

# Comparison of the Small Molecule Metabolic Pathways in *Escherichia coli* and *Saccharomyces cerevisiae*:

Non-orthologous displacements, Gene Fusions and Protein Interactions

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## ABSTRACT

We determined the domain structure and protein families of the enzymes in small molecule metabolism in *Escherichia coli* and *Saccharomyces cerevisiae* (yeast) using a combination of structural assignments and sequence comparisons. This allowed us to compare the evolutionary relationships between the proteins in the two organisms to determine the extent of conservation in pathways that are present in both yeast and *E. coli*. Among the 48 pathways and 232 enzymes shared between the two organisms, we identified twelve cases of non-orthologous displacement, where the enzymes carrying out identical functions belonged to entirely different protein families. Among the majority of enzymes which are conserved, we studied whether the subunit composition and gene structure were the same, looking for cases of gene fusions or fissions. We found fourteen cases where there is a multifunctional enzyme in one organism carrying out functions that are catalysed by several proteins in the other organism. Ten of the multifunctional enzymes were in the eukaryote yeast as expected, but another four of these multifunctional enzymes were in *E. coli*. In multifunctional enzymes, one of the advantages is the co-localisation of multiple active sites. In order to gain an insight into the role of protein interactions in metabolic pathways, we analysed the experimental data on protein-protein interactions available for the enzymes in yeast. In agreement with the small number of gene fusions identified in yeast, the extent of physical protein interactions between the enzymes is also limited, and most of the cases observed are between enzymes that are within a few reaction steps of each other within a pathway.