Chaos in Cancer: Analyzing Network Morphology to Predict Tumor Angiogenesis using Chaos Theory

The unpredictability of tumors is a problematic barrier to developing personalized cures, and a leading cause of cancer evolution and volatility is attributed to angiogenesis. Tumor angiogenesis exploits the formation of blood vessels that provide a supportive microenvironment rich in oxygen and nutrients required for cancer survival, malignancy, and metastasis. Chaos theory examines the underlying set of patterns and deterministic laws that are highly sensitive to the initial conditions of seemly random dynamical systems not unlike the anomalous branching of angiogenesis. Can a computational network reconstruction of tumor angiogenesis using coupled morphological, genomic, and physiological parameters when applied to chaos theory determine the extent of unpredictability in tumor angiogenesis? Using Breast Imaging Reporting and Data System (BIRADS) labeled mammograms, the magnitude of chaos in breast vasculature was uniquely determined using network science analysis and feature importance to generate modified Lorenz equations, which in turn were analyzed by bifurcation diagrams, fractal dimensions, and Lyapunov Characteristic Exponents. Further, a novel network-based drug discovery pipeline with r^2 of 0.512 was tested with aromatase, and in vitro validation with P. polycephalum was also investigated. Angiogenesis breast cancer vasculature exhibited a higher Lyapunov exponent than in nontumorous vasculature. Vasculature networks with a higher number of nodes from inferred vascular sprouting, segments from preferential attachment morphology, and smaller mean mesh size from endothelial and pericyte cell interplay were the most chaotic. Additionally, the newfound positive correlation between cancer and chaos indicates underlying chaotic patterns are yet to be explored in angiogenesis. Lastly, the application of chaos theory in clinical diagnosis, angiogenesis drug discovery, and bridging biochemical and mathematical research was proposed.