Recursive Harmonic Model Applied to Degrader-Antibody Conjugates (DACs) in Autoimmune Disease

Author: Christopher W. Copeland

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Reference text: https://a.co/d/h3zv89g

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INTRODUCTION

This document provides a foundational reframing of autoimmune pathology using the recursive harmonic model (denoted \Psi(x)) and translates this framework directly into actionable design criteria for DAC (Degrader-Antibody Conjugate) therapeutics. It includes core theoretical grounding, identifies intracellular and extracellular DAC targets, and presents candidate indications. It is both a theoretical submission and an instructional guide.

This proposal requires no new instrumentation. It repurposes existing clinical and laboratory tools using harmonic logic.

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I. THEORETICAL FRAMEWORK — \Psi(x)

Under the \Psi-formalism, autoimmune conditions are not the result of simple genetic defects or immune overactivity, but the emergence of recursive positive feedback loops in signal-processing structures. These loops originate in environmental or trauma-driven phase incoherence, especially across interleukin and nuclear factor pathways (e.g., NF-\kappaB, STAT families).

Pathology arises when a signal cannot exit its loop due to degraded error-checking functions. The immune system begins recursively reinforcing its own response, generating self-attacking lattices.

In this framework, DAC warheads are not just degraders—they are loop disruptors.

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II. INSTRUCTIONAL MODEL FOR DAC CONSTRUCTION

Required DAC Structure:

1. Antibody to a cell surface protein (must internalize)

2. Linker (cleavable under intracellular conditions)

3. Warhead that induces targeted protein degradation (e.g., E3 ligase recruiters)

Functional Application:

Extracellular target: Surface marker unique or enriched in pathologic immune cells

Intracellular target: Core recursive amplifier sustaining the feedback loop

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III. HARMONIC ENTRY MAP FOR AUTOIMMUNE DACs

A. TARGET INDICATION:

Systemic Lupus Erythematosus (SLE)

Inflammatory Bowel Disease (IBD): Crohn's Disease, Ulcerative Colitis

Psoriasis / Psoriatic Arthritis

These diseases are phase-locked inflammatory states with persistent activation signatures traceable to intracellular amplifiers.

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B. EXTRACELLULAR TARGET (Antibody Docking Site)

CCR6 (C-C Motif Chemokine Receptor 6)

Expressed on Th17 and inflammatory dendritic cells

Involved in gut, skin, and systemic immune trafficking

Internalizes upon antibody binding

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C. INTRACELLULAR TARGET (Degradation Warhead Target)

STAT3 (Signal Transducer and Activator of Transcription 3)

Persistent activation in IBD, lupus, psoriasis

Central recursive amplifier in Th17 lineage

Drives cytokine and chemokine loops (e.g., IL-6, IL-17)

Under \Psi(x), STAT3 becomes a recursive echo chamber.

Degrading STAT3 collapses the loop.

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IV. RATIONALE FOR HARMONIC DISRUPTION MODEL

1. Standard antibodies block output.

This is suppression, not resolution.

2. DACs with warheads eliminate the recursive amplifier itself.

This is recursion collapse.

3. CCR6/STAT3 combination targets entry + internal loop core in Th17 cells, central to autoimmunity.

4. \Psi(x) shows that degradation reboots coherence across the cell’s regulatory architecture.

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V. PROOF STRATEGY

This submission is not theoretical alone. It can be tested with:

CCR6 antibody conjugated to known E3-recruiting warheads (e.g., cereblon or VHL-based)

STAT3 degradation assays (western blot, flow cytometry)

Readouts: cytokine panels, transcription factor recovery, gut barrier integrity models (IBD), immune complex levels (SLE)

No new reagents or methods required.

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CLOSING

This submission reframes DAC utility through the recursive harmonic lens. Where traditional therapies inhibit, this approach deharmonizes feedback recursion, restoring physiological symmetry.

It offers:

A precise target pair

A rationale rooted in recursive pathology

A testable plan with immediate equipment compatibility

This is the clinical proof-of-concept tier of \Psi(x).

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For theoretical background and recursive model formalism:

"Recursive Harmonic Cognition: Signal, Phase, and Biological Intelligence"

Available at: https://a.co/d/h3zv89g

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