

DMT1, a physiologically relevant apical Cu^{1+} transporter of intestinal cells

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Despite important advances in the understanding of copper secretion and excretion, the molecular components of intestinal copper absorption remain a mystery. DMT1, also known as Nramp2 and DCT1, is the transporter responsible for intestinal iron uptake. Electrophysiological evidence suggests that DMT1 can also be a copper transporter. Thus we examined the potential role of DMT1 as a copper transporter in intestinal Caco-2 cells. Treatment of cells with a DMT1 antisense oligonucleotide resulted in 80 and 48% inhibition of iron and copper uptake, respectively. Cells incorporated considerable amounts of copper as Cu^{1+} , whereas Cu^{2+} transport was about 10-fold lower. Cu^{1+} inhibited apical Fe^{2+} transport. Fe^{2+} , but not Fe^{3+} , effectively inhibited Cu^{1+} uptake. The iron content of the cells influenced both copper and iron uptake. Cells with low iron content transported fourfold more iron and threefold more copper than cells with high iron content. These results demonstrate that DMT1 is a