Glucose metabolism in the antibiotic producing actinomycete Nonomuraea sp ATCC 39727

The actinomycete Nonomuraea sp. ATCC 39727, producer of the glycopeptide A40926 that is used as precursor for the novel antibiotic dalbavancin, has an unusual carbon metabolism. Glucose is primarily metabolized via the Entner-Doudoroff (ED) pathway, although the energetically more favorable Embden-Meyerhof-Parnas (EMP) pathway is present in this organism. Moreover, Nonomuraea utilizes a PPI-dependent phosphofructokinase, an enzyme that has been connected with anaerobic metabolism in eukaryotes and higher plants, but recently has been recognized in several actinomycetes. In order to study its primary carbon metabolism in further detail, Nonomuraea was cultivated with [1-C-13] glucose as the only carbon source and the C-13-labeling patterns of proteinogenic amino acids were determined by GC-MS analysis. Through this method, the fluxes in the central carbon metabolism during balanced growth were estimated. Moreover, a shift in the label incorporation pattern was observed in connection with phosphate limitation and increased antibiotic productivity in Nonomuraea. The shift indicated an increased flux through the EMP pathway at the expense of the flux through the ED pathway, a suggestion that was supported by alterations in intracellular metabolite levels during phosphate limitation. In contrast, expression levels of genes encoding enzymes in the ED and EMP pathways were not affected by phosphate limitation.

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