

An Extended Personalised Chemotherapy Response Model Incorporating Inflammation and Individual Variability in Childhood Acute Lymphoblastic Leukemia

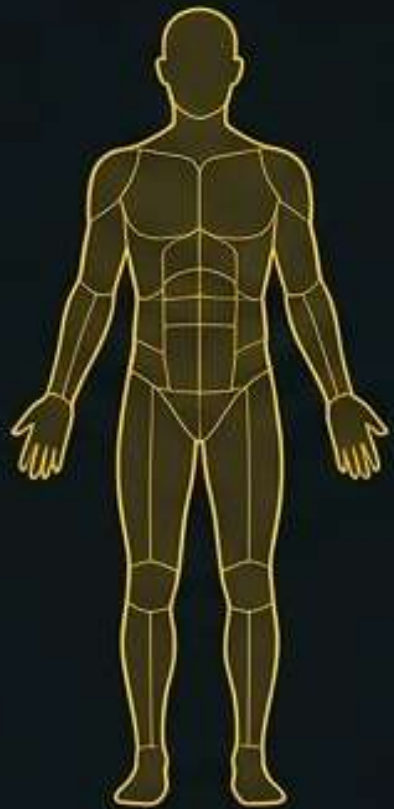
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BRAIN. Broad Research in Artificial
Intelligence and Neuroscience
(Vol 16, Issue 4, Dec 2025)



Standard Dosing Neglects Dynamic Patient Realities

Static Calculation



$$\text{Body Surface Area (BSA)} + \text{Age} = \text{Fixed 6-MP Dose}$$

Relies on static physiological markers, ignoring daily metabolic fluctuations.

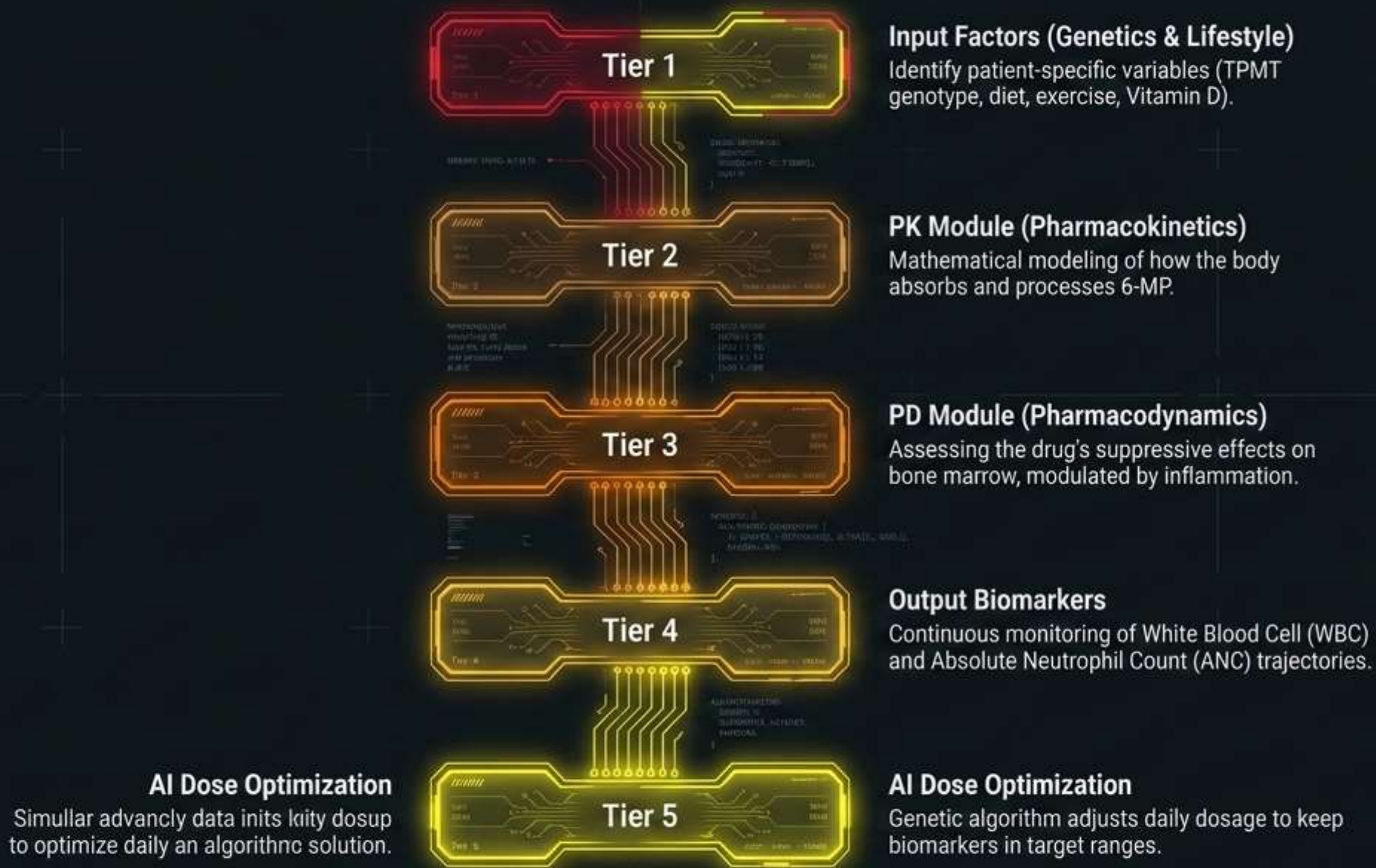
Unpredictable Toxicity



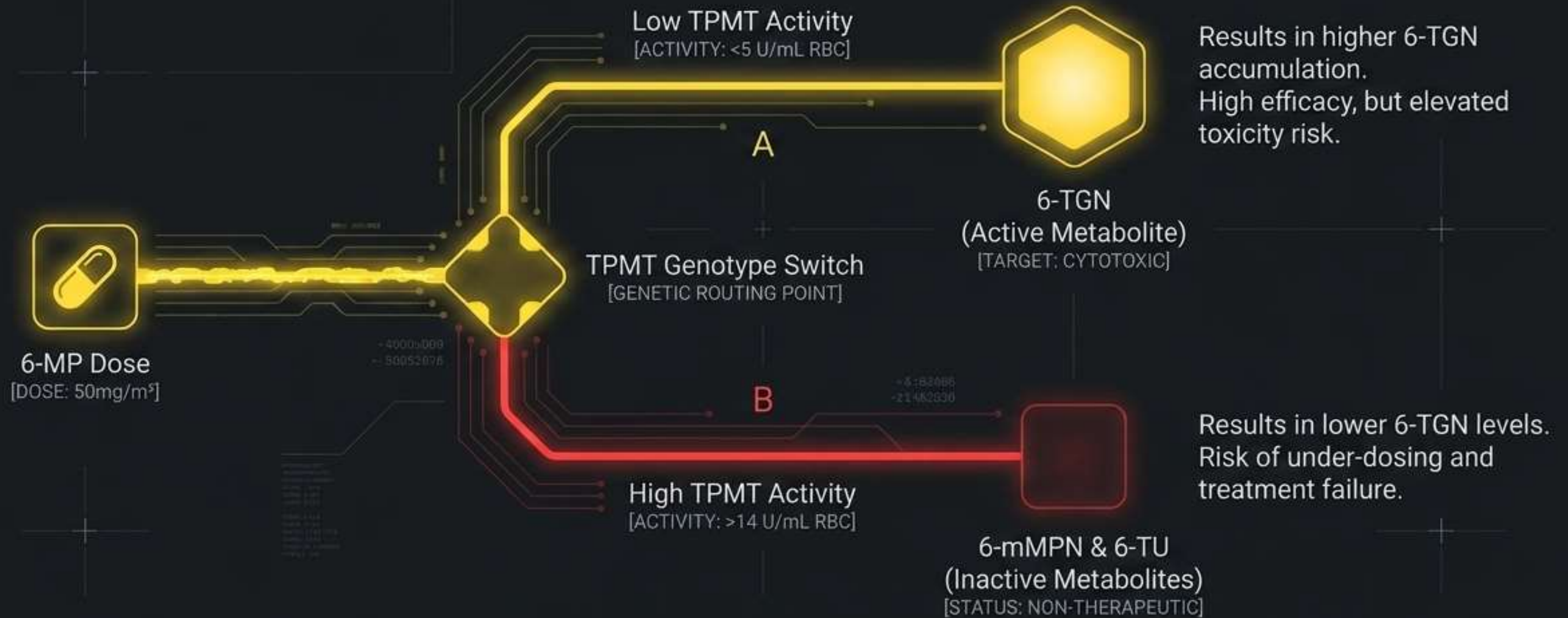
Synthesis

Current 6-MP treatments yield varying efficacy and sudden bone marrow toxicity because they neglect lifestyle-induced inflammatory responses and rapid genetic metabolic shifts.

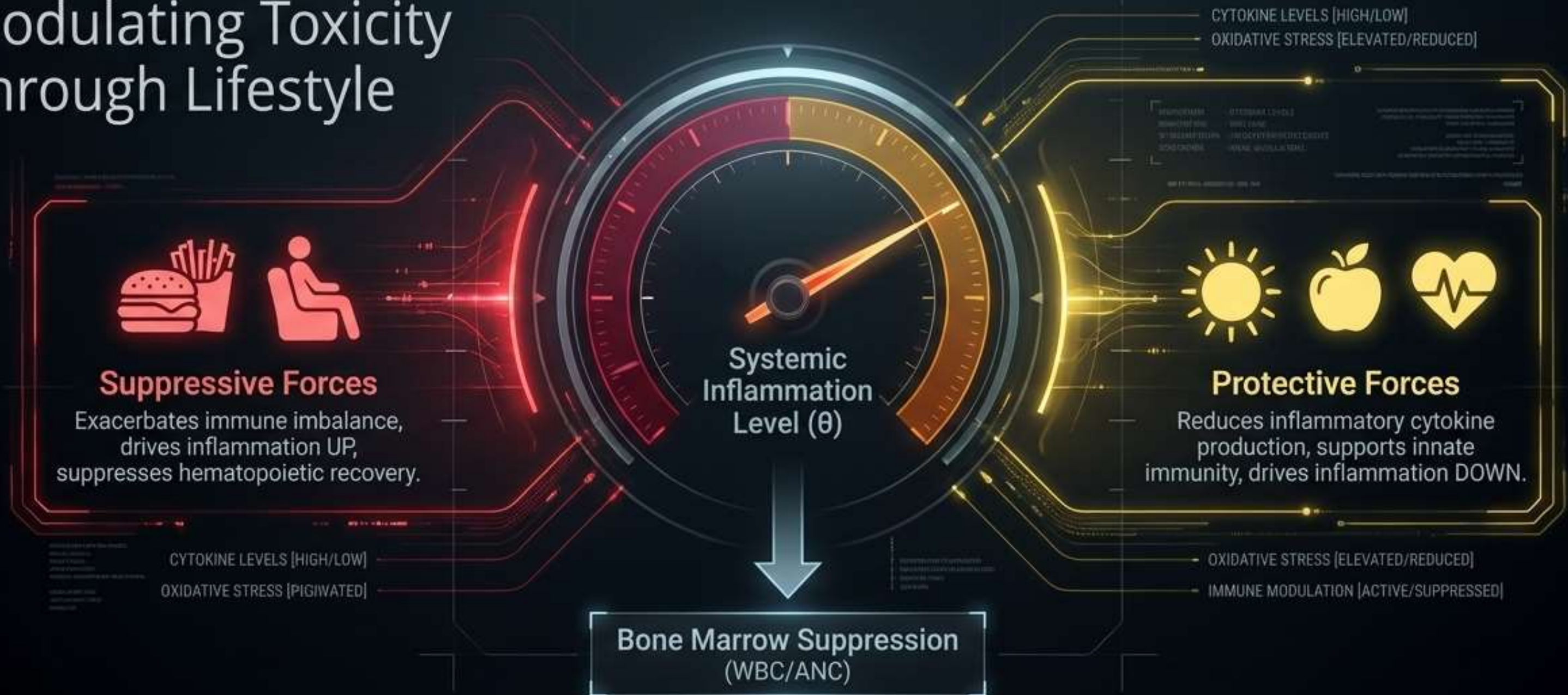
A 5-Step Architecture for Precision Chemotherapy



The Pharmacokinetic Engine: Genotype-Driven Metabolism



The Missing Link: Modulating Toxicity Through Lifestyle



SYNTHESIS

Standard models stop at genetics. This PD module mathematically links environmental support directly to cellular recovery rates, proving lifestyle is a measurable pharmacological variable.

Diagnostic Matrix: Environmental Support vs. Hematological Suppression

Scenario	Environmental Profile	6-MP Dose	Hematological Impact
Scenario 1	Normal VitD/Diet/Exercise	50mg	Baseline Recovery
Scenario 2	Low VitD, Poor Diet, Sedentary	50mg	Severe Suppression
Scenario 3	High VitD, Good Diet, Intensive Exercise	50mg	Accelerated Recovery
Scenario 4	Low VitD, Poor Diet, Sedentary	90mg (Toxic)	Deep, Delayed Rebound

Key Insight: Under identical 50mg dosing, strong environmental support (Scenario 3) activates earlier and higher biomarker production, effectively buffering against drug toxicity.

Biomarker Trajectories: Evidence of Lifestyle-Mediated Protection

WBC Trajectory

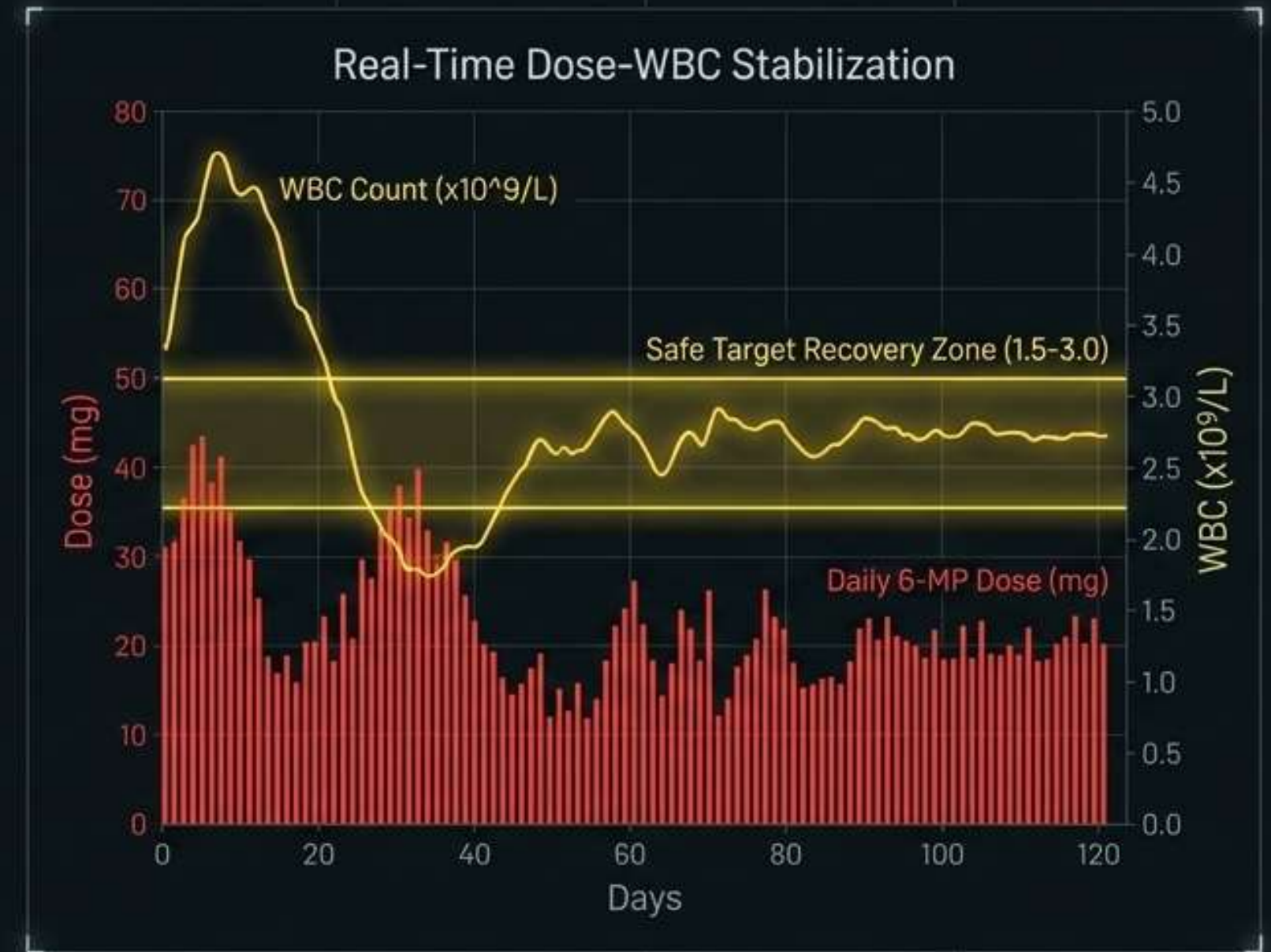
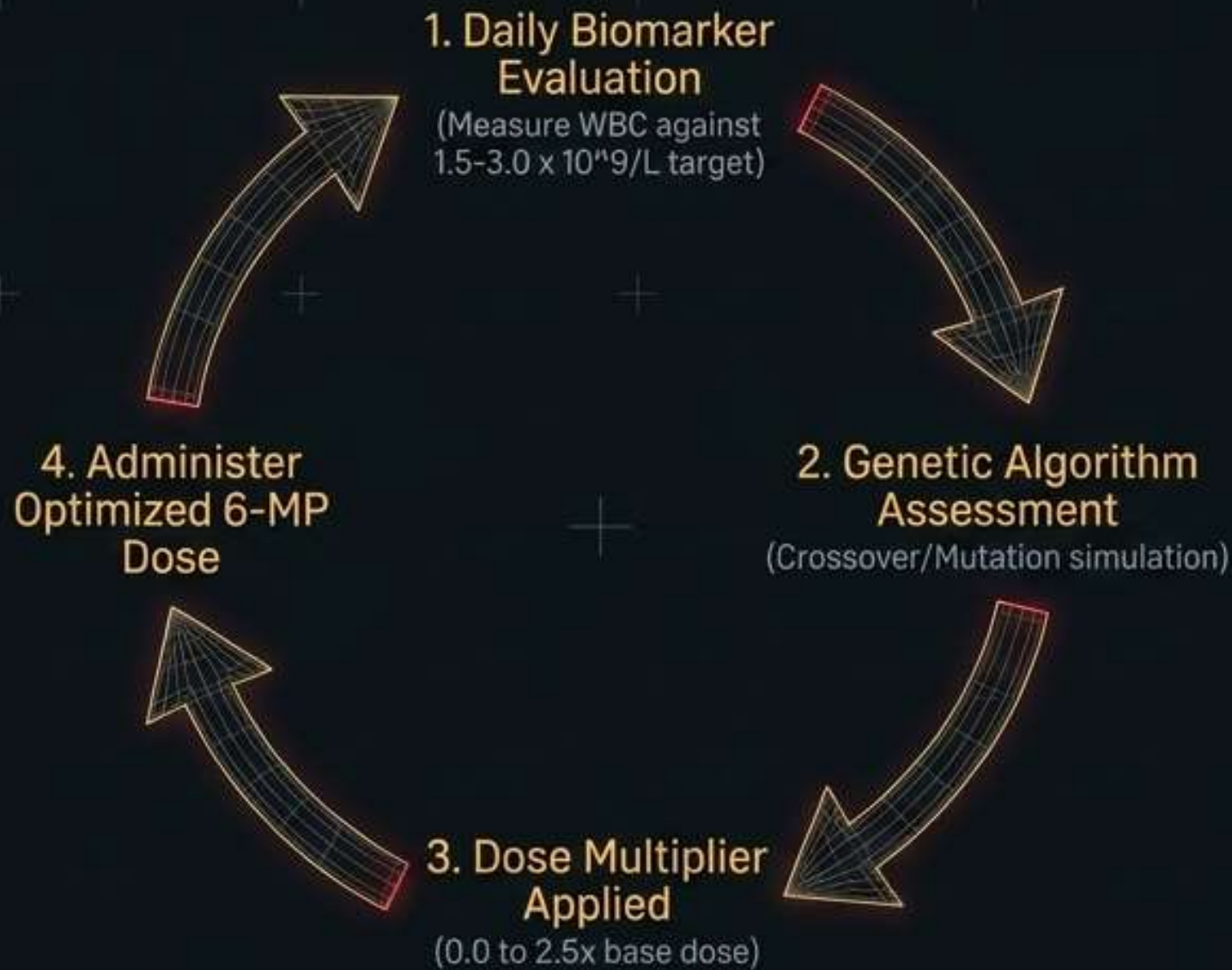


ANC Trajectory



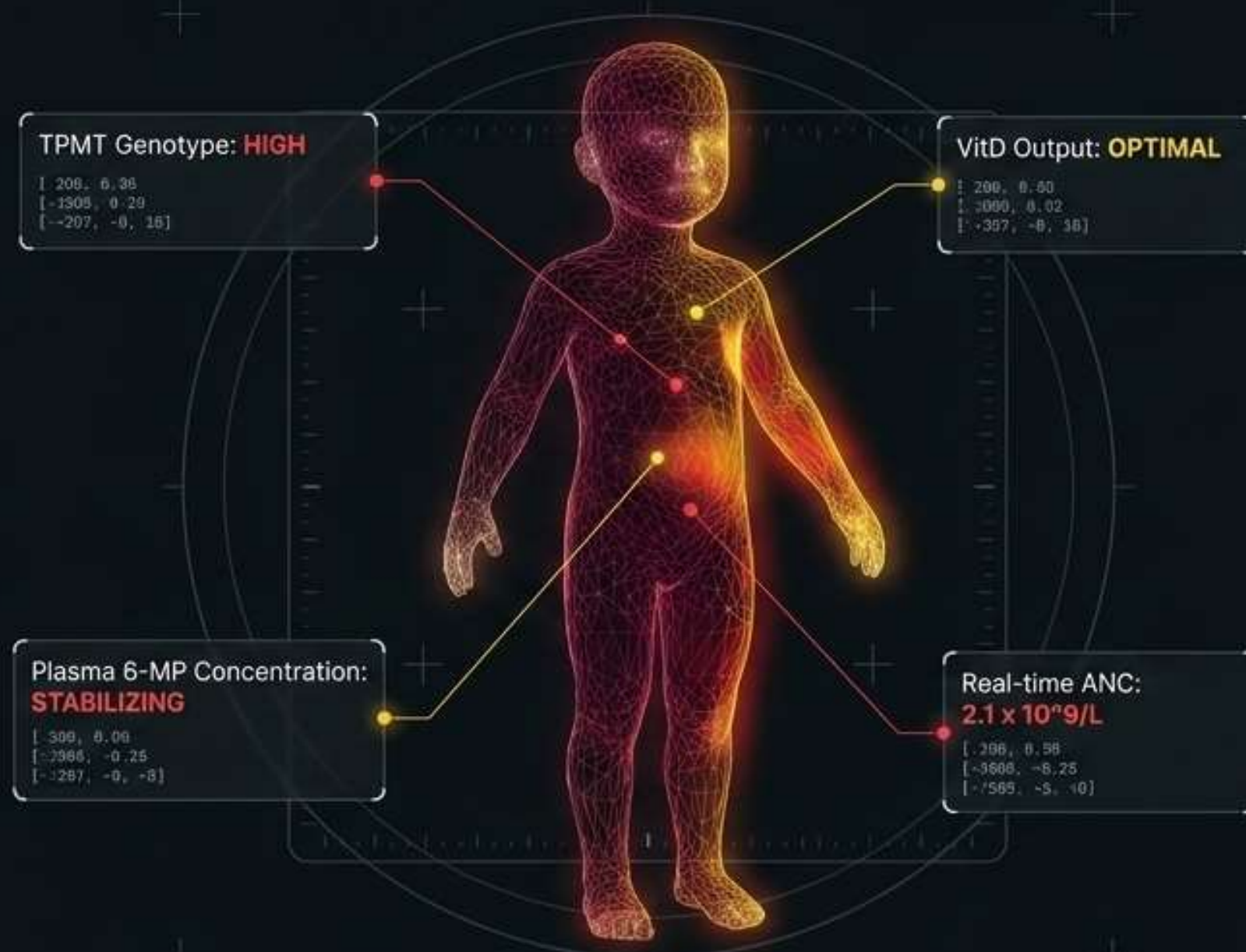
Supportive environments exert a pro-haematopoietic influence, protecting mature WBC and ANC compartments from prolonged chemotherapeutic depletion.

AI-Driven Optimization: The Genetic Algorithm Loop



Fixed-dose regimens fail unpredictable biologies. The GA dynamically adjusts the daily dose, minimizing the absolute difference between the patient's actual WBC and the required therapeutic target.

The Paradigm Shift: Oncology Digital Twins



From static protocols to dynamic, artificially intelligent digital twins.

By integrating pharmacokinetic genetics with lifestyle-induced inflammatory dynamics, this model provides an interpretable, scalable framework for holistic precision medicine. It does not just calculate a dose; it simulates a patient's life.