Author’s response to reviews

Title: Iron behaving badly: inappropriate iron chelation as a major contributor to the aetiology of vascular and other progressive inflammatory and degenerative diseases

Authors:

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Author’s response to reviews: see over
Dr Scott Edmunds,
Senior Editor,
BMC Journals,
BMC Medical Genomics.

Dear Scott,

Many thanks for your notes and for your two referees’ most helpful comments.

Apropos the formatting, I have added a list of abbreviations and a Competing Financial Interest section as per the instructions. I do note your point about a 350-word abstract, but I think I need to argue that given the considerable range (as well as length) of the ms it is reasonable to plead for a little latitude here, and I do so. I have tightened it up a little, and it is still less than a page of ms and only 487 words.

Referee Welch asks (section 5) whether the mitochondrial iron chaperone protein involved in Friedreich’s ataxia might be the mammalian siderophore. The answer is no, since the definition of siderophores (and indeed the ligands for NGAL fit this) assumes them to be small non-protein molecules. I have not added a comment in the ms since it would only raise a straw man.

Referee Kirkwood makes 3 main points where he requests some minor changes. Point 1 is that longevity is not a disease, such that it is slightly odd that it appears in the diseases section. I agree. However, as stated in the ms, it is usually treated in the ‘aging’ milieu since aging causes longevity and aging causes disease. I have added a couple of phrases to cover this. Point 2 is that the concluding remarks on systems biology and what a synthesis like the one attempted here can deliver. I accept this point too, and have added a little more material in the concluding remarks section. Point 3 is somewhat more woolly, to the effect that iron and metabolism should be considered in the context of other processes that may be contributing to the disorders discussed. While I accept the general thought, we don’t yet know enough to make that happen, and one is only inclined to start that process if one is convinced that it is worthwhile. Making available the present (weight of) evidence is designed to encourage the community to do just that.

I have also added a few pertinent references that came out since submission.

Once again, many thanks for your kind consideration, and I look forward to hearing from you before too long.

Very best wishes,

Yours ever,

Douglas Kell
Professor of Bioanalytical Science