Diversity of molecular defects expressed in porphyria

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Porphyrias are characterized biochemically by decreased formation of heme due to defects in certain enzyme activities involved in the heme biosynthesis. According to the defective enzyme, the inherited porphyrias are classified to eight types, five of which are known to be inherited dominantly. However, only a half of subjects who inherit an enzyme deficiency develop the symptom. Acute attacks of porphyria can be precipitated in susceptible persons by additional factors including drugs. One of the typical symptoms expressed in erythropoietic porphyria is photosensitivity, which is also observed in the side effect caused by certain drug administration. While identification of the molecular genetic abnormalities have greatly added to the understanding of the porphyrias, it is important to elucidate the additional factors to show the clinical expression. On the other hand, in most of the cases of recessively inherited porphyrias, gene defect was shown to be compound heterozygous. Besides the nature of the gene defect is highly heterogeneous. Each of the inherited porphyrias represents a single gene disorder, but some cases of dual porphyries associated with two enzymatic deficiencies have been reported. These cases indicated that some heterozygous gene defect, which is asymptomatic itself, become the additional factors to show the pathogenesis.

The elucidation of the mechanism of the regulation of the genes in heme biosynthesis would contribute greatly to the understanding of the pathogenesis of porphyria and might lead to the development of new drugs.