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Network model explains why cancer cells use inefficient pathway to produce energy JOO SANG LEE, Department of Physics and Astronomy, Northwestern University, JOHN MARKO, Department of Molecular Biosciences, Northwestern University, ADILSON MOTTER, Department of Physics and Astronomy, Northwestern University — The Warburg effect—the use of the (energetically inefficient) fermentative pathway as opposed to (energetically efficient) respiration even in the presence of oxygen—is a common property of cancer metabolism. Here, we propose that the Warburg effect is in fact a consequence of a trade-off between the benefit of rapid growth and the cost for protein synthesis. Using genome-scale metabolic networks, we have modeled the cellular resources for protein synthesis as a growth defect that increases with enzyme concentration. Based on our model, we demonstrate that the cost of protein production during rapid growth drives the cell to rely on fermentation to produce ATP. We also identify an intimate link between extensive fermentation and rapid biosynthesis. Our findings emphasize the importance of protein synthesis as a limiting factor on cell proliferation and provide a novel mathematical framework to analyze cancer metabolism.

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