



Supplementary Figure 1: Schematic work-flow used to dissect the molecular genetic cause of posterior polymorphous corneal dystrophy in the current study. Genome sequencing lead to the identification of the underlying molecular genetic cause in family C31, despite previous extensive genetic interrogation with Sanger and exome sequencing. Mutations identified by massively parallel sequencing were verified by Sanger sequencing in all cases.

Supplementary Table 1: Results of *in silico* prediction tools for c.469C>G; p.(His157Asp) variant identified in individual II:2 from family B13.

| | SNP&GO | PROVEAN | PolyPhen2 | MutationTaster | MutPred2 | SIFT |
|---------------|---------|---------|-------------------|-----------------|----------|-----------|
| p.(His157Asp) | Neutral | Neutral | Possibly damaging | Disease causing | Neutral | Tolerated |

Predictions were obtained using these web resources:

SNP&GO: <http://snps.biofold.org/snps-and-go/snps-and-go.html>

PROVEAN and SIFT: <http://provean.jcvi.org/index.php>

PolyPhen2: <http://genetics.bwh.harvard.edu/pph2/>

MutationTaster: <http://www.mutationtaster.org/>

MutPred2: <http://mutpred.mutdb.org/>

Supplementary Table 2: Summary of 49 *ZEB1* pathogenic variants reported as causative for posterior polymorphous corneal dystrophy type 3 in 54 families. All mutations were manually curated and aligned to NM_030751.5. Larger deletions were described based on the GRCh37/hg19 human genome assembly.

| No | Family ID* | DNA level | Protein level | Ethnicity | Country of residence | Reference |
|----|------------|--------------------|--------------------|--------------------|----------------------|-----------------------|
| 1 | Case # 6 | c.1A>G | p.(Met1?) | White | New Zealand | Vincent et al, 2009 |
| 2 | - | c.2T>G | p.(Met1?) | Not provided | US | Aldave et al, 2007 |
| 3 | - | c.34C>T | p.(Gln12*) | Not provided | US | Aldave et al, 2007 |
| 4 | - | c.449del | p.(Gly150Alafs*36) | White | US | Bakhtiari et al, 2013 |
| 5 | SW2 | c.454del | p.(Pro152Glnfs*34) | White | Switzerland | Current study |
| 6 | C36 | c.482-2A>G | p.Gly161Glufs*9 | White | Czech Republic | Current study |
| 7 | B7 | c.627del | p.(Phe209Leufs*11) | White | UK | Evans et al., 2015 |
| 8 | - | c.640C>T | p.(Gln214*) | Not provided | US | Aldave et al, 2007 |
| 9 | C34 | c.646G>T | p.(Glu216*); | White | Czech Republic | Current study |
| 10 | - | c.672del | p.(Gly225Glufs*7) | Not provided | UK | Nguyen et al, 2010 |
| 11 | S1 | c.685-2A>G | p.? | Asian (Sri Lankan) | UK | Evans et al., 2015 |
| 12 | - | c.689_690del | p.(His230Argfs*7) | Not provided | US | Bakhtiari et al, 2013 |
| | White | | | Czech Republic | Current study | |
| 13 | C20 | c.698dup | p.(Ser234Valfs*4) | White | Czech Republic | Liskova et al, 2013 |
| 14 | - | c.929dup | p.(Cys311Valfs*25) | Not provided | US | Aldave et al, 2007 |
| 15 | - | c.973C>T | p.(Arg325*) | Not provided | US | Aldave et al, 2007 |
| 16 | SK1 | c.1045G>T | p.(Glu349*) | White | Slovak Republic | Current study |
| 17 | B5 | c.1100C>A | p.(Ser367*) | White | UK | Evans et al., 2015 |
| 18 | B1 | c.1124del | p.(Phe375Serfs*31) | White | UK | Liskova et al, 2007 |
| 19 | B3 | c.1176dup | p.(Ala393Serfs*19) | White | UK | Evans et al., 2015 |
| 20 | UM:797 | c.1332_1335del | p.(Ile444Metfs*48) | White | US | Krafchak et al, 2005 |
| 21 | UM:A01 | c.1348C>T | p.(Gln450*) | White | US | Krafchak et al, 2005 |
| 22 | P5 | c.1381delinsGACGAT | p.(Ser461Aspfs*34) | Not provided | US | Chung et al, 2017 |
| 23 | B2 | c.1387_1390del | p.(Pro463Trpfs*29) | White | UK | Liskova et al, 2007 |
| 24 | - | c.1482dup | p.(Glu495Argfs*10) | Not provided | US | Aldave et al, 2007 |
| 25 | SW1 | c.1498_1501del | p.(Asn501Valfs*25) | White | Switzerland | Current study |

| Supplementary Table 2 continued | | | | | | |
|---------------------------------|--------|--|--------------------|--------------|------------------------------|-----------------------|
| 26 | UM513 | c.1576dup | p.(Val526Glyfs*3) | Not provided | US | Krafchak et al, 2005 |
| | B13 | | | Asian | UK | Current study |
| | B6 | | | White | UK | Evans et al., 2015 |
| | - | | | White | US | Bakhtiari et al, 2013 |
| | - | | | Not provided | Not provided (North America) | Lechner et al, 2013 |
| 27 | - | c.1569del | p.(Val526*) | Not provided | US | Aldave et al, 2007 |
| 28 | P1 | c.1613delC | p.(Pro538Glnfs*10) | Not provided | US | Chung et al, 2017 |
| 29 | B11 | c.1669C>T | p.(Gln557*) | White | UK | Current study |
| 30 | C24 | c.1717_1718del | p.(Val573Phefs*12) | White | Czech Republic | Evans et al., 2015 |
| 31 | C16 | c.1749_1750del | p.(Pro584*) | White | Czech Republic | Evans et al., 2015 |
| 32 | - | c.1913_1914del | p.(Ser638Cysfs*5) | White | US | Bakhtiari et al, 2013 |
| 33 | B10 | c.1918C>T | p.(Gln640*) | White | UK | Current study |
| 34 | C2 | c.2157C>G | p.(Tyr719*) | White | Czech Republic | Liskova et al, 2007 |
| 35 | UM:461 | c.2182G>T | p.(Glu728*) | White | USA | Krafchak et al, 2005 |
| 36 | - | c.2249C>A | p.(Ser750*) | Not provided | UK | Lechner et al, 2013 |
| 37 | C1 | c.2324dup | p.(Glu776Glyfs*44) | White | Czech Republic | Liskova et al, 2007 |
| 38 | B9 | c.2577del | p.(Val860*) | White | UK | Current study |
| 39 | C22 | c.2617dup | p.(Thr873Asnfs*2) | White | Czech Republic | Liskova et al, 2013 |
| 40 | - | c.2650del | p.(Gln884Argfs*37) | Not provided | USA | Bakhtiari et al, 2013 |
| 41 | B12 | c.2650C>T | p.(Gln884*) | White | UK | Current study |
| 42 | UM:139 | c.2916_2917del | p.(Gly973Valfs*14) | White | US | Krafchak et al, 2005 |
| 43 | - | c.2990_2991del | p.(Glu997Alafs*7) | Not provided | US | Aldave et al, 2007 |
| 44 | - | c.3116_3117del | p.(Glu1039Glyfs*6) | Not provided | US | Bakhtiari et al, 2013 |
| 45 | C27 | chr10.hg19:31,784,795_31,855,747delinsACACACAC | p.? | White | Czech Republic | Liskova et al, 2016 |
| 46 | C17 | chr10.hg19:g.29,277,299_32553,577del | p.? | White | Czech Republic | Liskova et al, 2016 |
| 47 | B8 | chr10.hg19:g.(31,298,325_31,350,494)_(32,214122_32,285,574)del | p.? | White | UK | Liskova et al, 2016 |
| 48 | - | deletion at 10p11.23p11.22 | p.? | White | Canada | Chaudhry et al, 2017 |
| 49 | C31 | chr10.hg19:31,476,839_31,812,954 | p.? | White | Czech Republic | Current study |

*as designated in the original reports, US = United States of America, UK = United Kingdom

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