

Ishida *et al.* reply:

We thank Ferguson and Stuart for their comments and appreciate the opportunity to respond. Our data show that leukocytes mediate physiological retinal vascular pruning and pathological vaso-obliteration. These effects were demonstrated in both CD18-deficient mice and in rats treated with antibody to CD18 (ref. 1). The results, therefore, transcend a single species.

Our data also identify a role for FasL as an apoptosis-inducing molecule in vascular pruning and vaso-obliteration. We generated the data by antibody-based blockade¹ and did not rely on *gld* mice. In the discussion of our paper¹, we noted the possibility of the existence of redundant molecular or cellular mechanisms in the processes of pruning and vaso-obliteration.

Although our data and the data obtained from *gld* mice^{2,3} are seemingly contradictory, they may in fact be complementary. Additional studies are required to confirm this. The phenomena that Ferguson and Stuart describe in *gld* mice are similar to those observed in our experiments. In our CD18-deficient mice, leukocyte adhesion and vascular pruning were delayed by approximately two days, but were not indefinitely suppressed. Thus, the retinal vasculature of the adult CD18-deficient mice was essentially normal¹, as was the neural retina. We have learned that the timing of the analyses is criti-

cal, as vascular modeling occurs quickly. When placed in a hyperoxic environment for 72 hours, the CD18-deficient mice showed vaso-obliteration similar to that seen in wild-type mice (S.I., K.Y., T.U. and A.P.A., unpublished data), but significantly less vaso-obliteration was seen in CD18-deficient mice at 48 hours¹.

Both vascular pruning and vaso-obliteration may represent defense mechanisms aimed at protecting the sensory retina from oxidative stress. As noted in our paper, compensatory systems may be used *in vivo* to preserve this important defense mechanism. We hypothesize that the *gld* mice data^{2,3} reflect this biological redundancy. FasL blockade did not suppress leukocyte adhesion in our experiments¹. Under prolonged oxidative stress, we speculate that known leukocyte products, such as perforin and TRAIL, have a similar role in endothelial cell apoptosis in *gld* mice. We also noted¹ that FasL-bearing blood-borne cells of nonleukocytic origin may have a role in pruning and vaso-obliteration^{4,5}. It is therefore possible that leukocyte cytotoxicity does not depend on a single molecular pathway, and that FasL expression in the retina is not from a single cell type. A temporal examination of the role of blood-borne cells in pruning and vaso-obliteration is required in the genetically altered mice that Ferguson and Stuart describe.

The fact that *gld* mice show increased pathological neovascularization after hyperoxia-induced retinal ischemia^{2,3} is also consistent with our published data⁶. In our model of oxygen-induced retinopathy, T lymphocytes served as negative regulators of pathological neovascularization.

COMPETING INTERESTS STATEMENT

The authors declare competing financial interests (see the *Nature Medicine* website for details).

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How to submit microarray data

Nature Medicine has implemented a new policy regarding microarray experiments as of 1 December 2002. As discussed in a recent editorial in *Nature* (**419**, 323; 2002), *Nature Medicine* will now require authors to submit microarray data in accordance with the Minimal Information About a Microarray Experiment guidelines issued by the Microarray Gene Expression Data society. The guidelines include a checklist of relevant information that should be included with every new microarray submission, and can be found online at http://www.mged.org/Workgroups/MIAME/miame_checklist.html. The supplementary information must be supplied with the manuscript on five compact discs, at the time of submission, in a format compatible with commonly available software packages. We will also require that data central to the paper's conclusions be deposited in a public database for microarray data and accession numbers provided, where available, at or before acceptance for publication. By adopting this policy, we hope that the explicit description of experimental design and methods will facilitate the review and replication of microarray results.