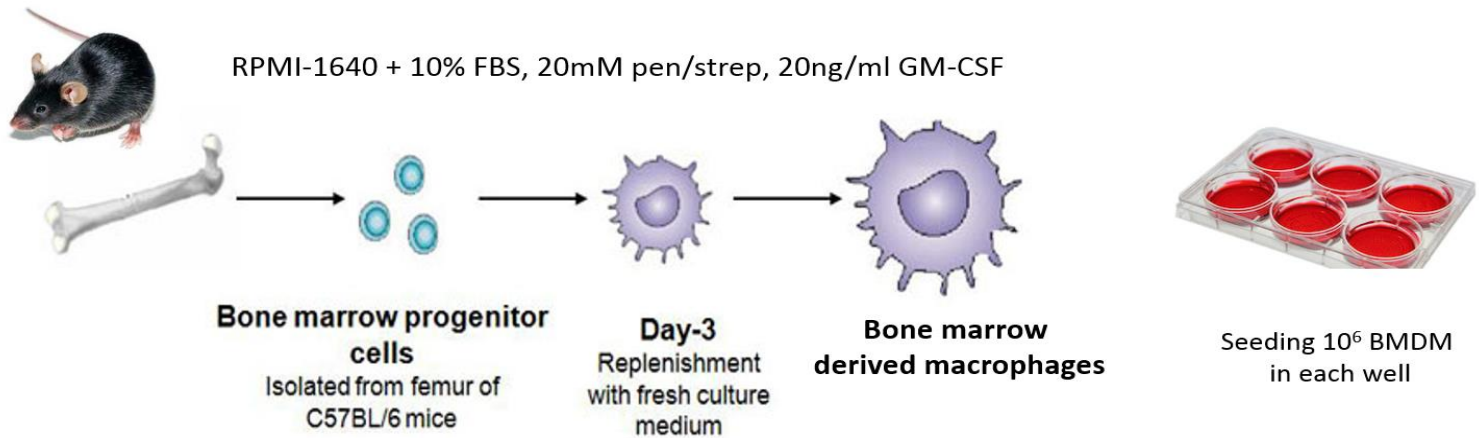


TREM-1 expression

Materials

Part 1

WT vs.
TR1 KO



Part 2

BMDM: 5×10^5 cells/well



Stimulation 6~24 hours

	Dose
RPMI	-
ESAT-6	0.625~10ug/ml
H37Rv cell lysate	120ug/ml
ESAT6+TB lysate	

Cytokine expression
Inflammation marker: NO,
TNF-a, IL-1b, IL-12

Protein expression
M1 marker: iNOS
(Western Blot)

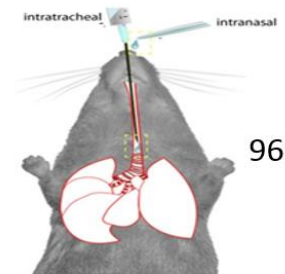
mRNA expression
iNOS, TREM1, TNF-a,
IL-10, Arg-1

Part 3

TREM1-KO mice



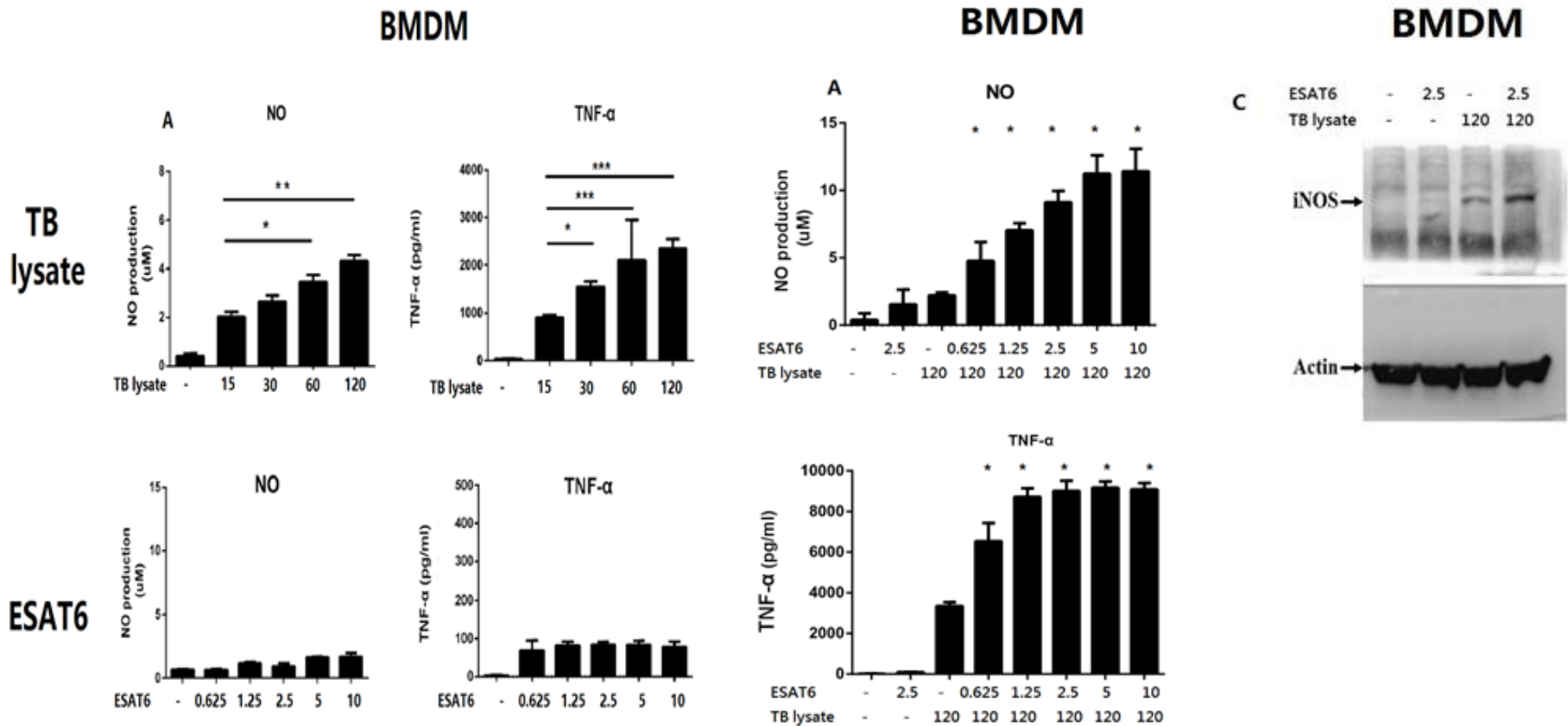
TREM1-WT mice



- IT injection of
1. PBS
 2. HKMTB (6ug/kg)

Q1

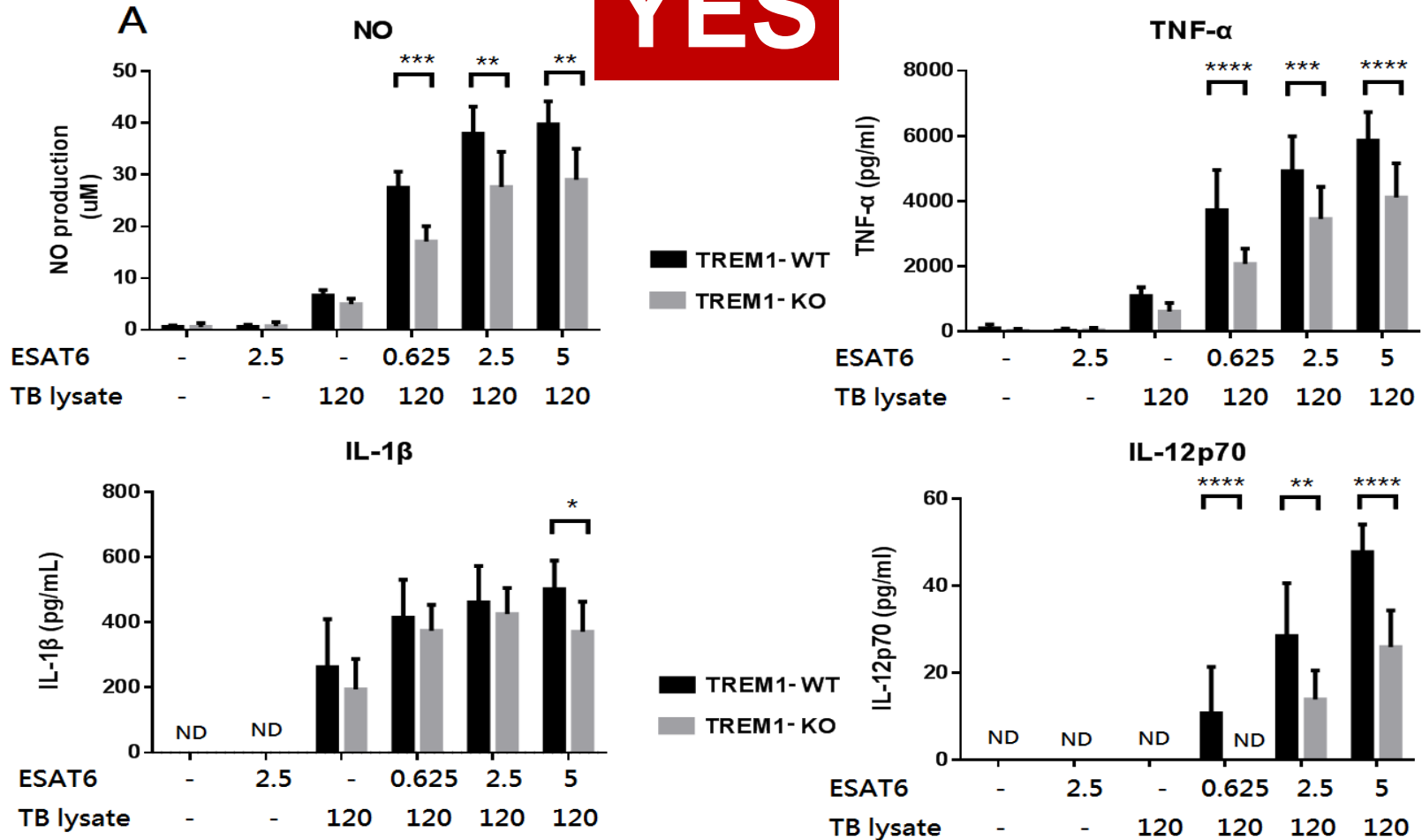
Will TB lysate/ESAT6 enhance proinflammatory responses in BMDM



ESAT6 has synergistic effects

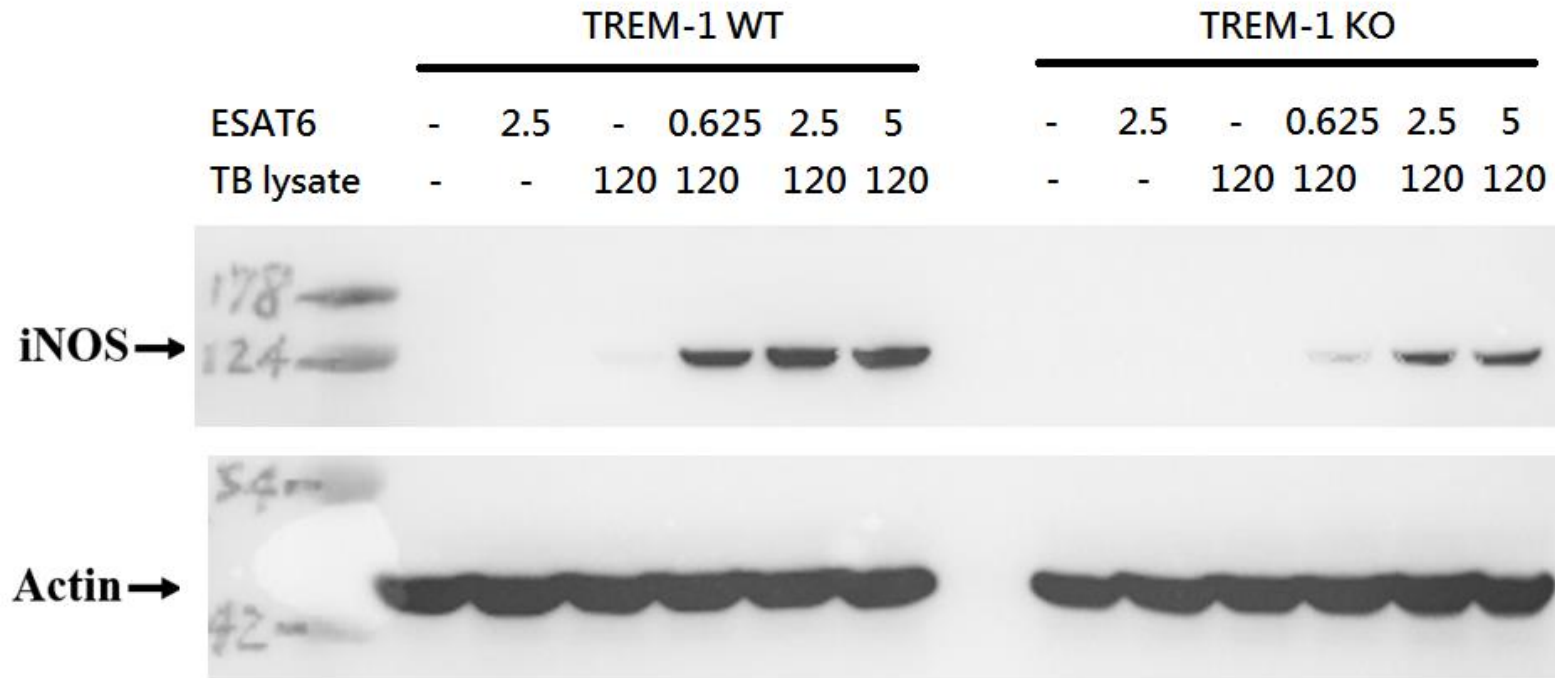
Q2 Will TREM-1 amplify TB lysate/ESAT6 related inflammatory responses in BMDM

YES

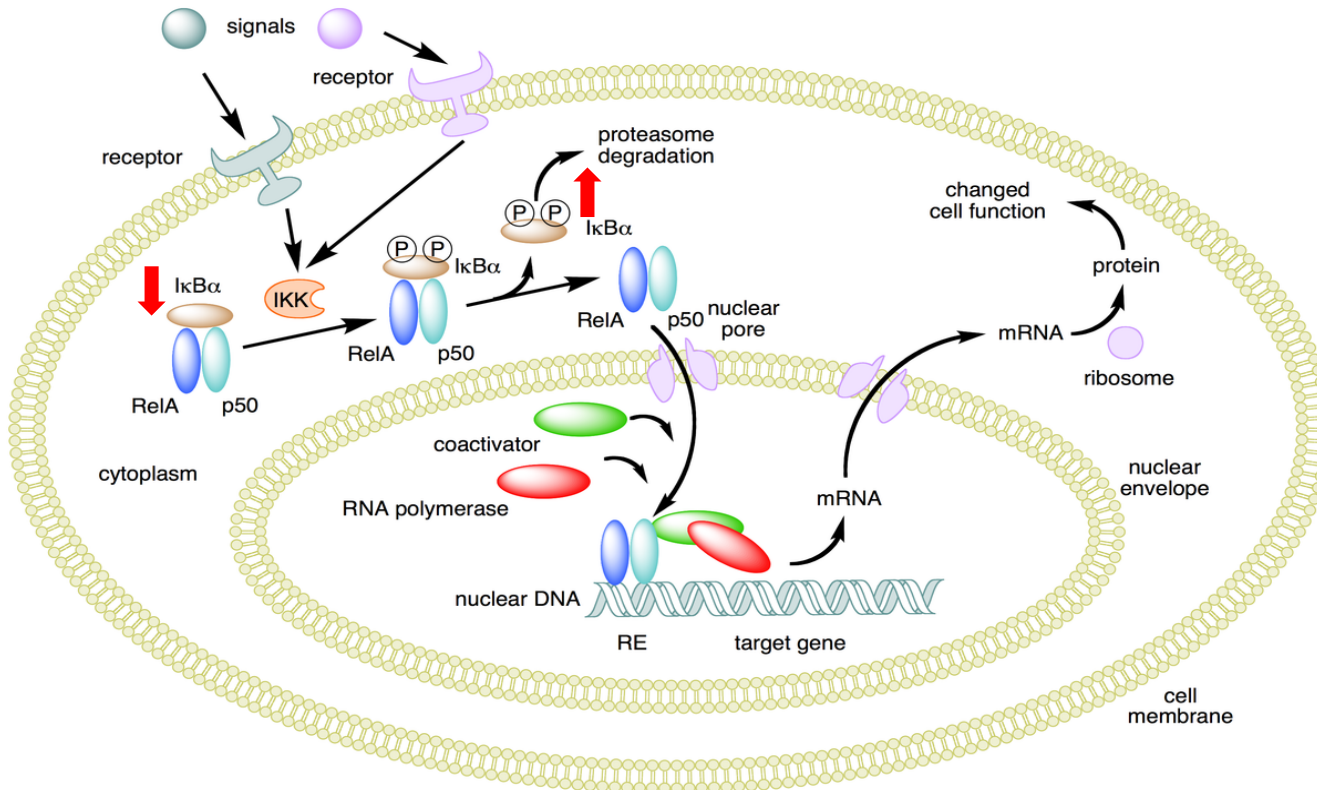


TREM-1 amplify TB lysate/ESAT6 related inflammatory responses in BMDM

B



Q3 Is **TLR/NF- κ B pathway** involved in TB lysate/ ESAT6 mediated proinflammatory responses

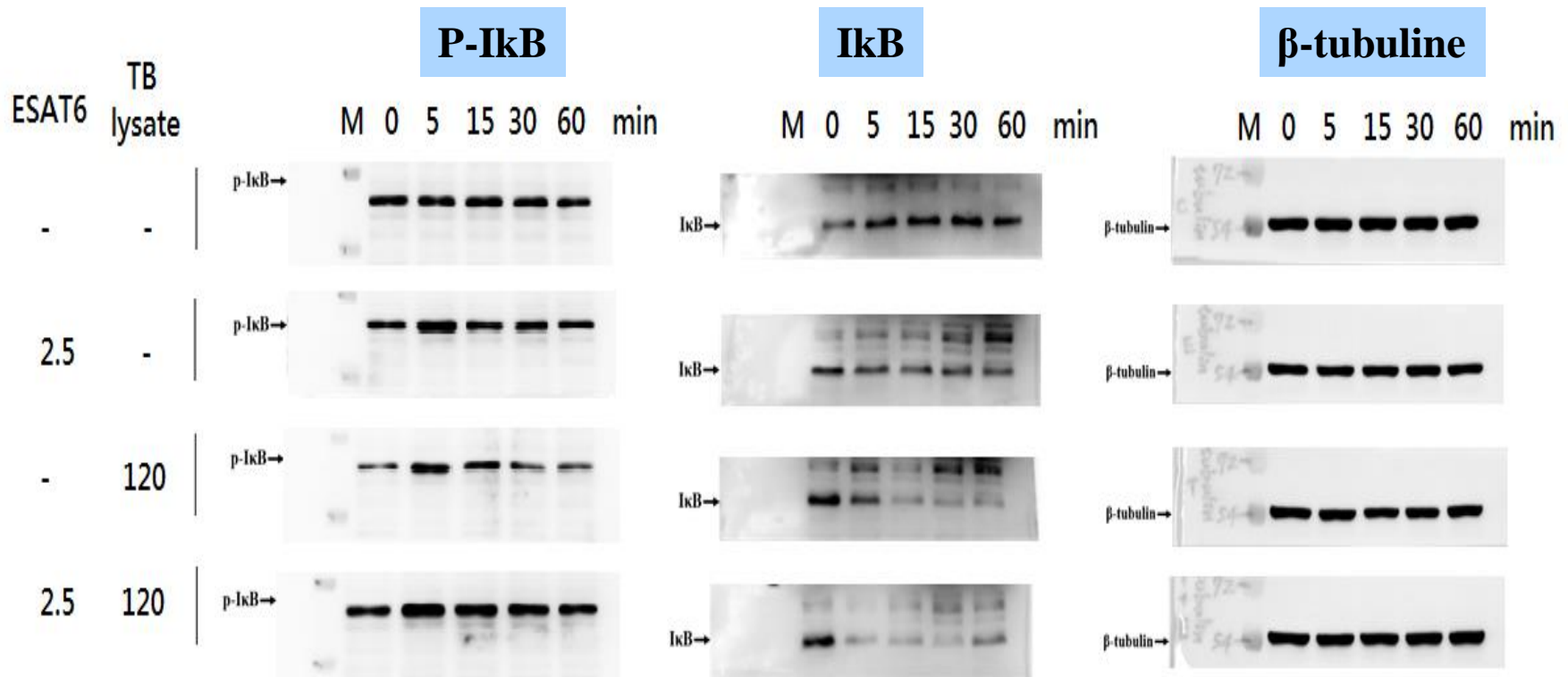


Phosphorylation Western Blot

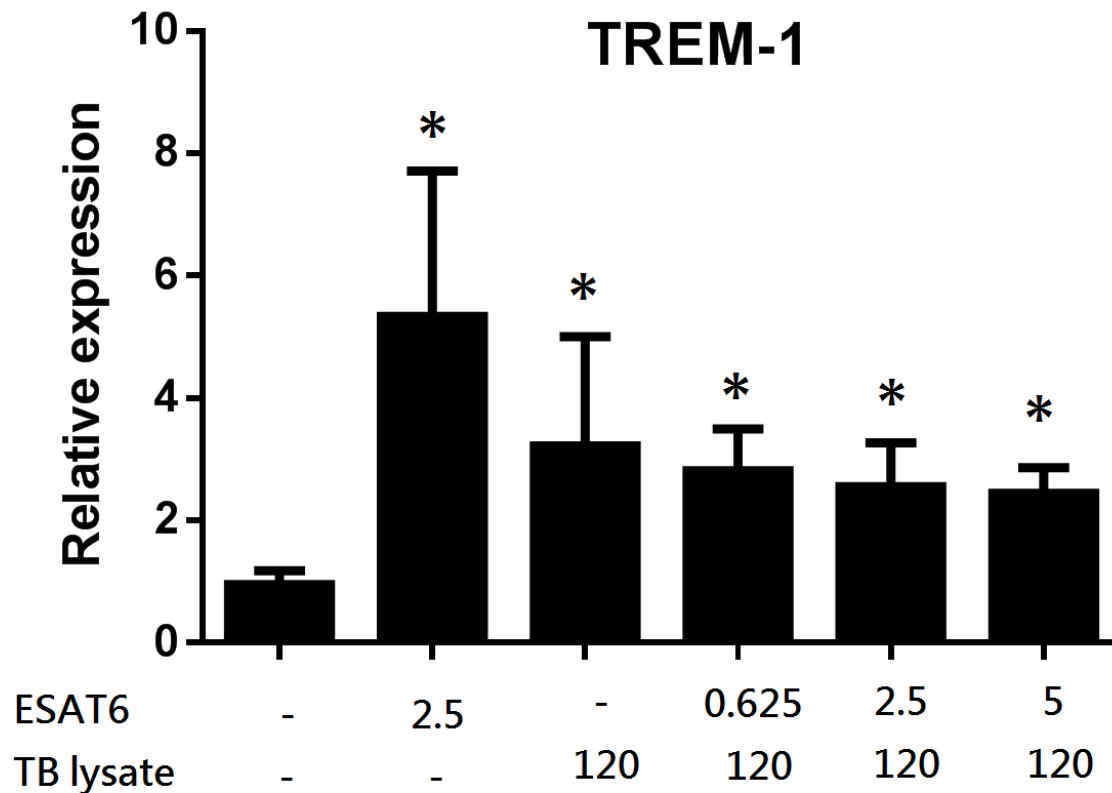
NF- κ B pathway activation

- P-I κ B \uparrow
- I κ B \downarrow

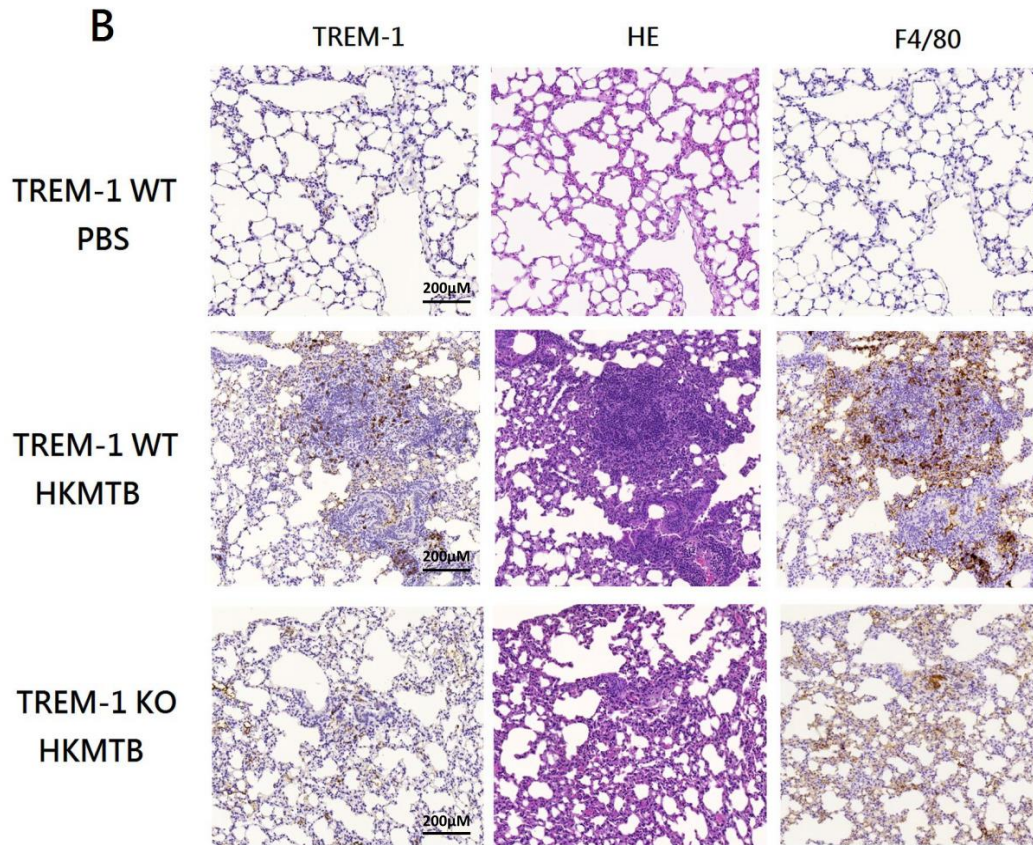
Is **TLR/NF- κ B pathway** involved in TB lysate/ESAT6 mediated proinflammatory responses



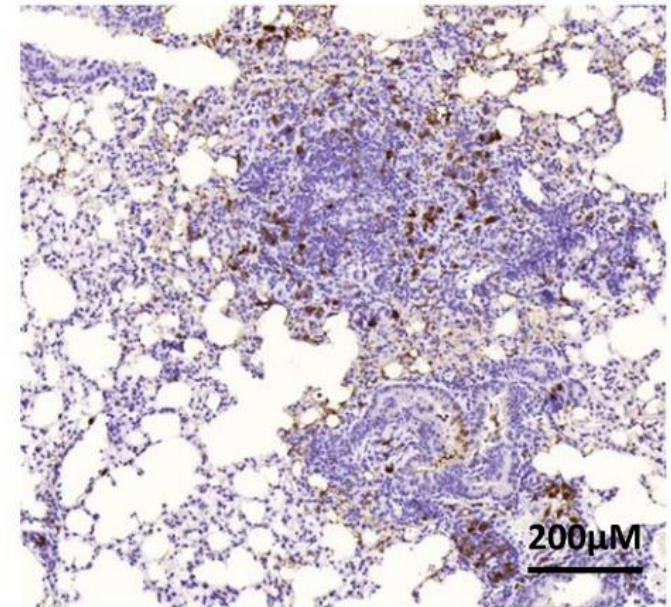
Q4 Is **TREM-1 expression** enhanced by TB lysate/ESAT6



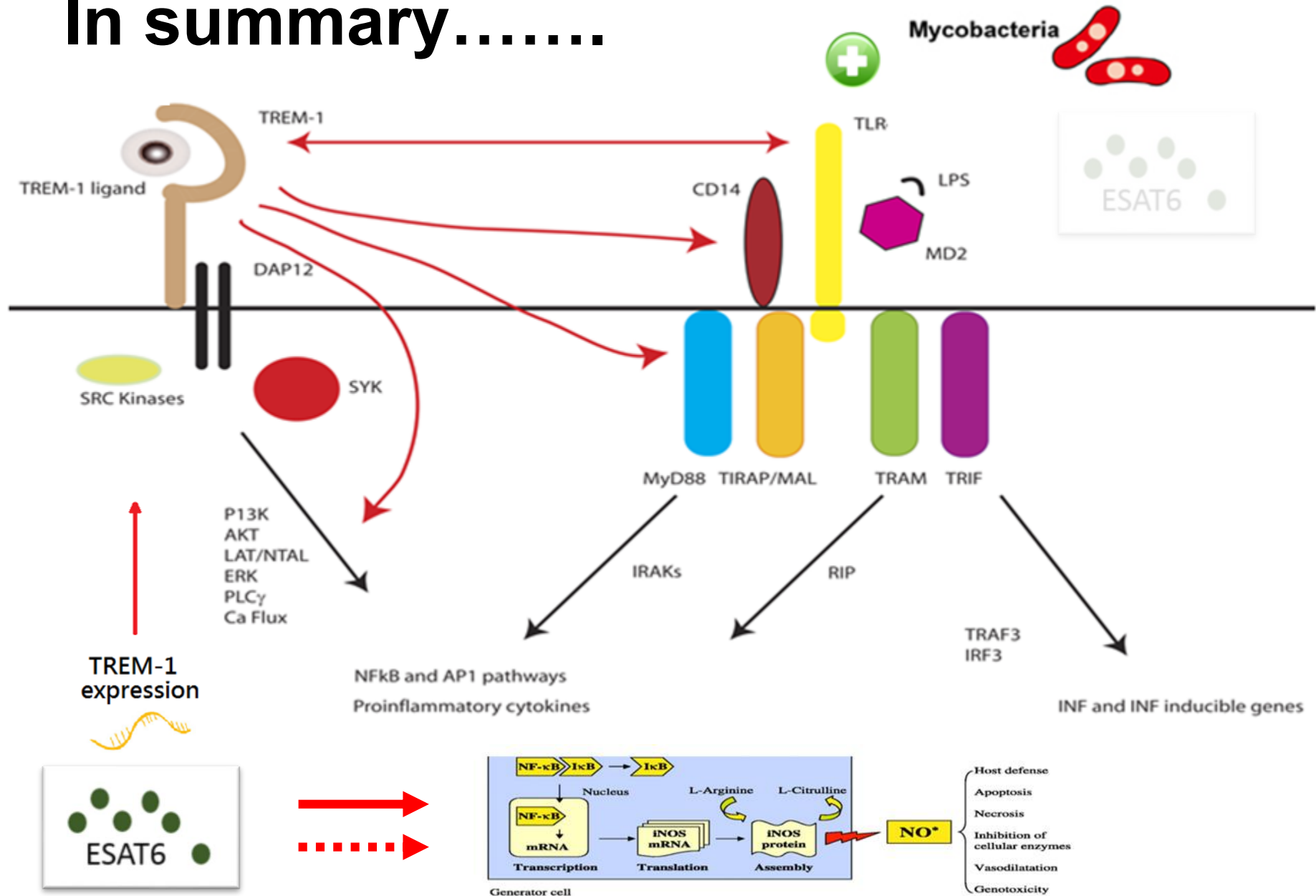
Detection of TREM-1(+) macrophages in lung tissues exposed to HKMTB



TREM-1 IHC



In summary.....



Conclusion

- In mice model

- TB lysate induce NO and TNF- α production in mice macrophages
 - ✓ Limited effect of ESAT6
- ESAT6 have synergistic effects in TB lysate induced pro-inflammatory responses
- TREM-1 amplify the synergistic effects of ESAT6 in inducing pro-inflammatory responses
- TLR/NF- κ B pathway is involved in ESAT6 related synergistic effects
- TREM-1 expression can be significantly induced by ESAT6

Acknowledgement

陽明大學

台北榮總

林永煬教授

陳念榮教授

胸腔部

蘇維鈞教授

陽光耀教授

潘聖衛醫師

林辰昱

賈浩倫

TREM-1 enhances inflammatory responses in TB-related inflammatory responses

