Predicting Cancer Pathway Shifts via Dietary Carotenoid–Mediated Retinoid Signaling: A Systems Biology Model Integrating Breast, Lung, and Leukemia With Patient-Derived Genomic Data

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Carotenoids are lipid-soluble dietary pigments and vitamin A precursors that regulate gene transcription via RARA and RXRA nuclear receptors. Retinoid signaling controls differentiation, proliferation, and apoptosis, and its dysregulation drives cancers including acute promyelocytic leukemia, breast, and lung cancers. Although carotenoid intake correlates with reduced cancer risk, the quantitative, systems-level impact on oncogenic signaling remains unclear. A computational systems biology model was developed to predict how carotenoids modulate proliferative pathways. Ordinary differential equations in Python simulated absorption, intracellular retinoic acid production, receptor activation, differentiation signaling, and MAPK/PI3K-AKT activity. Parameters were curated from biochemical literature and validated against transcriptomic datasets, including The Cancer Genome Atlas. Simulations indicate that increased carotenoid intake elevates retinoic acid, amplifies differentiation signals, and suppresses oncogenic MAPK/PI3K-AKT activity in a tissue-specific manner. A composite disease signaling index revealed protective and therapeutic thresholds—~4.5 μM in lung tissue and ~5.0 μM in leukemia—where malignant cells shift from proliferative to differentiated states, while breast tissue exhibits a graded, dose-dependent response. Sensitivity analysis highlights receptor kinetics and phosphatase regulation as key modulators. These findings establish a quantitative framework linking diet to cancer prevention and therapy through direct modulation of oncogenic signaling, providing a roadmap for tissue-specific precision nutrition strategies to complement conventional treatments.

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