



Figure 3 Multiplex PCR to detect *NEMO* gene deletion of exons 4–10. (a) Using primers Int3s, Rep3s, and L2Rev, which determine deletion of exons 4–10 in either *NEMO* or delta *NEMO*, double bands at 733 and 1045 bp each were seen in mother (lane 3) and proband (lane 4), whereas single 733 bp band in her unaffected (lane 2) father and healthy control (lane 1). (b) Subsequent PCR using *NEMO*-specific primers In2 and JF3H. Single band was obtained only in the affected two individuals (lanes 3 and 4) indicating the deletion is originated from *NEMO* gene. No band was seen in her father and healthy control (lanes 1 and 2). M = size marker.

One of the most common ocular lesions in IP is vascular abnormalities in the peripheral retina.³ The similarities of avascularization in both patients suggest that *NEMO* may be involved in angiogenesis of the human retina. The formation of retinal vessels involves either vasculogenesis or angiogenesis, and the latter may be responsible for the formation in the perifoveal and peripheral regions.⁴ Therefore, we postulated that the perifoveal degeneration observed in the mother may be a result from perifoveal vascular abnormality. This is consistent with our previous report⁵ that NF- κ B signalling is closely associated with retinal angiogenesis. In contrast, phenotypic variations suggest the presence of other genetic factors.

It was recently reported that in the West, an identical genomic deletion accounted for 90% of the identified mutations in the *NEMO* gene. Because the same gene deletion was found in Japanese, the deletion may be the most common mutational hot spot irrespective of race, although further genetic analysis of Japanese IP patient is required.

Acknowledgements

This work was supported in part by grants from the Ministry of Education, Science, Sports and Culture, Japan (TI and SY), The Japan Health Foundation (SY), and Kanae Foundation for Life and Socio-medical Science (SY).

References

- 1 Aradhya S, Woffendin H, Jakins T, Bardaro T, Esposito T, Smahi A *et al.* A recurrent deletion in the ubiquitously expressed *NEMO* (IKK- κ) gene accounts for the vast majority

of incontinentia pigmenti mutations. *Hum Mol Genet* 2001; **10**: 2171–2179.

- 2 Steffann J, Raclin V, Smahi A, Woffendin H, Munnich A, Kenwrick ST *et al.* A novel PCR approach for prenatal detection of the common *NEMO* rearrangement in incontinentia pigmenti. *Prenat Diagn* 2004; **24**: 384–388.
- 3 Goldberg M, Custis P. Retinal and other manifestations of incontinentia pigmenti (Bloch–Sultsberger syndrome). *Ophthalmology* 1993; **100**: 1645–1654.
- 4 Suzanne H, Huijun Y, Tailoi C. Vascularization of the human fetal retina: roles of vasculogenesis and angiogenesis. *Invest Ophthalmol Vis Sci* 2000; **41**: 1217–1228.
- 5 Yoshida S, Ono M, Shono T, Izumi H, Ishibashi T, Suzuki H *et al.* Involvement of interleukin-8, vascular endothelial growth factor, and basic fibroblast growth factor in tumor necrosis factor alpha-dependent angiogenesis. *Mol Cell Biol* 1997; **17**: 4015–4023.

H Tada, S Yoshida, Y Yamaji, K Fujisawa and T Ishibashi

Department of Ophthalmology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

Correspondence: S Yoshida

Tel: +81 92 642 5648;

Fax: +81 92 642 5663.

E-mail: yosida@eye.med.kyushu-u.ac.jp

Eye (2007) **21**, 888–890; doi:10.1038/sj.eye.6702770;
published online 30 March 2007

Sir,

Bevacizumab: a compassionate way of doing business?

We agree with Canning and Lotery¹ that a clinical trial of bevacizumab in the treatment of neovascular age-related macular degeneration (AMD) could reveal important safety issues, but for rarer diseases randomised controlled trials are not always appropriate.

Neovascular glaucoma is another disease where bevacizumab is promising. It is, however, uncommon compared with AMD, and fortunately most cases respond to panretinal photocoagulation (PRP) when timely performed.² For the minority in whom PRP is either not possible or not effective, the prognosis is dire.

Bevacizumab has several possible roles in the management of this vexing condition. Used early it may prevent intractable glaucoma; later when the angle is closed, it may be used as an adjunct to glaucoma drainage surgery reducing the risk of intraocular bleeding. Finally by causing regression of new vessels and reducing leakage of inflammatory mediators, it may help in the treatment of painful blind eyes.³

Faced with the alternatives of a painful blind eye or enucleation, patients are unlikely to be willing to accept the control arm of a trial, nor would we be willing to offer it.

On this basis we have been given approval by our Regional Ethics Committee to use bevacizumab for the treatment of neovascular glaucoma unresponsive to PRP. Where randomised placebo-controlled clinical trials are not appropriate, one should not underestimate the power of a well-conducted, prospective, observational case series.

References

- 1 Canning C, Lotery A. Bevacizumab: a new way of doing business? *Eye* 2006; **20**: 985–987.
- 2 The Central Vein Occlusion Study. Natural history and clinical management of central retinal vein occlusion. *Arch Ophthalmol* 1997; **115**: 486–491.
- 3 Grisanti S, Peters S, Tatar O, Ziemssen F, Bartz-Schmidt K. Intracameral bevacizumab for iris rubeosis. *Am J Ophthalmol* 2006; **142**: 158–159.

A Spratt, L Ogunbowale and W Franks

Glaucoma Research Unit, Moorfields Eye Hospital,
162 City Road, London EC1V 2PD, UK

Correspondence: W Franks,
Tel: +44 20 7566 2059;
Fax: +44 20 7566 2826.
E-mail: wendy.franks@moorfields.nhs.uk

None of the authors has a financial interest in any of the products mentioned.

Eye (2007) **21**, 890–891; doi:10.1038/sj.eye.6702776;
published online 16 March 2007

Sir,
Bevacizumab: a new way of doing business?

We wish to thank Franks for her insightful contribution to the debate on the indications and evidence for the use of bevacizumab in the eye.

One of the prerequisites for an ethical randomised controlled trial is the state of clinical equipoise—the researchers should not be biased strongly in favour of one treatment option or the other.¹ This implies a degree of uncertainty regarding the outcome for both treatment options.

Unfortunately there is little doubt about the natural history of rubeotic glaucoma unresponsive to laser. It is a dire condition with devastating consequences for the

quality of the patient's life and their family. It is only natural to wish to do everything one can under such conditions. There is a good theoretical basis for the use of bevacizumab in this condition and so far the safety profile seems good.

We agree with Franks therefore that ranibizumab or bevacizumab in rubeotic glaucoma would be justified in the context of a carefully documented observational study. The wholesale use of this drug in a raft of conditions where other options exist remains a cause for comment. Bevacizumab might well be a very effective and cost-effective drug for much vascular eye pathology—let's just prove it!

Reference

- 1 Hansson SO. Uncertainty and the ethics of clinical trials. *Theor Med Bioethics* 2006; **27**(2): 149–167.

C Canning and A Lotery

Southampton General Hospital, Human Genetics
Division, Tremona Road, Southampton-SO16 6YD,
UK

Correspondence: A Lotery
Tel: +41 02 38 079 4590;
Fax: +44 38 079 4120.
E-mail: a.j.lotery@soton.ac.uk

Eye (2007) **21**, 891; doi:10.1038/sj.eye.6702777;
published online 16 March 2007

Sir,
Spontaneous resolution of retinal pigment epithelial tears and pigment epithelial detachment following blunt trauma

Retinal pigment epithelium (RPE) tear mostly occurs as a complication of age-related macular degeneration but may also develop as a rare complication after trauma.^{1–5} Patients with traumatic RPE tear involving the fovea usually have poor visual prognosis.^{1,2} We report the spontaneous resolution of traumatic RPE tears and pigment epithelial detachment (PED) in a patient after blunt trauma who subsequently had good visual recovery.

Case report

A 63-year-old woman presented with left blurred vision after being hit by a badminton racquet. Her left eye