Role of Peroxisome proliferator-activated receptors (PPARs) in autoimmunity, immunocompromised, and infectious states: a Review

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Introduction

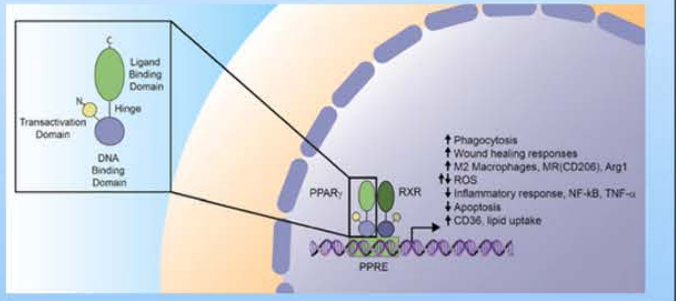
- Peroxisome proliferator-activated receptors (PPARs) are a family of nuclear receptors that activate a large array of genetic pathways.
- Different subtypes, including α, β, and γ1, γ2, and γ3
- We continue to learn more about the involvement of PPARs in immune modulation.

Autoimmunity

- myocarditis and PPAR-α may play a more critical role after all
- **Allergic rhinitis:** type II immune responses in allergies (and nematode infections) are promoted by PPAR-γ[1]; polymorphisms affect symptom severity[2]
- **T1DM:** PPAR antagonists were shown to reduce the risk of development of t1d in genetically predisposed line NOD[3]

Immunodeficiency

- **HIV** have decreased PPAR-γ expression and increased NADPH oxidases leading to enhanced oxidative stress
- impairment of the alveolar macrophages' ability to phagocytize and clear infection in the alveolar space and increased risk for lung infections.



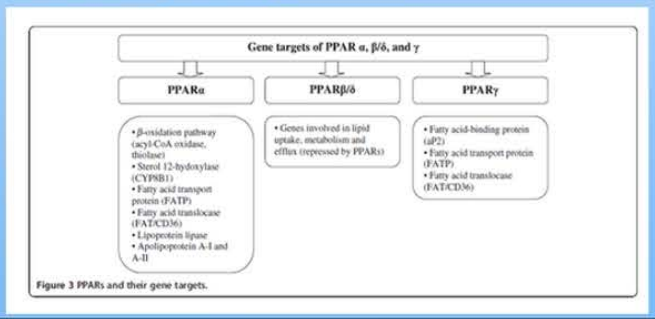


Figure 3 PPARs and their gene targets.

Pharmacology

- Treatment of M.tb infected cells with Vitamin B1 showed increased expression levels of CD86 and MHC-II, but decreased expression levels of CD206[4]
- Treatment with PPAR-γ agonist has been shown to attenuate the biofilm formation via the induction of paraoxoanse-2 (PON-2), an enzyme that degrades QS molecules involved in biofilm formation[5, 6]

Infections

- **Influenza**: PPAR-γ decreases fibrotic remodeling and inflammation, and promotes host recovery
- **TB**: PPAR-γ activation plays a role through induction of IL-10 and repression of pro-inflammatory cytokines; PPAR-α upregulates and translocates TFEB (Transcription factor EB) to the nucleus to perform its downstream effects of lysosomal biogenesis and autophagosomal antimicrobial responses against M.tb[7, 8]
- **Pseudomonas aeruginosa** (PA) infection: PPAR-α prevents excessive inflammatory response to PA infection by controlling NLP3; also has an inhibitory effect on TLR4, which recognizes pathogens and activates pro-inflammatory cytokines[9, 10]

Conclusion

- Further understanding PPARs upstream pathways and interactions can contextualize pathophysiology in immunocompromised states
- There is a relationship between PPARs and infections
- Pharmacological evidence targeting these PPARs is prevalent to accelerate clearance of these pathogens but also assist in pharmacologic therapy for autoimmunity and immunocompromised states