Response to: Dietary and pharmacological factors affecting iron absorption in mice and man

We agree with the comments of Kontoghiorghe *et al.*[1] on the effects of various dietary and pharmacological factors in iron absorption. There is no doubt that lipophilic iron compounds can be relatively efficiently absorbed by the gastrointestinal tract, while hydrophilic iron complexes are impermeable to cellular membranes. Nevertheless, even though heme shares some physicochemical similarities to other lipophilic iron-binding compounds, it is a molecule with distinct and unique biological properties. Thus, gastrointestinal absorption,[2] intracellular transport[3] and extracellular neutralization[4] of heme are mediated by specific pathways. Moreover, heme can only release iron in cells following its enzymatic degradation by heme oxygenases.[5]

As Kontoghiorghe *et al.* point out, and as is also demonstrated by epidemiological data,[6] iron deficiency anemia is quite common in vegetarian and malnourished populations of developing countries, but is not frequently observed in Western populations consuming heme-rich diets. Consistently, nutritional studies have suggested that heme iron is more bioavailable to humans than inorganic iron.[7] We showed that heme is a poor dietary iron source for mice.[8] which is in line with the fact that these animals are not predators and rarely have access to heme-rich sources of nutrition. We identified the rate-limiting step in the transport of luminal heme across the apical membrane of murine enterocytes. Based on these findings, we speculated that efficient heme absorption mechanisms may have evolved preferentially in carnivores and omnivores, and not in *de facto* vegetarian species. Future identification of the long-sought intestinal heme transporter(s) could provide experimental support to this hypothesis, if this molecule is differentially expressed in human and murine enterocytes.

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