epitope was interpreted to be discontinuous, comprising three segments that occupy ~20% of the sequence of the PrP structured domain. If YYR were the 15B3 epitope, this sequence would have been centrally located in all three segments; however, only one segment contained the complete YYR motif at the extreme N terminus (segment II). In addition, the peptide-spotting method for epitope mapping revealed that several peptides recognized by 15B3 do not contain a YYR motif, whereas several peptides not recognized by 15B3 do contain YYR. The data, as presented[2], indicate that YYR is not the 15B3 epitope.

The usefulness of the YYR epitope in prion immunotherapy or immunoprophylaxis remains open until confirmed by experimental tests, as do its potential diagnostic applications.

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

Eustache Paramithiotis[1], Marc Pinard[1], Trebor Lawton[2], Sylvie LaBoissiere[1], Valerie L Leathers[2], Wen-Quan Zou[3], Lisa A Estey[2], Julie Lamontagne[1], Marty T Lehto[3], Leslie H Kondejewski[1], Gregory P Francoeur[2], Maria Papadopoulos[1], Ashkan Haghighat[1], Stephen J Spatz[2], Mark Head[4], Robert Will[4], James Ironside[4], Katherine O'Rourke[5], Quentin Tonelli[2], Harry C Ledebur[1], Avi Chakrabartty[6] & Neil R Cashman[1,3,6,7]

[1]Caprion Pharmaceuticals, 7150 Alexander-Fleming, St-Laurent, Quebec H4S 2C8, Canada. [2]IDEXX Laboratories, 1 IDEXX Drive, Westbrook, Maine 04092, USA. [3]Centre for Research in Neurodegenerative Diseases, 6 Queen's Park Crescent West, University of Toronto, Toronto, Ontario M5S 3H2, Canada. [4]The National Creutzfeldt-Jakob Disease Surveillance Unit, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK. [5]USDA-ARS-ADRU, 3003 ADBF, Washington State University, Pullman, Washington 99164-6630, USA. [6]Department of Medical Biophysics, University of Toronto, Ontario Cancer Institute, 610 University Avenue, Toronto, Ontario M5G 2M9, Canada. [7]Sunnybrook & Women's College Health Sciences Centre, University of Toronto, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada.

1. Paramithiotis, E. *et al. Nat. Med.* **9**, 893–899 (2003).
2. Korth, C. *et al. Nature* **390**, 74–77 (1997).

FasL, leukocytes and vascular modeling

To the editor:

The recent paper by Ishida *et al.*[1] examines the role of leukocytes, specifically T lymphocytes, in vascular remodeling and vaso-obliteration in the rat eye. The authors conclude that T lymphocytes bind to the vasculature and model it by using Fas ligand (FasL) to prune the developing vessels. The authors also conclude from their examination of oxygen-induced vaso-obliteration that FasL on T lymphocytes induces apoptosis of hyperoxygenated endothelial cells. For these observations to have biological relevance, they should transcend species specificity. Because similar models of retinal angiogenesis exist in the mouse, one should be able to use the mouse to test predictions arising from these important observations. First, if Fas-FasL interactions are involved in retinal vessel development, Fas-deficient (*lpr*) and FasL-deficient (*gld*) mice should show vascular defects. Second, vessels in mice without these proteins should not undergo vaso-obliteration to the same degree as do wild-type animals. Third, rodents without T lymphocytes ($Rag^{-/-}$ or severe combined immunodeficient mice and T-cell-deficient rats) and/or cytotoxic lymphocytes (MHC class I– or CD8-deficient) should show aberrant retinal vessel development. Fourth, if the retinal vessels in these mice do not develop normally, this should severely impair normal development of the retina. Fifth, examination of these strains for vaso-obliteration should reveal that this process is severely impaired compared with wild-type animals.

Some of these issues have been addressed in recent publications using mouse models. First, retinal vessel development is normal in *lpr* and *gld* mice[2]. Second, the retinal vessels develop normally in these strains[3]. Third, the vaso-obliteration stage of oxygen-induced retinopathy is identical in *lpr*, *gld* and wild-type mice[3,4]. Thus, the *lpr* and *gld* mutations do not affect any of these three parameters. This has been tested with the *lpr* and *gld* mutations on both the C57BL/6 and BALB/c backgrounds.

We have examined numerous strains with targeted deletions of molecules involved in immune responses (including those mentioned above). These strains have shown no obvious defects in retinal development or oxygen-induced retinopathy (unpublished observations).

Our studies have shown that Fas and FasL exert influence only when neovascularization is induced in the eye. Retinal vessel growth in response to hyperoxia is accelerated in *gld* mice[3]. Laser-induced choroidal neovascularization is accelerated in *gld* and *lpr* mice[2]. Corneal angiogenesis induced by suture is intensified by the *gld* mutation[5].

It should also be noted that FasL expression is found only on activated T cells, not on resting or circulating T cells, but it is not restricted to T cells. It is constitutive and inducible in numerous sites throughout the body[6]. In the eye, abundant FasL is a key mediator in immune privilege[7], corneal graft acceptance[8] and control of angiogenesis[2,3]. It also regulates the extent of neovascularization in the cornea[5]. Thus, we favor the idea that FasL acts as a barrier to Fas^{+} leukocytes and endothelial cells after full organ development. This is the only way to account for the fact that mice bearing the *lpr* and *gld* mutations do not show notable developmental defects in the eye.

COMPETING INTERESTS STATEMENT
The authors declare that they have no competing financial interests.

Thomas A Ferguson & Patrick M Stuart
Department of Ophthalmology & Visual Sciences, Washington University School of Medicine, St. Louis, Missouri 63110, USA.

1. Ishida, S. *et al. Nat. Med.* **9**, 781–788 (2003).
2. Kaplan, H.J., Leibole, M.A., Tezel, T. & Ferguson, T.A. *Nat. Med.* **5**, 292–297 (1999).
3. Barreiro, R., Schadlu, R., Herndon, J., Kaplan, H.J. & Ferguson, T.A. *Invest. Ophthalmol. Vis. Sci.* **44**, 1282–1286 (2003).
4. Davies, M.H., Eubanks, J.P. & Powers, M.R. *Invest. Ophthalmol. Vis. Sci.* **44**, 3202–3210 (2003).
5. Stuart, P.M., Pan, F., Plambeck, S. & Ferguson, T.A. *Invest. Ophthalmol. Vis. Sci.* **44**, 93–98 (2003).
6. Green, D.R. & Ferguson, T.A. *Nat. Rev. Mol. Cell. Biol.* **2**, 917–924 (2001).
7. Griffith, T.S., Brunner, T., Fletcher, S.M., Green, D.R. & Ferguson, T.A. *Science* **270**, 1189–1192 (1995).
8. Stuart, P.M. *et al. J. Clin. Invest.* **99**, 396–402 (1997).