P011 The Mitochondrial Pyruvate Carrier

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The ability of cells to transport pyruvate across the inner mitochondrial membrane is essential for a variety of metabolic processes, from the funnelling of the products of glycolysis to the TCA cycle, to supplying substrate to pyruvate carboxylase for gluconeogenesis, yet while a considerable body of literature has been assembled about this process (including inhibitor and substrate specificity, tissue expression levels and kinetic properties) the carrier protein involved has long remained unidentified. By screening a bank of deletion mutants for loss of inhibitor-sensitive mitochondrial pyruvate uptake, work in our lab has identified the YIL006w gene as the carrier responsible for pyruvate transport in the yeast *Saccharomyces cerevisiae*. YIL006w encodes a protein of 41.9 kDa that is a member of the mitochondrial carrier family (MCF). YIL006w possess an N-terminal extension of ≈66αα of unknown function that is not uncommon among yeast MCF members, but the sequence from residue 67 onwards shares significant protein-level homology with the yeast mitochondrial flavin carrier (FLX1) and the unannotated YEL006w gene, and with the human mitochondrial folate carrier, and two as yet-unannotated human genes (accession nos. NP_115691 and NP_060625).

We hope to use combinations of heterologous gene expression and gene silencing to further characterise the yeast carrier and to identify the human homologue of this carrier protein.