**Table S6. Brow lab suppressor substitutions in Prp8**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Prp8**  **domain** | **Yeast Prp8**  **substitution** | **Human**  **residue** | **U4-cs1a**  **(*PRP8*)** | **U4-cs1b**  **(genome)** | ***brr2-1*c**  **(*PRP8*)** | ***prp28-1*d**  **(*PRP8*)** |
| NTD1 | I222R | I149 |  |  |  | S |
| NTD1 | I222V | I149 |  |  |  | S |
| NTD1 | R226G | R153 |  |  |  | S |
| NTD1 | R226S | R153 |  |  |  | S |
| NTD1 | R229Q | R156 |  |  |  | S |
| NTD1 | R236G | R163 | S |  |  |  |
| NTD1 | L261P | L188 | S |  |  |  |
| NTD1 | P263L | A190 |  |  |  | S |
| NTD1 | I264R | I191 |  |  |  | S |
| NTD1 | L266P | L193 |  |  |  | S |
| NTD1 | L268S | L195 |  |  |  | S |
| NTD1 | D273G | D200 |  |  |  | S |
| NTD1 | D273N | D200 |  |  |  | S |
| NTD1 | W279G | W206 |  |  |  | S |
| NTD1 | L280P | F207 | S |  |  | S |
| NTD1 | Y281C | Y208 |  |  |  | S |
| NTD1 | L314S | L241 |  |  |  | S |
| NTD1 | E362**** | E291 | S |  |  |  |
| NTD1 | K611R | K536 | S |  |  |  |
| NTD1 | E624G | E549 | S |  |  |  |
| NTD1 | N643S | N568 | S |  |  |  |
| NTD1 | V644A | V569 | S |  |  |  |
| NTD1 | D651G | D576 | S |  |  |  |
| NTD1 | D651N | D576 | S |  |  |  |
| NTD1 | H659P | H584 | S |  |  |  |
| NTD2 | K684E | K609 | S |  |  |  |
| NTD2 | E788A | E715 |  | S |  |  |
| NTD2 | E788G | E715 | S |  |  |  |
| NTD2 | E788V | E715 | S |  |  |  |
| NTD2 | N796S | N723 | S |  |  |  |
| NTD2 | W856R | Y783 | S |  |  |  |
| NTD2 | E860K | E787 | S |  |  |  |
| NTD2 | Q861P | Q788 |  | S |  |  |
| NTD2 | Q861R | Q788 | S |  |  |  |
| RT-like | L1066P | L993 |  |  | S |  |
| RT-like | N1067K | N994 |  |  | S |  |
| RT-like | N1087H | N1014 |  |  | S |  |
| RT-like | D1094A | D1021 | S |  |  |  |
| RT-like | D1094N | D1021 | S |  |  |  |
| RT-like | D1094V | D1021 | S |  |  |  |
| RT-like | V1098D | T1025 | S |  | S |  |
| RT-like | V1098I | T1025 |  |  | S |  |
| RT-like | N1099K | N1026 |  | S |  |  |
| RT-like | L1107T | L1034 |  |  | S |  |
| RT-like | P1191A | P1118 |  | S |  |  |
| RT-like | P1191L | P1118 | S | S |  |  |
| RT-like | P1191S | P1118 | S |  |  |  |
| RT-like | P1191T | P1118 | S |  |  |  |
| RT-like | D1192Y | D1119 | S |  |  |  |
| RT-like | N1194D | N1121 | S |  |  |  |
| Linker | L1624M | Q1552 | S |  |  |  |
| Linker | L1634F | M1562 | S | S |  |  |
| Linker | T1640K | T1568 |  | S |  |  |
| Linker | L1641F | L1569 | S |  |  |  |
| Endonuc. | T1685I | T1613 | S |  |  |  |
| Endonuc. | P1688L | P1616 | S |  |  |  |
| Endonuc. | P1688R | P1616 | S | S |  |  |
| Endonuc. | A1754V | A1682 | S |  |  |  |
| Endonuc. | N1809D | N1737 | S |  |  |  |
| RNase H | F1851L | F1779 | S |  |  |  |
| RNase H | V1860D | V1788 | S |  |  |  |
| RNase H | V1860N | V1788 | S |  |  |  |
| RNase H | T1861P | T1789 | S | S\* |  |  |
| RNase H | V1862A | I1790 | S |  |  |  |
| RNase H | V1862D | I1790 | S |  |  |  |
| RNase H | V1862Y | I1790 | S |  |  |  |
| RNase H | T1872A | T1800 |  | S |  |  |
| RNase H | T1872K | T1800 |  | S |  |  |
| RNase H | I1875T | I1803 | S |  |  |  |

a Kuhn & Brow 2000, b This study or (\*) Kuhn *et al.* 1999, c Kuhn *et al.* 2002, d Price *et al.* 2014