# PPARγ SIGNALLING IN VIRUS-INDUCED RESPIRATORY DISEASES: MODE OF ACTION NETWORKING

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## INTRODUCTION & AIMS

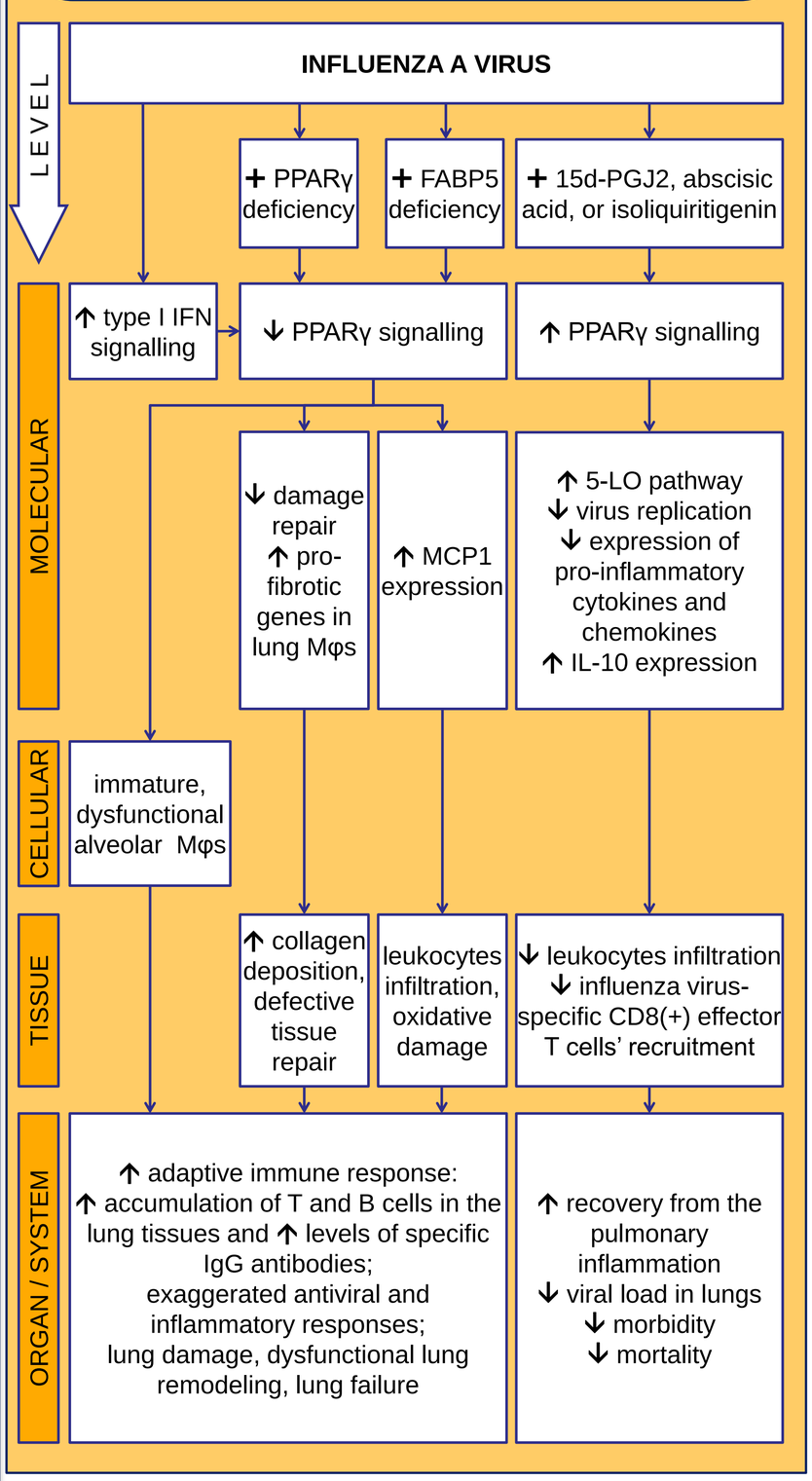
- The peroxisome proliferator-activated receptor γ (PPARγ) is a key regulator of inflammatory responses and is ubiquitously expressed in many tissues and organs including lung. Several studies were reported in the last two decades pointing out the role of PPARγ signalling in respiratory viral infections.
- The aim of this study was development of mode of action networks, reflecting the relationships between the progression or alleviation of virus-induced respiratory diseases and PPARγ activity or PPARγ expression levels.

## DATA & METHODS

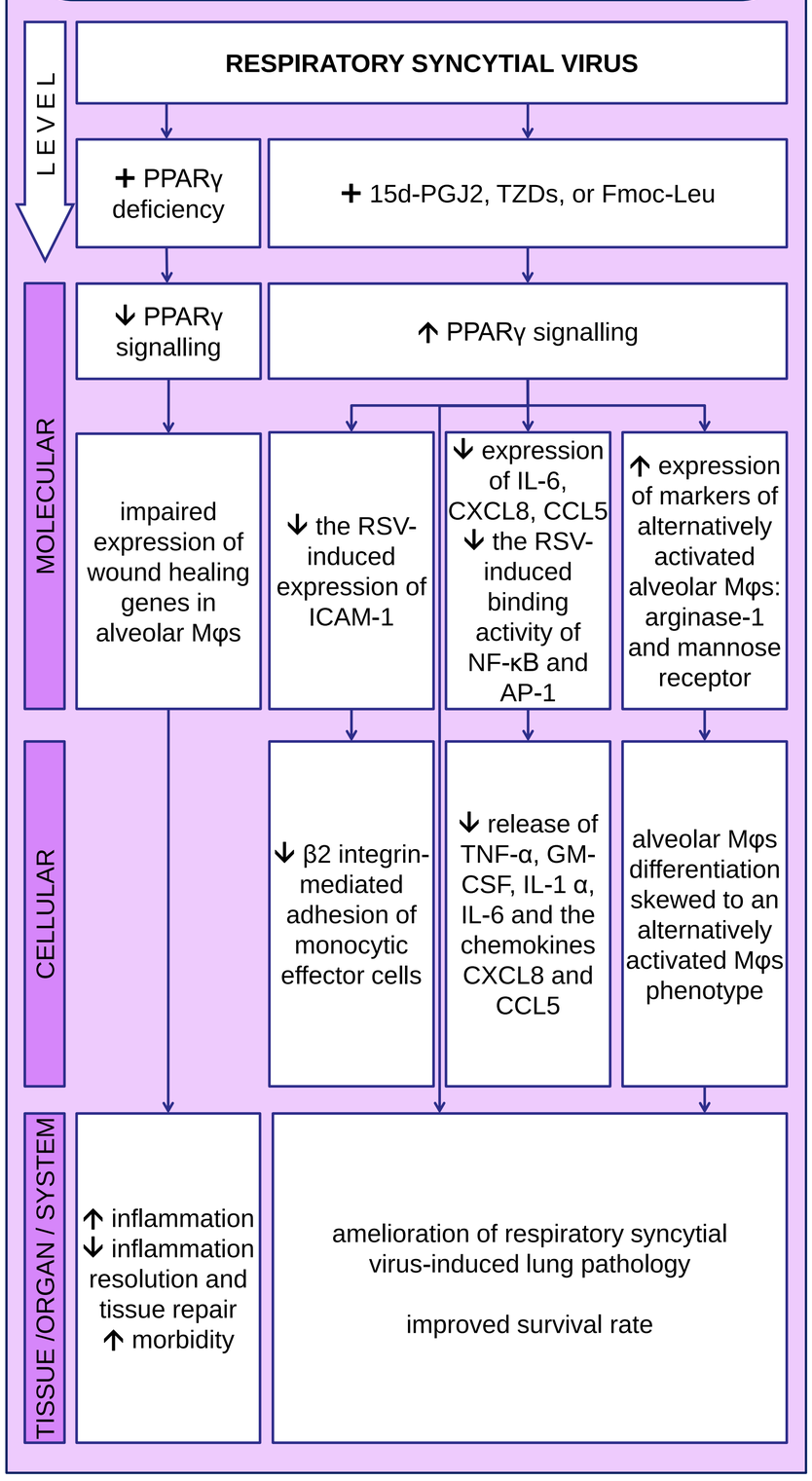
- The NIH PubMed and PubChem systems (https://www.ncbi.nlm.nih.gov/) were searched for available experimental evidence supporting PPARγ targeting in virus-induced pulmonary disorders. An initial pool of 31 publications was processed to select 19 relevant papers for a detailed analysis and data extraction.
- The mode of action networking approach was then applied to link the observed biological effects associated with signalling pathways and biomarkers of relevance at different levels of biological organisation.

## RESULTS: MODE OF ACTION NETWORKS

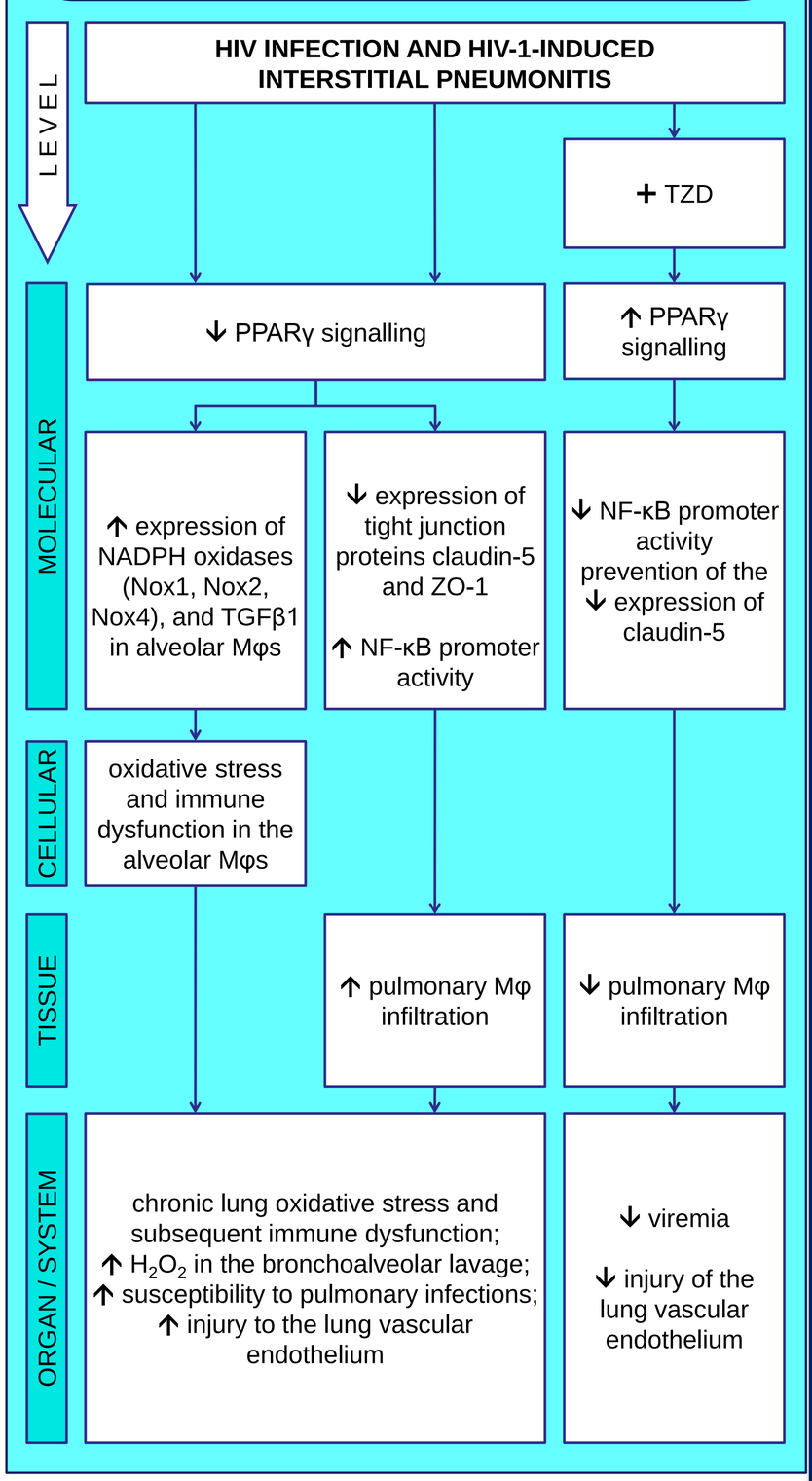
### 1. PPARγ AND INFLUENZA A VIRUS




### 2. PPARγ AND RESPIRATORY SYNCYTIAL VIRUS




### 3. PPARγ AND HIV-INDUCED RESPIRATORY DISORDERS




***Symbols and abbreviations:*** ↑ – increased; ↓ – decreased; + – additional factor (genetic, chemical) to the disease state; 15d-PGJ2 – 15-deoxy-$\Delta^{12,14}$-prostaglandin J2; 5-LO – 5-lipoxygenase; AP-1 – activation protein-1; CD8(+) effector T cells – cytotoxic MHC class I-restricted T lymphocytes; CCL5 – chemokine ligand 5; CXCL8 – IL8 or chemokine (C-X-C motif) ligand 8; FABP5 – fatty acid binding protein 5; Fmoc-Leu – N-(9-fluorenylmethoxycarbonyl)-L-leucine; GM-CSF – granulocyte macrophage colony-stimulating factor; ICAM-1 – intercellular adhesion molecule-1; IFN – interferon; IL – interleukin; MCP1 – monocyte chemotactic protein 1; Mφ – macrophage; NF-κB – nuclear factor κ light chain enhancer of activated B cells; TGFβ1 – transforming growth factor β1; TNF-α – tumor necrosis factor-α; TZD – thiazolidinedione; ZO-1 – zonula occludens-1, tight junction protein-1.

## CONCLUSIONS

- Three **mode of action networks** were outlined, linking **PPARγ modulation to pulmonary diseases induced by influenza A virus, respiratory syncytial virus, and HIV infection**. Multiple levels of biological organisation were discriminated in the developed networks to reflect known molecular, cellular, tissue, organ and system effects.
- The reported results allow for a better understanding of the potential role of PPARγ in virus-induced pulmonary pathologies.
- The proposed mode of action networks present a **mechanistically justified basis for subsequent *in silico* drug design studies focused on PPARγ-targeting in virus-induced respiratory diseases**.

## ACKNOWLEDGEMENTS

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