Supplementary Table 1. The *MUTYH* variants of probands

|  |  |  |
| --- | --- | --- |
| Variant 1 | Variant 2 | No of probands |
| **Biallelic carriers** |  | **41** |
| c.1187G>A p.(Gly396Asp) | c.1187G>A p.(Gly396Asp) | 14 |
| c.536A>G p.(Tyr179Cys) | c.536A>G p.(Tyr179Cys) | 6 |
| c.1187G>A p.(Gly396Asp) | c.536A>G p.(Tyr179Cys) | 10 |
| c.1187G>A p.(Gly396Asp) | c.821G>A p.(Arg274Gln) | 1 |
| c.1187G>A p.(Gly396Asp) | c.933+3A>C p.(Gly264TrpfsX7) | 2 |
| c.536A>G p.(Tyr179Cys) | c.933+3A>C p.(Gly264TrpfsX7) | 1 |
| c.536A>G p.(Tyr179Cys) | c.721C>T p.(Arg241Trp) | 2 |
| c.536A>G p.(Tyr179Cys) | c.312 C>A p.(Tyr104Ter) | 1 |
| c.536A>G p.(Tyr179Cys) | c.1437\_1439delGGA p.(Glu480del) | 1 |
| c.536A>G p.(Tyr179Cys) | c.1147delC p.(Ala385ProfsTer23) | 2 |
| c.1171C>T p.(Gln391Ter) | c.1437\_1439delGGA p.(Glu480del) | 1 |
| **Monoallelic carriers** |  | **225** |
| c.1187G>A p.(Gly396Asp) |  | 153 |
| c.536A>G p.(Tyr179Cys) |  | 54 |
| c.821G>A p.(Arg274Gln) |  | 13 |
| c.1437\_1439delGGA p.(Glu480del) |  | 2 |
| c.1147delC p.(Ala385ProfsTer23) |  | 2 |
| c.933+3A>C p.(Gly264TrpfsX7) |  | 1 |

Supplementary Table 2. Verification of cancers diagnoses in the first- and second-degree relatives (combined) of probands

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Site of cancer | Pathology report | Medical record | Death certificate | Cancer registry | Self or relative report | Unknown | Total |
| Stomach | 2 | 0 | 2 | 3 | 45 | 1 | 53 |
| Hepatobiliary tract | 2 | 0 | 0 | 1 | 22 | 0 | 25 |
| Brain | 1 | 0 | 0 | 1 | 19 | 1 | 22 |
| Urinary bladder | 2 | 0 | 0 | 0 | 7 | 0 | 9 |
| Renal pelvis/Kidney | 1 | 0 | 1 | 2 | 11 | 0 | 15 |
| Pancreas | 0 | 1 | 0 | 1 | 7 | 1 | 10 |
| Ovary | 1 | 0 | 0 | 1 | 8 | 0 | 10 |
| Endometrium | 5 | 0 | 0 | 2 | 15 | 0 | 22 |
| Breast | 12 | 1 | 0 | 2 | 90 | 1 | 106 |
| Prostate | 9 | 0 | 0 | 5 | 49 | 0 | 63 |

Supplementary Table 3. Cumulative risks % (95% confidence interval) to age 70 years of extracolonic cancers for carriers of germline monoallelic and biallelic mutations in *MUTYH* living in Canada and Australia

|  |  |  |
| --- | --- | --- |
|  | Canada | Australia |
| Site of cancer | Males | Females | Males | Females |
| **Biallelic carriers** |  |  |  |  |
| Urinary bladder | 17 (3.7–63) | 5.7 (1.2–26) | 8.4 (1.7–36) | 2.7 (0.5–13) |
| Ovary |  | 15 (2.3–66) |  | 12 (1.8–57) |
| **Monoallelic carriers** |  |  |  |  |
| Stomach | 5.8 (4.2–8.0) | 2.4 (1.7–3.3) | 6.6 (4.8–9.1) | 2.9 (2.1–4.0) |
| Hepatobiliary tract | 2.3 (1.4–3.8) | 1.1 (0.7–1.9) | 2.3 (1.4–3.8) | 1.1 (0.7–1.8) |
| Endometrium |  | 3.2 (1.7–5.8) |  | 2.4 (1.3–4.4) |
| Breast |  | 11 (7.6–14) |  | 11 (7.7–15) |