

**Supplementary Table 1: Oligonucleotides.**

| <b>Name</b>                 | <b>Sequence (5' -&gt; 3')</b>                                                                                                          |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| API-Delta_F                 | TTCCCGGCCCTG                                                                                                                           |
| API-Delta_R                 | GGGCCGGGAACCGGAAAAAACGAGTTG                                                                                                            |
| ERSEA-Delta_F               | CTTAACTTAAACCTCGGCC                                                                                                                    |
| ERSEA-Delta_R               | CCGAGGTTTAAGTTAAAGAGCGCTGCCAACC                                                                                                        |
| SP1-Delta_F                 | CGGGGGCACAGAGTG                                                                                                                        |
| SP1-Delta_R                 | CTGTGCCCCCGCCGGCCGAGGTTTAAG                                                                                                            |
| MRE-Delta_F                 | GCGCGGCAATTG                                                                                                                           |
| MRE-Delta_R                 | ATTGCCGCGCGGCCCACTCTGTGCCCCC                                                                                                           |
| ERSEB-Delta_F               | TCCGCCCGCG                                                                                                                             |
| ERSEB-Delta_R               | GCGGGCGGAGCGCGGGGACC                                                                                                                   |
| API-Mut_F                   | TAAATGATTCCCGGCCCTG                                                                                                                    |
| API-Mut_R                   | CCGGAATCATTACCGGAAAAAACGAGTTG                                                                                                          |
|                             |                                                                                                                                        |
| HsPrnp-gRNA-U6-pLenti_F     | CTTGTGAAAAGGACGAAACACCGCTGGGGGCAGCCGATACCCG                                                                                            |
| HsPrnp-gRNA-U6-pLenti_R     | CTTGCTATTTCTAGCTCTAAAACCGGGTATCGGCTGCCCCCAGC                                                                                           |
| HsPrnp-API-gRNA1-U6-pgRNA_F | <b>CTATAAGTATCCCTTGGAGAACCGACTCATTCCCGGCCCTGCTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTTTTTC</b> |
| HsPrnp-API-gRNA1-U6-pgRNA_R | CTAATGGATCCTAGTACTCGA G AAAAAAAGCACCGACTCGGTGCCACTTTTTCAAGTTGATAACGGACTAGCCTATTTTAACTTGCTATTTCTAGCTCTAAAACAGCAGGGCCGGGAATGAGTC         |