BEYOND THE SKIN: TRYPTOPHAN REROUTING IN PSORIASIS

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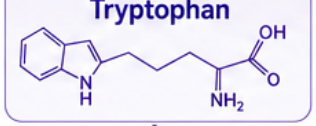
1 TRYPTOPHAN METABOLISM AND KYNURENNASE DYSREGULATION

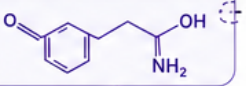
Essential Amino Acid

Tryptophan



IDO
(Indoleamine 2,3-dioxygenase)

L-Kynurenine



KYNU
(Kynureninase)

PSORIATIC DEFECT:
Kynureninase (KYNU) Overexpression

Rapid depletion of kynurenine before it can activate AhR

Kynurenic Acid
(KYNA)

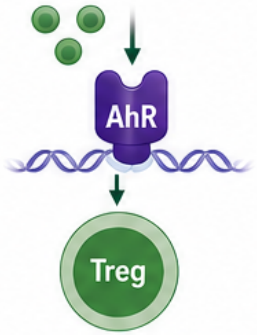


Kynurenine and KYNA are endogenous agonists of the Aryl Hydrocarbon Receptor (AhR)

2 T-CELL DIFFERENTIATION: Th17 vs. Treg BALANCE

PHYSIOLOGIC CONDITION (Healthy Skin)

Stable kynurenine levels activate AhR

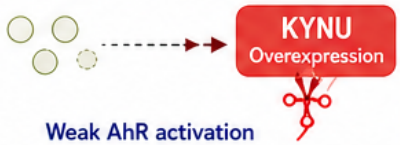


FoxP3+ Regulatory T cells

IMMUNE BRAKE
Suppresses excessive inflammation and maintains immune balance

PSORIASIS (Active Lesional Skin)

Kynureninase overexpression rapidly depletes kynurenine



Weak AhR activation



Treg (Impaired)

Th17 (Pathogenic)

↑ IL-17, IL-22
Drives inflammation

LOSS OF IMMUNE BRAKE
Decreased Treg generation + Increased Th17 differentiation → Chronic inflammation

3 DOWNSTREAM CONSEQUENCES IN PSORIASIS

↑ IL-17 and IL-22
Promote keratinocyte proliferation, recruitment of immune cells, and sustained inflammation

Keratinocyte Hyperproliferation and Barrier Dysfunction
Leads to psoriatic plaque formation

Oxidative Stress and Mitochondrial Dysfunction
Further amplify inflammatory signaling and tissue damage

Neuroimmune Connections
Altered tryptophan metabolism and reduced serotonin availability may contribute to depression and anxiety in psoriasis

4 MODIFIABLE INFLUENCES

NUTRITIONAL FACTORS (DIRECTLY LINKED)

Trp · B6 · B3 (Niacin)

- Tryptophan intake: substrate availability
- Vitamin B6: cofactor for kynurenine pathway enzymes
- Niacin (B3): influences tryptophan use for NAD⁺ synthesis vs. other metabolic pathways

IMMUNOMETABOLIC MODIFIERS (MAY REDUCE INFLAMMATION)

D · Zn

- Vitamin D: modulates immune responses and may lower IDO activation
- Zinc: supports immune regulation and antioxidant defenses

KEY TAKEAWAY

In psoriasis, overexpression of kynureninase (KYNU) depletes kynurenine, weakening AhR activation. This impairs Treg generation and shifts the immune balance toward pathogenic Th17 cells, driving IL-17 and IL-22 production, skin inflammation, and systemic effects. Targeting this pathway and supporting key nutritional and lifestyle factors may offer complementary strategies for disease control.

IDO = indoleamine 2,3-dioxygenase *KYNU = kynureninase* *AhR = aryl hydrocarbon receptor* *KYNA = kynurenic acid* *Treg = regulatory T cell* *Th17 = T helper 17 cell*