Autosomal recessive lissencephaly with cerebellar hypoplasia is associated with human *RELN* mutations

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In a recent *Letter*, we mapped a gene that causes human lissencephaly with cerebellar hypoplasia (LCH), and identified two independent splicing mutations in the human gene *RELN*. Each mutation causes skipping of an exon with a consequent translational frameshift and deficiency of the reelin protein. It has recently been brought to our attention that the numbering system we used for the 65 exons of *RELN* differs from the convention adopted for exon numbering in the mouse[1]. The DNA sequences that are skipped in the human mutations are not altered, and the relationship of the mutations to the cDNA sequence, the translational frameshifts caused, or the predicted protein sequence are not changed in any way. Only the numbering of these exons, and thus the comparison of human exon-skipping mutations with mouse exon-skipping mutations, is slightly different than indicated in our paper. We therefore would like to clarify the human-mouse comparison so that a single numbering system can be used for both species.

The British mutation skips a 148-bp exon that corresponds to exon 43, rather than exon 42. We have also detected a second linked polymorphism in this British family whose significance is uncertain but that might also be pathogenic. At position 9840 of the cDNA (numbered according to GenBank NM_005045; ref. 2), in exon 60, there is a T to G change that changes amino acid 3222 (in the eighth reelin repeat) from isoleucine to serine. Although this mutation alters a highly conserved amino acid in a region critical for reelin secretion, and although the mutation was not seen in 200 normal chromosomes, we assume that it might be an alteration that occurred after the primary splicing mutation. However, this polymorphism might be useful in the future for genotyping purposes. The second (Saudi Arabian) mutation skips an 85-bp exon that corresponds to exon 37, rather than exon 36. Interestingly, exon 37 is the exact same exon skipped in the mouse *Reln*$^{rl\text{-}Alb2}$ allele, although the mechanism of these two splicing mutations is different: in the human, the abnormal splicing results from a splice acceptor mutation rather than the retrotransposon insertion that occurs in the mouse[3]. We apologize for any confusion we might have caused.

1. Royaux, I., Lambert de Rouvroit, C., D'Arcangelo, G., Demirov, D. & Goffinet, A.M. Genomic organization of the mouse reelin gene. *Genomics* **46**, 240–250 (1997).
2. DeSilva, U. *et al*. The human reelin gene: isolation, sequencing, and mapping on chromosome 7. *Genome Res.* **7**, 157–164 (1997).
3. Royaux, I., Bernier, B., Montgomery, J.C., Flaherty, L. & Goffinet, A.M. Reln(rl-Alb2), an allele of reeler isolated from a chlorambucil screen, is due to an IAP insertion with exon skipping. *Genomics* **42**, 479–482 (1997).