Appendix A: Table explaining mechanisms involved in chronic itch in psoriasis and the novel finding of a neuroimmune itch loop.

Table 1: Summary of key mechanisms involved in chronic itch in psoriasis.

Mechanism	Description	Key players	References
Neuroimmune interactions	Interactions between immune cells and sensory neurons contribute to itch perception.	IL-31, IL-33, TSLP, Sensory neurons	[6,7,9-11]
JAK-STAT pathway	Mediates pruritogenic cytokine effects on sensory neurons; JAK inhibitors target this pathway.	IL-31, JAK-STAT pathway	[12-14]
Peripheral sensitization	Exaggerated itch response due to sensitized sensory neurons in psoriatic skin.	NGF, TRPV1, TRPA1	[15-17]
Skin barrier dysfunction	Compromised skin barrier in psoriasis leads to increased penetration of irritants.	Ceramides, PAR-2, Filaggrin	[18-24]
Central sensitization	Heightened responsiveness of CNS neurons to itch stimuli.	Substance P, Spinal Cord, Cortex	[25-33]

This table provides an overview of the primary biological mechanisms responsible for chronic itch in psoriasis. Each row identifies a specific mechanism, describes its role in the sensation of itch, and lists the key molecular players or pathways involved. The references included offer a detailed foundation and support for the mechanisms outlined, drawing from recent research and clinical studies. IL: Interleukin, TSLP: Thymic stromal lymphopoietin, NGF: Nerve growth factor, TRP: Transient receptor potential, PAR-2: Protease-activated receptors, JAK: Janus kinase, CNS: central nervous system

Table 2: Proposed neuroimmune itch loop model.

Component	Description	Interaction details	References
Immunogenic activation	Cytokines from immune cells (e.g., IL-31) activate sensory neurons.	IL-31, IL-33, TSLP, Substance P	[60,61]
Nerve sensitization	Activated sensory neurons release peptides like substance P, perpetuating itch.	Sensory neuron activation, Hyperactivity	[60-62]
Chronic itch maintenance	Continuous cycle of immune activation and sensory neuron sensitization.	Persistent pruritus cycle	[63]
Therapeutic implications	Targeting the neuroimmune itch loop can disrupt chronic itch cycle.	JAK inhibitors, Neuromodulators	[64,65]

This table illustrates the proposed neuroimmune itch loop model, which integrates various components involved in the chronic itch cycle in psoriasis. It details each component's role and interactions within the model, explaining how these elements work together to perpetuate the itch sensation. The references cited provide foundational research and theoretical support for the model. IL: Interleukin, TSLP: Thymic stromal lymphopoietin, JAK: Janus kinase