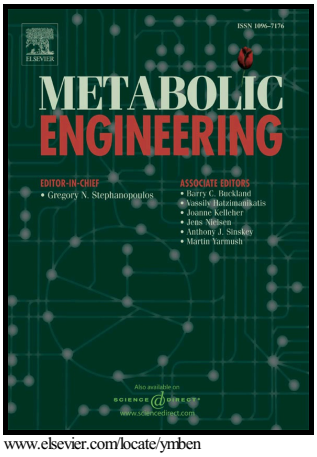

www.elsevier.com/locate/ymben

Metabolic Flux Analyses of *Pseudomonas aeruginosa* Cystic Fibrosis Isolates

Michael J. Opperman, Yair Shachar-Hill

PII: S1096-7176(16)30125-2
DOI: http://dx.doi.org/10.1016/j.ymben.2016.09.002
Reference: YMBEN1148

To appear in: *Metabolic Engineering*

Received date: 22 March 2016
Revised date: 7 June 2016
Accepted date: 11 September 2016

Cite this article as: Michael J. Opperman and Yair Shachar-Hill, Metabolic Flux Analyses of *Pseudomonas aeruginosa* Cystic Fibrosis Isolates, *Metabolic Engineering,* http://dx.doi.org/10.1016/j.ymben.2016.09.002

Metabolic Flux Analyses of Pseudomonas aeruginosa Cystic Fibrosis Isolates

Michael J. Opperman[1,2], Yair Shachar-Hill[1*]

[1]Department of Plant Biology, Michigan State University, 612 Wilson Road, East Lansing, MI 48824, USA
[2]Cell and Molecular Biology graduate program, 2240A Biomedical Physical Sciences Building, East Lansing Michigan State University 48824, USA

[*]Corresponding author: yairhill@msu.edu

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 ^{13}C 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