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CORRESPONDENCE

Sir,

Involvement of circulating endothelial progenitor cell and vasculogenic factors in the pathogenesis of diabetic retinopathy

The first point of their letter is that our study is not novel, and they suggest their studies confirmed the presence of abnormally high levels of circulating plasma markers of angiogenesis/vasculogenesis in patients with and without retinopathy. In their study, circulating plasma markers were confined to angiopoietin-1, angiopoietin-2, their soluble receptor Tie-2, vascular endothelial growth factor (VEGF) and its soluble receptor Flt-2, and they did not comment about the role of stem cells in the pathologic neovascularization. However, we tried to look at the mechanism of neovascularization from a different point of view in stem cell level, even though we could not conclude the exact mechanism of diabetic retinopathy.

We apologize for any confusion caused by the use of term serum instead of plasma in part of VEGF. Enzyme-linked immunosorbant assay samples were collected into ethylenediaminetetraacetic acid tubes with minimal stasis and centrifuged to obtain plasma. Indeed, VEGF was measured not in serum but in plasma. The correlation between the plasma level of VEGF and diabetic retinopathy were reported differently from many investigators. Shimada *et al*[1] found no association between the plasma VEGF level and retinopathy status in a larger number of type II diabetic patients (no retinopathy $n=30$, retinopathy $n=34$). We observed similar plasma level of VEGF in patients with and without established diabetic retinopathy.

We strongly agree that many associated co-morbidities (hypertension, cardiovascular disease, etc) and drug treatments (ACE inhibitors and statins) have to be fully taken into consideration in diabetic patients. As noted in our publication, we excluded patients from the beginning if they had a history of cardiovascular disease, administration of statin or ACE inhibitors, and human recombinant erythropoietin treatment.

To address the concerns of our study, it must be noted that 15 numbers of samples in each four groups were too small to elucidate complete statistical consequences. However, the findings that CD34+ cells and c-kit+ cells were elevated in diabetic retinopathy patients supports the hypothesis that neovascularization of diabetic retinopathy is a systemic vasculogenesis rather than a local angiogenesis. We believe that it is also likely that marrow-derived endothelial progenitor cells play an increasingly important role as a vasculogenic factors in diabetic retinopathy, although we acknowledge that more research and data to support this assertion are needed. We thank Dr KY Goon and YH Lip for having read and commented on our article.

Reference

1 Shimada K, Baba T, Neugebauer S, Onozaki A, Yamada D, Midorikawa S *et al*. Plasma vascular endothelial growth factor in Japanese Type 2 diabetic patients with and without nephropathy. *J Diabetes Complications* 2002; **16**: 386–390.

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Sir,

Involvement of circulating endothelial progenitor cells and vasculogenic factors in the pathogenesis of diabetic retinopathy

In the May 2006 issue of *Eye,* Lee *et al*[1] present their findings from a small study which adds to our current understanding of pathological neovascularization in diabetic retinopathy. However, certain issues related to their study merit further discussion.

Their investigation of *systemic* (rather than local) angiogenic factors in diabetic retinopathy is not novel, as claimed by the authors. In 2000 and 2004, our research group reported plasma levels of vascular endothelial growth factor (VEGF), soluble VEGF receptor (Flt-1), angiopoietin-2 and its receptor tie-2 in patients with and without retinopathy.[2,3] Our studies confirmed the presence of abnormally high levels of circulating plasma markers of angiogenesis/vasculogenesis in these patients, suggesting an association between plasma indices of angiogenesis and the presence of diabetic retinopathy.

Of note, Lee *et al*[1] found no correlation between the severity of diabetic retinopathy and *serum* VEGF levels,