**Supporting Information Listing**

**Supplementary Figure 1. Insertion (A) and deletion (B) frequencies of early passage and deeply senescent cells.**

*P* values were estimated using the Wilcox Rank Sum test, two-tailed. Box plot elements are: center line, median; box limits, upper and lower quartiles; whiskers, 1.5× interquartile range; points, all data points.

**Supplementary Figure 2. Rainfall plot illustrating distances of neighboring mutations.** Mutations of single cells from each group were pooled in this analysis. (Top) Density of mutations in kilobase bins. Distances of each mutation to its closest other mutation.

**Supplementary Figure 3. Aneuploidy and large copy number variation in early passage single cells.**

Each panel indicates one single cell. Curved lines indicate normalized sequencing depth, and horizontal straight lines indicate estimated copy numbers. Of note, some parts of the genome do not have an estimated copy number. This is due to high fluctuation of sequencing depth in these regions, and the SCCNV pipeline did not report their copy numbers due to lack of statistical confidence. This is a typical problem of single-cell whole-genome amplification, and affects mainly copy number estimation. The arrow indicates a large copy deletion in chromosome 2 of a single cell.

**Supplementary Figure 4. Aneuploidy and large copy number variation in deep senescent single cells.**

The four black arrows indicate four aneuploidies observed in the single cells. In addition to the four events, cell “IMR90\_P38\_02\_10” has potentially a copy-number-loss on chromosome 22 (blue arrow), although it is not called by SCCNV due to the high fluctuation in sequencing depth in this single cell. The fluctuation of sequencing depth is a result of whole-genome amplification, which affects mainly copy number estimation.