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Letter to the Editor

Response to letter by Bakker et al.

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We appreciate the Letter of Drs. Bakker, Melgert, and Faas regarding our article [1], which reported the down-regulation of proinflammatory cytokines from macrophages by hemopexin, and their comments suggesting that hemopexin may have several different properties. There is no discrepancy with our data. Consistent with the efficiency of evolution, many proteins perform several different functions. As noted, a primary role of hemopexin is likely to scavenge heme, thereby limiting its potential toxicity from oxidant stress [2]. Dr. Bakker and colleagues have reported that hemopexin could be involved in some renal diseases through certain isoforms that possess enhanced protease activity [3–5]. We believe that the question of whether the properties of hemopexin are "anti-inflammatory" or not may be a question of semantics, depending on what is meant by inflammation. It is worth noting that not all protease activity is proinflammatory. For example, activated protein C, which is approved by the U.S. Food and Drug Administration for the treatment of sepsis, is a serine protease that is reported to have anti-inflammatory properties. Given the different properties reported for hemopexin, it will be interesting to study isoforms of hemopexin for differences in protease activity, heme binding, and macrophage suppression to better understand structure-function relationships. Finally, there may be additional properties for hemopexin. For example, a recent article [6] suggests that hemopexin may play a novel, anti-inflammatory role in protecting against atherosclerosis as part of high-density lipoprotein, a finding generally consistent with what we reported.

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