

# Apical distribution of HFE- $\beta$ 2-microglobulin is associated with inhibition of apical iron uptake in intestinal epithelia cells

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Mutations in the HFE gene result in hereditary hemochromatosis, a disorder of iron metabolism characterized by increased intestinal iron absorption. Based on the observation that ectopic expression of HFE strongly inhibits apical iron uptake (Arredondo et al., 2001, FASEB J 15, 1276-1278), a negative regulation of HFE on the apical membrane transporter DMT1 was proposed as a mechanism by which HFE regulates iron absorption. To test this hypothesis, we investigated: (i) the effect of HFE antisense oligonucleotides on apical iron uptake by polarized Caco-2 cells; (ii) the apical/basolateral membrane distribution of HFE,  $\beta$ -2 microglobulin and DMT1; (iii) the putative molecular association between HFE and DMT1. We found that HFE antisense treatment reduced HFE expression and increased apical iron uptake, whereas transfection with wild-type HFE inhibited iron uptake. Thus, an inverse relationship was established between HFE levels and apical iron uptake activity. Selective apical or basolat