

.0012 PI M(MALTON) [PI, PHE52DEL ON M2]

Liver disease, as well as emphysema, has been described only with PI*Z and PI*M(Malton). [Fraizer et al. \(1989\)](#) studied the molecular defect in M(Malton), a deficiency allele which, like the Z allele, is associated with hepatocyte inclusions and impairs secretion. They found that the M(Malton) allele contains a deletion of the codon for 1 of the 2 adjacent phenylalanine residues (amino acid 51 or 52 of the mature protein). Judging from the haplotype data, the M(Malton) mutation must have derived from the normal M2 allele. Deletion of the 1 amino acid would be expected to shorten 1 strand of the beta-sheet, B6, apparently preventing normal processing and secretion. Like the common Z deficiency mutation (glu342-to-lys), the M(Malton) allele is associated with both alpha-1-antitrypsin deficiency and hepatic disease. [Curiel et al. \(1989\)](#) also showed that the M(Malton) allele differs from the normal M2 allele by deletion of the entire codon (TTC) for residue phe52. They demonstrated abnormal intracellular accumulation of newly synthesized AAT protein in a homozygote who also showed, on liver biopsy, inflammation, mild fibrosis, and intrahepatocyte accumulation of the protein. Furthermore, [Curiel et al. \(1989\)](#) showed by retroviral gene transfer of AAT cDNA with the M(Malton) phe52 deletion into murine cells that abnormal accumulation of the newly synthesized protein occurred. This provides further evidence that abnormal intrahepatocyte AAT accumulation is responsible for the liver injury. By means of gene amplification and direct DNA sequencing, [Graham et al. \(1989\)](#) identified the same mutation, pointing out that it could be either phenylalanine-51 or phenylalanine-52 that is deleted. [Dry \(1991\)](#) described a method for detecting the single base substitution in PiZ useful for same-day diagnosis of AAT deficiency in chorion villus samples. 💡