Genomic mutations associated with mild and severe deficiencies of transcobalamin I (haptocorrin) that cause mildly and severely low serum cobalamin levels.
Title: Genomic mutations associated with mild and severe deficiencies of transcobalamin I (haptocorrin) that cause mildly and severely low serum cobalamin levels.

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Abstract: Transcobalamin (TC) I deficiency, like the function of TC I itself, is incompletely understood. The concept of mild deficiency is an important but poorly understood entity. While there have been reports of mild deficiency, there has been very little study of the mutational, population genetic, and clinical features of patients who present with severe low levels of serum cobalamin. We describe 24 patients with a diagnosis of transcobalamin I deficiency and their pedigrees. Subjects were classified into groups with mildly or severely low serum cobalamin levels. Seventeen patients had evidence for mild deficiency based on low levels of serum cobalamin with normal or near-normal values of transcobalamin I activity. Seven patients had severe deficiency, with serum cobalamin levels below 25 nmol/l. Twenty-three patients had mutations in the haptocorrin gene. Two patients, homozygous for the same mutation, presented as typical cases with severe cobalamin deficiency and neurologic symptoms. The remainder were heterozygous for different mutations, and the phenotypic features of the patients varied widely. The mutations in the haptocorrin gene were significantly different between the two groups. The mutations in the severely low group were predominantly small insertions and deletions, whereas that in the mildly low group were larger insertions and deletions, insertions of unknown function, and non-synonymous substitutions.

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