

| Study | Cases | Total | Mutation Rate | 95% CI |
|-------|-------|-------|---------------|--------|
|-------|-------|-------|---------------|--------|

|                      |      |      |      |              |
|----------------------|------|------|------|--------------|
| Dimitriadis, K. 2014 | 167  | 253  | 0.66 | [0.60; 0.72] |
| Du, W. D. 2011       | 10   | 12   | 0.83 | [0.52; 0.96] |
| Kim, J. Y. 2003      | 46   | 60   | 0.77 | [0.64; 0.86] |
| Kirkman, M. A. 2009  | 132  | 196  | 0.67 | [0.60; 0.74] |
| Klopstock, T. 2011   | 57   | 85   | 0.67 | [0.56; 0.76] |
| Majander, A. 2017    | 13   | 27   | 0.48 | [0.30; 0.66] |
| Ramos Cdo, V. 2009   | 45   | 66   | 0.68 | [0.56; 0.78] |
| Spruijt, L. 2006     | 145  | 325  | 0.45 | [0.39; 0.50] |
| Ueda, K. 2017        | 38   | 44   | 0.86 | [0.73; 0.94] |
| Tonagel, F. 2021     | 18   | 22   | 0.82 | [0.60; 0.93] |
| Ishikawa, H. 2021    | 54   | 57   | 0.95 | [0.85; 0.98] |
| Marotta, R. 2020     | 52   | 76   | 0.68 | [0.57; 0.78] |
| Li, J. K. 2020       | 84   | 96   | 0.88 | [0.79; 0.93] |
| Ahn, Y. J. 2020      | 38   | 44   | 0.86 | [0.73; 0.94] |
| Poincenot, L. 2020   | 1044 | 1497 | 0.70 | [0.67; 0.72] |
| Zhao, X. 2020        | 29   | 33   | 0.88 | [0.72; 0.95] |
| Dokrungkoon, T. 2019 | 10   | 13   | 0.77 | [0.48; 0.92] |

**Random effects model**

**0.75 [0.67; 0.81]**

Heterogeneity:  $I^2 = 88\%$ ,  $\tau^2 = 0.4849$ ,  $\chi^2_{16} = 133.20$  ( $p < 0.01$ )

