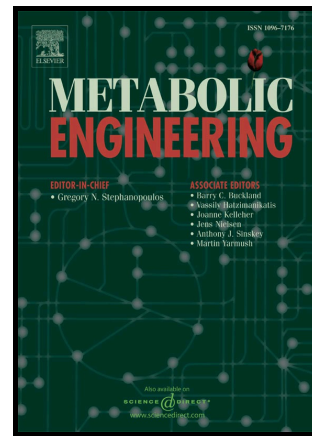


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Metabolic Flux Analyses of *Pseudomonas aeruginosa* Cystic Fibrosis Isolates

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Abstract

Pseudomonas aeruginosa is a metabolically versatile wide-ranging opportunistic pathogen. In humans *P. aeruginosa* causes infections of the skin, urinary tract, blood, and the lungs of Cystic Fibrosis patients. In addition, *P. aeruginosa*'s broad environmental distribution, relatedness to biotechnologically useful species, and ability to form biofilms have made it the focus of considerable interest. We used ¹³C metabolic flux analysis (MFA) and flux balance analysis to understand energy and redox production and consumption and to explore the metabolic phenotypes of one reference strain and five strains isolated from the lungs of cystic fibrosis patients. Our results highlight the importance of the oxidative pentose phosphate and Entner-Doudoroff pathways in *P. aeruginosa* growth. Among clinical strains we report two divergent metabolic strategies and identify changes between genetically related strains that have emerged during a chronic infection of the same patient. MFA revealed that the magnitude of fluxes through the glyoxylate cycle correlates with growth rates.

Abbreviations: CCE – Carbon Conversion Efficiency; CF – Cystic Fibrosis; EDP – Entner-Doudoroff Pathway; EMPP – Embden Meyerhof Parnas Pathway; FBA – Flux Balance Analysis; FVA – Flux Variability Analysis; HCA – Hierarchical Clustering Analysis; MFA – Metabolic Flux Analysis; OPPP – Oxidative Pentose Phosphate Pathway; PCA – Principal Component Analysis; SS_{res} – sum of squared residuals; TCA – Tricarboxylic acid cycle

Keywords: Cystic Fibrosis, Entner-Doudoroff, Flux Balance Analysis, Glyoxylate Cycle, Metabolic Flux Analysis, *Pseudomonas aeruginosa*

1. Introduction

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