Novel association to the proprotein convertase PCSK7 gene locus revealed by analysing soluble transferrin receptor (sTfR) levels.

The level of body iron storage and the erythropoietic need for iron are indicated by the serum levels of ferritin and soluble transferrin receptor (sTfR), respectively. A meta-analysis of five genome-wide association studies on sTfR and ferritin revealed novel association to the PCSK7 and TMPRSS6 loci for sTfR and the HFE locus for both parameters. The PCSK7 association was the most significant (rs236918, P = 1.1 × 10E-27) suggesting that proprotein convertase 7, the gene product of PCSK7, may be involved in sTfR generation and/or iron homeostasis. Conditioning the sTfR analyses on transferrin saturation abolished the HFE signal and substantially diminished the TMPRSS6 signal while the PCSK7 association was unaffected, suggesting that the former may be mediated by transferrin saturation whereas the PCSK7-associated effect on sTfR generation appears to be more direct.