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UNIVERSIDADE DE SÃO PAULO  
FACULDADE DE CIÊNCIAS  
FARMACÉUTICAS

# Toll-like Receptor 1 (TLR1)

## Reconhecimento Molecular pelo Sistema Imune - 2025

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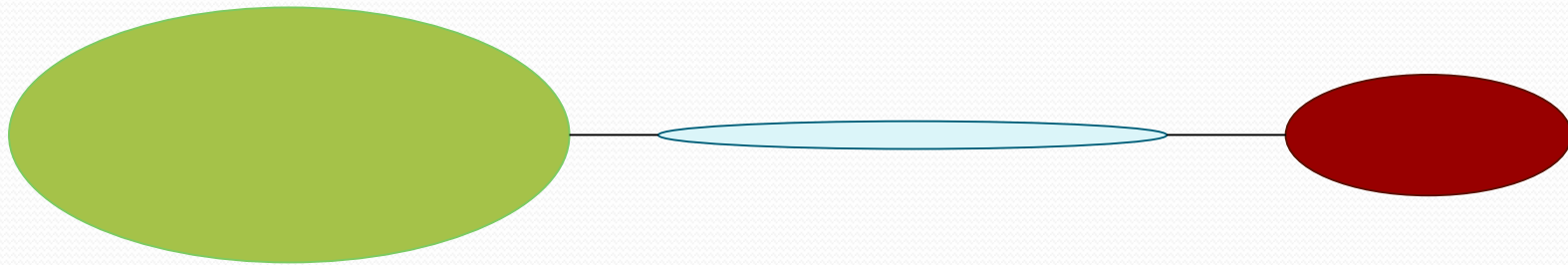
# Toll-like Receptor 1 (TLR)

- Transmembrane Pattern Recognition Receptor (PRR)
- Type I transmembrane glycoprotein
- Localizes to the cell membrane
- Expressed in immune cells such as dendritic cells and macrophages as well as non-immune cells such as fibroblasts and epithelial cells
- PAMP receptor
- Mostly binds bacterial lipoproteins, specifically try-acylated lipoproteins and peptides

# Toll-like Receptor 1 (TLR)

- The active form is an heterodimer with TLR2
- Together with TLR2, it is essential for the immune response associated to the recognition of bacterial try-acylated lipoproteins and peptides
- The heterodimer can also recognize Lipoteichoic acid (LTA)
- LTA is a major component of the cell wall of gram-positive bacteria
- Its activation induces strong proinflammatory signals in macrophages
- TLR2-deficient mice do not respond to the lipoproteins and are more susceptible to septicemia due to *S. aureus*, meningitis due to *S. pneumoniae* and *L. monocytogenes*, and infection with *M. tuberculosis*

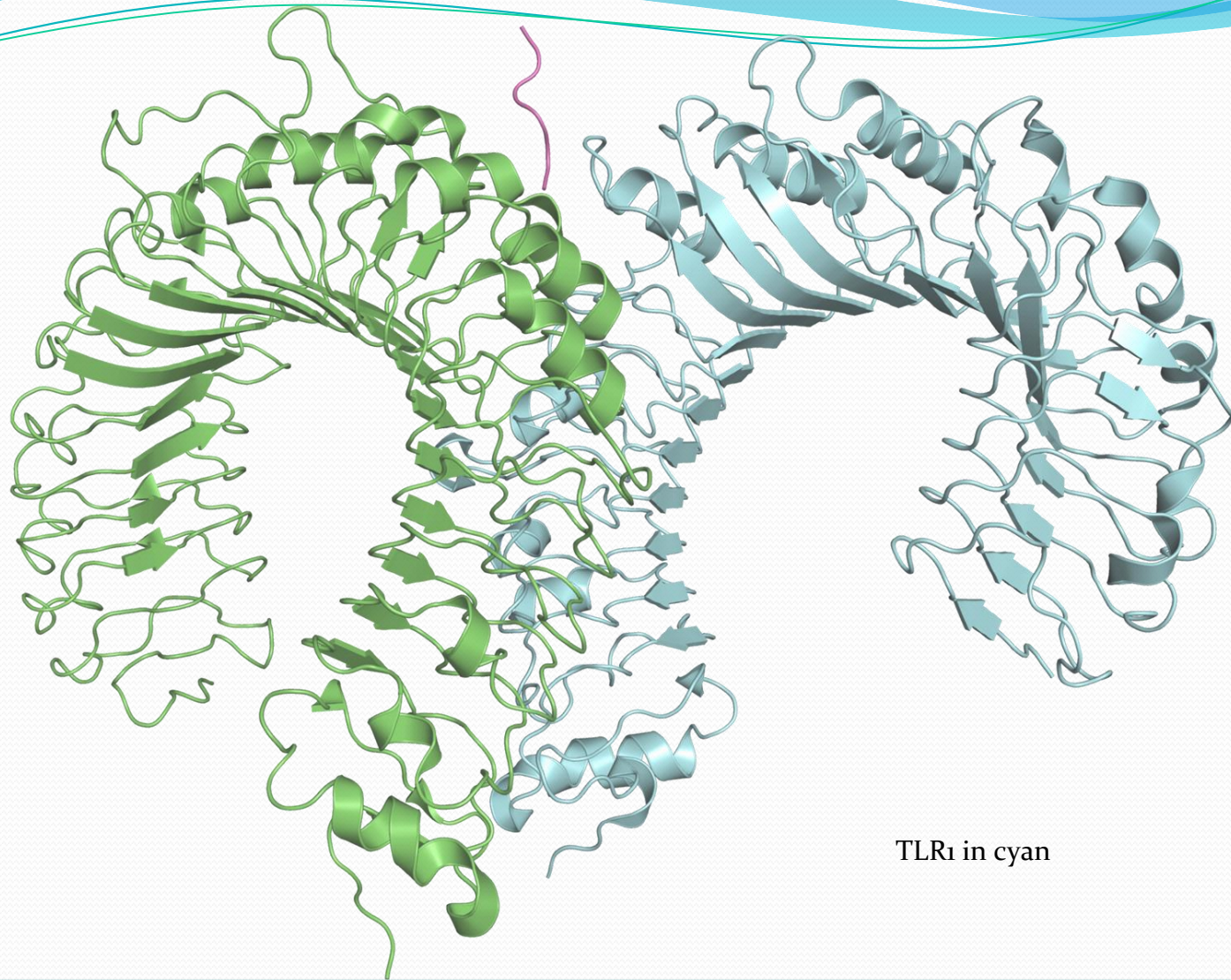
# Toll-like Receptor 1 (TLR)



Large extracellular Ligand-binding Domain, containing leucine-rich repeats (LRRs)

single-pass transmembrane domain

globular intracellular Toll-interleukin 1 Receptor homology domain (TIR)

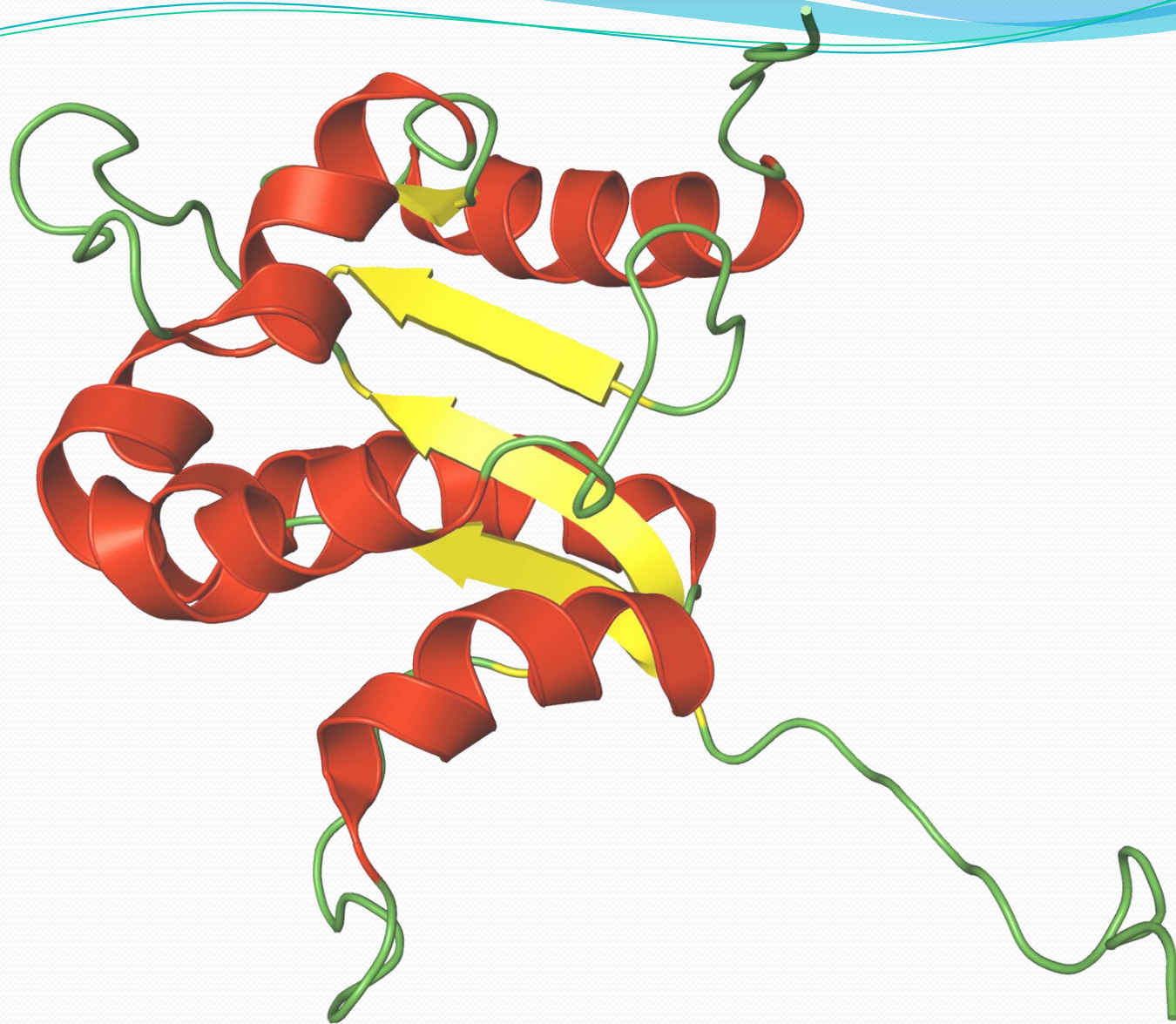


TLR1 in cyan

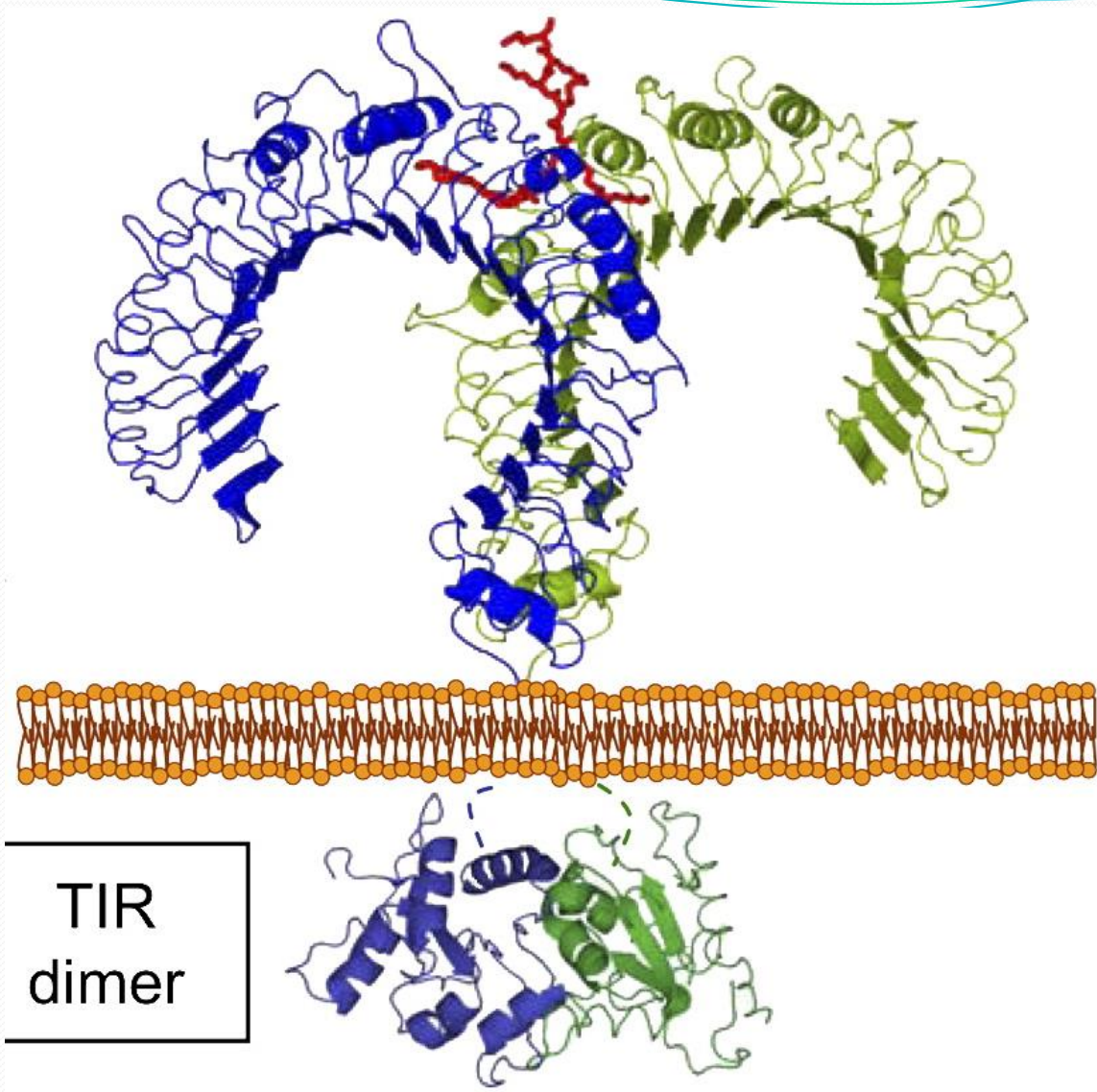
**Crystallographic structure of the ectodomains of human TLR1-TLR2 heterodimer complex bound to tri-acylated lipopeptide, Pam<sub>3</sub>CSK<sub>4</sub>**

PDB accession code: **2Z7X**

Resolution: 2.10 Å



**MNR-resolved structure of the human globular intracellular Toll-interleukin 1 receptor homology domain (TIR)**  
PDB accession code: **7NT7**



Ligand induced dimer

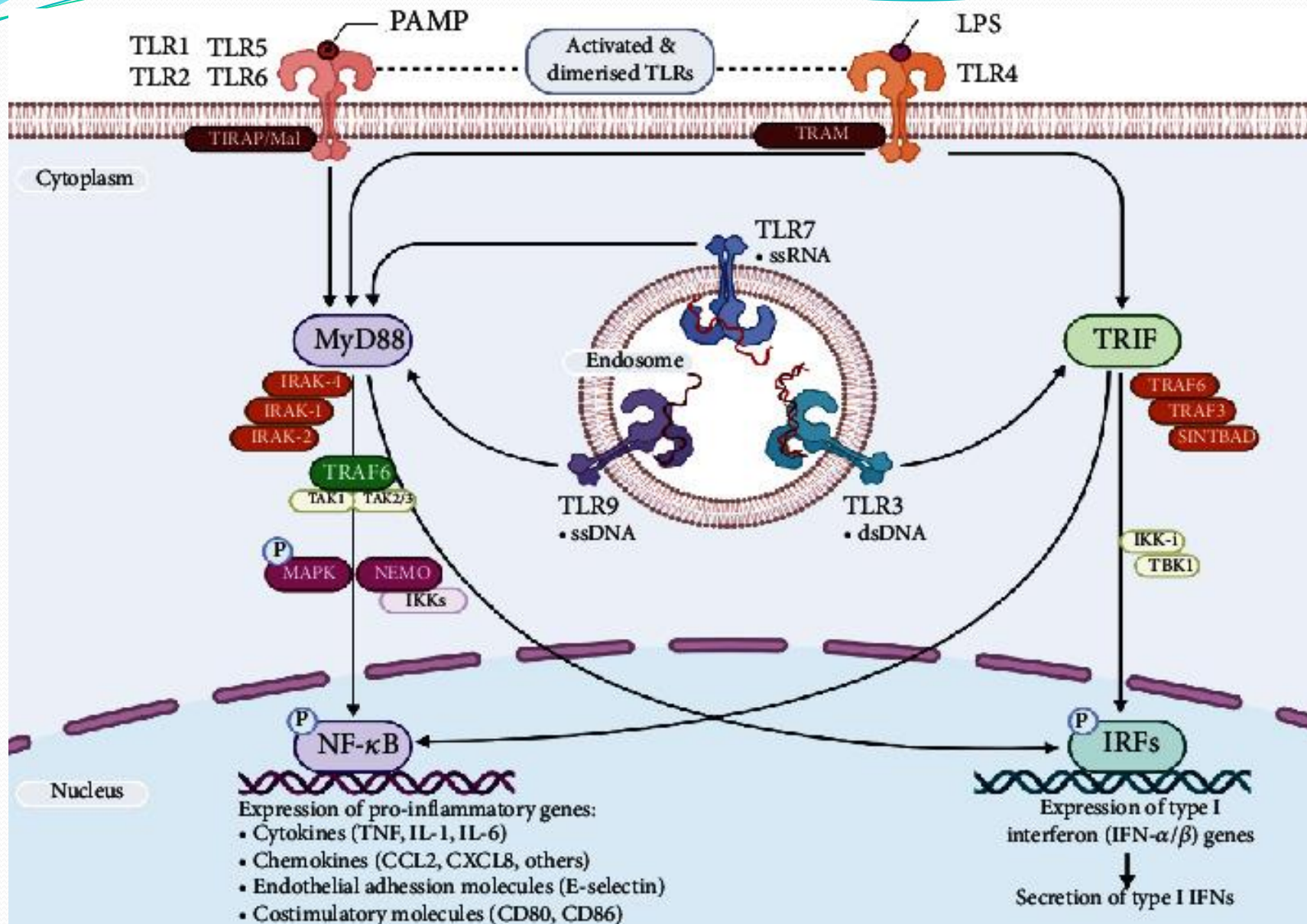
# Toll-like Receptor 1 (TLR)

- Activated TLR<sub>1</sub>-TLR<sub>2</sub> heterodimer interacts through their TIR domains with intracellular adaptor proteins, such as:
- TIR domain-containing adaptor protein (TIRAP);
- Myeloid differentiation primary response 88 protein (MyD88);
- Forming the so-called “Myddosome” complex



# Toll-like Receptor 1 (TLR)

- Interaction of TLR<sub>1</sub>-TLR<sub>2</sub> heterodimer with MyD88 and TIRAP adaptor proteins activate a cascade involving:
- The kinase complexes TRAF6/TAK<sub>1</sub> and then MAPK and IKK/NEMO, which in turn activate:
- The transcription factors AP<sub>1</sub> and NF-κB, which ultimately leads to the:
- Transcription of inflammatory cytokines genes and Type I Interferons, respectively



# Bibliography

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**THANKS!!!**