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Response to van Koppen *et al*

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We thank Dr van Koppen and colleagues for their interest in our work. We reported that compared with healthy controls, circulating bone marrow derived fibrocyte levels were elevated in the plasma of individuals with hypertensive heart disease, and that in these individuals, increased fibrocyte levels correlated with increased left ventricular hypertrophy assessed by cardiac MRI [1]. In their letter, Dr van Koppen and colleagues present data from studies performed using a rat model of hypertensive chronic kidney disease. They reported the following: a single dose of autologous bone marrow cells (from healthy or hypertensive donors) administered via the renal artery did not contribute to cardiac fibrosis; and there was a trend (not statistically significant) towards more cardiac fibrosis in rats that received hypertensive compared with vehicle or healthy control bone marrow cells. They concluded that autologous bone marrow cell therapy in hypertension and chronic kidney disease is less effective in reducing renal disease progression and may induce cardiac fibrosis.

We submit that these conclusions should be tempered by the following methodological limitations. First, the letter appears to report the results of a single experiment with only five animals per group; thus, firm conclusions should be deferred until the data are reproduced in repeat experiments. Second, it is difficult to extrapolate from transfer of unselected bone marrow cells to the effect of fibrocytes *per se*, which are a small subset of total bone marrow cells, particularly as the proportion of fibrocytes may have differed between the bone marrow cells obtained from healthy and hypertensive donors. Third, a single administration of a large number of cells is unlikely to replicate the physiologic egress of fibrocytes from the bone marrow to the target organs via the blood stream in hypertension, which likely occurs over months; generating bone marrow chimeric animals is a more robust experimental approach in this regard. Fourth, administration of the bone marrow cells into the renal artery will presumably result in entrapment of the majority of the cells in the renal capillaries; this may be desirable if the renal phenotype of the animals is of interest, but is not well suited to the study of the heart. Fifth, a quantitative method of enumerating blood and tissue fibrocytes, such as flow cytometry, is preferable (and complimentary) to

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Conflicts of interest

The authors have no conflicts of interest to declare.

qualitative measures such as histologic assessment. In summary, although we find Dr van Koppen and colleagues' work interesting, we are not convinced that their observations can be directly linked to fibrocytes.

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