**Supplementary file 1**: HR-based repair was also able to rescue in somatic tissues like eye. High-level eye-antennal disc expression of both mito-BglII and mito-XhoI using ey-Gal4 at 29°C resulted in pupal lethality (headless pupa) in wild-type flies or in flies carrying mt genomes resistant to only one of the two enzymes. A few (about 1%) escapers eclosed and the majority of eclosed flies had no eye or small eye phenotype (rows 1 and 2). Having both genomes increased the eclosion rate to 10% (row 3) and most of the eclosed flies had normal sized eyes (not shown).

|  |  |  |  |
| --- | --- | --- | --- |
| Mitochondrial genotype | Total # of pupa | Total # of flies eclosed | % of flies eclosed |
| mt:CoIR301Q | 584 | 7 | 1.20 |
| mt:ND2del1 | 420 | 4 | 0.95 |
| mt:ND2del1/mt:CoIR301Q | 418 | 42 | 10.05 |