Red Blood Cell Extreme Pathways

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ABSTRACT

Extreme pathways are a mathematically defined set of generating vectors that describe the conical steady state solution space for flux distributions through metabolic networks. The extreme pathways of the well-characterized human red blood cell metabolic network were calculated and interpreted in a biochemical and physiological context. The red cell metabolic network was found to have a total of 36 Type I extreme pathways that exchange mass with the environment, one of which is the classical glycolytic pathway. These extreme pathways were divided into groups based on such criteria as their cofactor and by-product production, and carbon inputs including those that: 1) convert glucose to pyruvate, 2) interchange pyruvate and lactate, 3) produce 2,3-diphosphoglycerate that binds to hemoglobin, 4) convert inosine to pyruvate, 5) induce a change in the total adenosine pool, and 6) dissipate ATP. Furthermore, divisive hierarchical clustering was used to classify the extreme pathways in a manner that was consistent with their physiological roles. In addition, results from a full kinetic model of red cell metabolism were anticipated based solely on an interpretation of the extreme pathway structure. The extreme pathways for the red blood cell thus gave a concise representation of red cell metabolism as well as a way to interpret its metabolic physiology.