The biogenesis of peroxisomes requires a group of protein factors referred to as peroxins which are encoded by the PEX genes. Peroxisomal proteins are synthesized on free polyribosomes and imported posttranslationally. The transport of peroxisomal matrix proteins from the cytoplasm to the peroxisome is mediated by two peroxisome-targeting signal sequences. Peroxisomal membrane proteinsare imported independently of the matrix proteins by a distinct mechanism mediated by the membrane PTS signal.Pex10p is a peroxisomal membrane protein required for peroxisome biogenesis and peroxisomal matrix protein import. It exhibits E3 ubiquitin ligase activity in vitro, and is required for Ubc4p-dependent ubiquitination of Pex5p, but not for Pex4p-dependent ubiquitination of Pex5p.Two subcomplexes of the peroxisomal import machinery have been defined: the docking subcomplex comprises Pex14p, Pex17p, and Pex13p, while the translocation subcomplex contains Pex2p, Pex10p, and Pex12p. The proteins of the translocation complex expose their RING finger domains to the outer face of the peroxisomal membrane, and act downstream of Pex14p, Pex17p, and Pex13p during the peroxisomal protein import process. Association of both subcomplexes into a larger import complex requires Pex8p, an intraperoxisomal protein. Pex8p organizes the formation of the larger import complex from the trans side of the peroxisomal membrane and thus might enable functional communication between both sides of the membrane.Pex10p also plays a central role in the peroxisomal protein interaction network by connecting the ubiquitin conjugating enzyme Pex4p to the other members of the peroxisomal protein import machinery, and is required for the ubiquitination of the PTS1receptor Pex5p. pex10 null mutants are viable but peroxisome deficient, mislocalize peroxisomal matrix proteins to the cytosol, and accumulate Pex5p at the cytosolic face of the peroxisomal membrane.The human peroxisome biogenesis disordersare a group of genetically heterogeneous diseases characterized by severe mental retardation, neuronal, hepatic and renal abnormalities, and death in early infancy. Clinical features of PBD patients vary, but all exhibit a defect in the import of one or more classes of peroxisomal matrix proteins. This cellular phenotype is shared by yeast pex mutants, and human orthologs of yeast PEX genes are defective in some groups of PBD patients.Mutations in human PEX10 have been associated with Zellweger Syndrome and adrenoleukodystrophy.