**Table S3.** List of 54 variants that cause de novo 5’ or 3’ ectopic splice site activation. Variants were obtained from DBASS5 and DBASS3. References can be found in the main text of the paper.

| SNP No. | Chr | Position | Gene       | Potential Coding effect | Splice site activation | Variant (DNA) | max(Δss) | Reference |
|---------|-----|----------|------------|--------------------------|------------------------|---------------|----------|-----------|
| 1       | 3   | 15651990 | BTD        | Missense                 | 3’                     | G->A          | 7.96     | [106]     |
| 2       | 4   | 155708309| FGB        | Missense                 | 3’                     | T->A          | 8.37     | [107]     |
| 3       | 6   | 31432182 | HLA-B      | Missense                 | 3’                     | G->C          | 9.95     | [108]     |
| 4       | 11  | 107511124| ACAT1      | Missense                 | 3’                     | C->T          | 2.11     | [109]     |
| 5       | 15  | 41282727 | EPB42      | Missense                 | 3’                     | G->T          | 13.31    | [110]     |
| 6       | 19  | 17860260| SLC5A5     | Missense                 | 3’                     | C->G          | 8.06     | [111]     |
| 7       | X   | 32238252 | DMD        | Nonsense                 | 3’                     | T->G          | 8.59     | [112]     |
| 8       | 11  | 67567654 | TCIRG1     | Synonymous               | 3’                     | G->A          | 7.95     | [113]     |
| 9       | 19  | 11084983 | LDLR       | Synonymous               | 3’                     | C->A          | 8.04     | [114]     |
| 10      | X   | 153838609| F8         | Synonymous               | 3’                     | G->T          | 2.51     | [115]     |
| 11      | 1   | 154375026| LMNA       | Missense                 | 5’                     | G->A          | 1.53     | [4]       |
| 12      | 4   | 89215079 | PKD2       | Nonsense                 | 5’                     | C->T          | 0        | [116]     |
| 13      | 5   | 70980772 | COL1A1     | Missense                 | 5’                     | A->G          | 8.18     | [117]     |
| 14      | 7   | 91702781 | MBB        | Missense                 | 5’                     | C->G          | 1.81     | [118]     |
| 15      | 7   | 91703738 | KRIT1      | Missense                 | 5’                     | A->G          | 8.18     | [118]     |
| 16      | 10  | 89682830 | PTEN       | Missense                 | 5’                     | C->G          | 8.27     | [119]     |
| 17      | 11  | 107708775| ATM         | Missense                 | 5’                     | C->T          | 7.75     | [85]      |
| 18      | 16  | 67413594 | CDH1       | Missense                 | 5’                     | C->T          | 7.75     | [120]     |
| 19      | 17  | 26551666 | NF1        | Missense                 | 5’                     | C->T          | 7.75     | [121]     |
| 20      | 17  | 26580523 | NF1        | Missense                 | 5’                     | G->A          | 3.81     | [122]     |
| 21      | 17  | 26565668 | NF1        | Nonsense                 | 5’                     | A->G          | 8.18     | [122]     |
| 22      | 17  | 26583297 | NF1        | Missense                 | 5’                     | T->A          | 5.33     | [121]     |
| 23      | 17  | 38512021 | BRCAl      | Missense                 | 5’                     | T->G          | 8.6      | [123]     |
| 24      | 17  | 45619024 | COL1A1     | Missense                 | 5’                     | A->G          | 8.18     | [124]     |
| 25      | X   | 100516810| BTK        | Nonsense                 | 5’                     | A->G          | 8.18     | [125]     |
| 26      | X   | 13343695 | HPRT1      | Missense                 | 5’                     | G->T          | 7.65     | [126]     |
| 27      | X   | 135560190| CD40L      | Nonsense                 | 5’                     | G->T          | 4.23     | [127]     |
| 28      | X   | 148392770| IDS        | Missense                 | 5’                     | C->G          | 0        | [128]     |
| 29      | X   | 153235823| FLNA       | Missense                 | 5’                     | C->T          | 0        | [129]     |
| 30      | 1   | 154375028| LMNA       | Synonymous               | 5’                     | C->T          | 0.49     | [130]     |
| 31      | 1   | 153474560| GBA        | Synonymous               | 5’                     | A->G          | 8.18     | [131]     |
| 32      | 1   | 156912581| SPTA1      | Synonymous               | 5’                     | A->G          | 8.18     | [132]     |
| 33      | 2   | 219382723| CYP27A1    | Synonymous               | 5’                     | G->T          | 7.65     | [133]     |
| 34      | 3   | 48593334 | COL7A1     | Synonymous               | 5’                     | C->T          | 7.75     | [134]     |
| 35      | 3   | 143757971| ATR        | Synonymous               | 5’                     | A->G          | 0        | [37]      |
| 36      | 3   | 185449258| ALG3       | Synonymous               | 5’                     | C->T          | 0.75     | [135]     |
| 37      | 5   | 42747170 | GHR        | Synonymous               | 5’                     | C->T          | 7.76     | [136]     |
| 38      | 5   | 42735837 | GHR        | Synonymous               | 5’                     | A->G          | 4.8      | [137]     |
| 39      | 7   | 65070189 | GUSB       | Synonymous               | 5’                     | C->T          | 7.76     | [138]     |
|   |   |     |     |     |     |     |     |     |     |
|---|---|-----|-----|-----|-----|-----|-----|-----|-----|
| 40| 11| 5204749| HBB | Synonymous | 5’ | G->A | 2.24 | [139] |
| 41| 11| 5204753| HBB | Synonymous | 5’ | T->A | 2.28 | [140] |
| 42| 12| 108497085| MVK | Synonymous | 5’ | C->T | 7.75 | [141] |
| 43| 12| 46535733| VDR | Synonymous | 5’ | C->G | 3.5  | [142] |
| 44| 15| 70428488| HEXA| Synonymous | 5’ | T->A | 4.52 | [143] |
| 45| 16| 162980| HBA2 | Synonymous | 5’ | C->T | 7.76 | [144] |
| 46| 16| 66027759| HSD11B2| Synonymous | 5’ | C->G | 2.51 | [145] |
| 47| 17| 42731797| ITGB3| Synonymous | 5’ | C->T | 7.76 | [146] |
| 48| 17| 26580468| NF1 | Synonymous | 5’ | G->A | 3.51 | [121] |
| 49| 17| 26586877| NF1 | Synonymous | 5’ | C->T | 7.75 | [121] |
| 50| 19| 17808957| JAK3 | Synonymous | 5’ | C->T | 7.75 | [147] |
| 51| 19| 806755| ELA2 | Synonymous | 5’ | C->A | 7.03 | [148] |
| 52| X | 100500293| BTK | Synonymous | 5’ | A->G | 0    | [149] |
| 53| X | 153301140| TAZ | Synonymous | 5’ | G->A | 0    | [150] |
| 54| X | 148376419| IDS | Synonymous | 5’ | C->T | 7.75 | [151] |