Targeting key angiogenic pathways with a bispecific CrossMAb optimized for neovascular eye diseases

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In July 2017, the journal issued an editorial expression of concern (https://doi.org/10.15252/emmm.201707895) to alert readers that the data in Figs 4 and 5 needed further analysis and verification. Researchers at Roche have since confirmed in an independent study based on independently obtained data that the conclusions from these figures are valid (Foxton et al., 2019).

The journal analysed source data for Figs 1, 4, 5, 6 and 9 of Regula et al., 2016; inconsistencies and omissions between the published data and the source data are corrected as follows.

Figures 4 and 5 contain panels that derive from different mice but show highly similar whole-mount retinae preparations. David Shima shared available source data related to these figures with the journal. The editors of the journal were not able to find matches for the majority of the panels displayed in the published figures. There was no institutional investigation of this matter.

As a result, Figs 4 and 5A–G are herewith retracted and marked accordingly in the published article.

Additionally, the following figures are corrected:

Figure 1A
The archived source data were reanalysed independently by Christoph Ullmer and Sascha Fauser at Roche and shared with the journal. The Prism file with P-values and ANOVA corrected with multiple testing for this figure has been published with this correction. The revised Fig 1A is below. A single data point diverges between the published figure and the source data provided (ANG1, control value = 314); the reanalysed data confirm that there are no significant differences compared to the control experiment. Note that the scale of the y-axis is ln2.

Figure 6A
The authors omitted detailing the software used to generate this figure. For the structural representation of RG7716, a homology model of RG7716 was generated and visualized with the software Discovery Studio (Dassault Systèmes Bioliva, San Diego, USA) using the X-ray structures of an anti-ANG-2 CrossFab (PDB accession number 4iml), an anti-VEGF Fab (PDB accession number 1cz8), as well as the structure of a complete IgG1 (PDB accession number 1hzh) as templates. The highlighted positions were identified by their sequence position. A semi-transparent molecular surface was generated with a 1.4 Å probe radius.

Figure 9B
The corresponding author states that a subanalysis based on a subset of 15 monkeys out of 30 was published. The full, original source data...
for 30 monkeys (5 subgroups of 2 × 3 monkeys each) were re-plotted by C. Ullmer and S. Fauser to show the correct values, error bars and changes in statistical significance for all animals. The values and P-values in the figure legend have been updated. The source data for this figure are published with this correction. The authors state that the conclusions of the figure do not change in the light of these changes to the displayed data analysis.

**Figure 6A. Revised figure legend.**
Structural presentation of CrossMAb RG7716 with substituted amino acids highlighted and coloured. Amino acids corresponding to individual point mutations ensuring correct and efficient heavy-chain heterodimerization (“knobs-into-holes” [green] and additional disulphide bridge [yellow]), abolishing Fc receptor functionality (Fcγ receptors I, II and III [pink] and FcRn [blue]), are highlighted. The structure modelling was obtained using the DiscoveryStudio Pro software (Dassault Systèmes).

JTR, PLvL, RF, VAB, CMGC, SBBT, YSW, DI, JM, KGS, EN, GW, PS, CK, DTS and GH agree with this corrigendum in its entirety. MD and MK did not provide a response.

**Reference**
Foxton RH, Uhles S, Grüner S, Revelant F, Ullmer C (2019) Efficacy of simultaneous VEGF-A/ANG-2 neutralization in suppressing spontaneous choroidal neovascularization. *EMBO Mol Med* 11: e10204