

**Table S1 Cochran-Armitage Trend Test across each mutation load for age-related changes in cell population distributions.**

| <b>ISC mutation load</b> | <b>z-value<br/>(m.G5081A)</b> | <b>p.adjust<br/>(m.G5081A)</b> | <b>z-value<br/>(m.G12918A)</b> | <b>p.adjust<br/>(m.G12918A)</b> |
|--------------------------|-------------------------------|--------------------------------|--------------------------------|---------------------------------|
| mut ≤60%                 | 3.0415                        | 0.0059                         | 6.9315                         | <0.0001                         |
| 60% <mut ≤70%            | 1.0771                        | 0.1759                         | -4.0799                        | <0.0001                         |
| 70% <mut ≤80%            | -1.6623                       | 0.0804                         | -4.2533                        | <0.0001                         |
| 80% <mut ≤90%            | -2.0210                       | 0.0541                         | -1.9700                        | 0.0305                          |
| 90% <mut ≤100%           | 0.3873                        | 0.3493                         | -0.0916                        | 0.4635                          |