

Vitamin B6 biosynthesis: mechanistic insights derived from structural and functional aspects of the participating proteins.

Teresa B. Fitzpatrick

University of Zurich, Institute of Plant Biology, 8008 Zurich, Switzerland

Vitamin B6 is well known in its biochemically active form as pyridoxal 5'-phosphate (PLP), an essential cofactor of numerous metabolic enzymes. The vitamin is also implicated in numerous human body functions ranging from modulation of hormone function to its recent discovery as a potent antioxidant. Its *de novo* biosynthesis occurs only in bacteria, fungi and plants, making it an essential nutrient in the human diet. Despite its paramount importance, its biosynthesis was predominantly investigated in *Escherichia coli*, where it is synthesized from the condensation of deoxyxylulose-5-phosphate and 4-phosphohydroxy-L-threonine catalysed by the concerted action of PdxA and PdxJ. However, it has now become clear that the majority of organisms capable of producing this vitamin do so via a different route, utilizing ribose 5-phosphate, glyceraldehyde 3-phosphate and glutamine. This alternative pathway is characterized by the presence of two genes, *Pdx1* and *Pdx2*. Their discovery has sparked renewed interest in vitamin B6 and numerous studies have been conducted over the last few years to characterise the new biosynthesis pathway. Indeed, enormous progress has been made in defining the nature of the enzymes involved and important insights have been provided into their mechanisms of action, where Pdx1 and Pdx2 function together as a glutamine amidotransferase now known as PLP synthase. The structure of a bacterial PLP synthase complex has been solved and displays an ornate architecture made up of 24 subunits, two hexameric rings of 12 Pdx1 subunits to which 12 Pdx2 subunits attach, with the glutaminase and synthase active sites remote from each other. The multiple catalytic ability of Pdx1, the remote glutaminase and synthase active sites, as well as the elaborate structure provide a fertile and challenging area of research on several levels. A summary of the current advances in our knowledge of the biosynthesis of this versatile molecule and the most recent results from the laboratory will be provided.