



**Supplemental Figure S3. Schematic of an alternate SMASH method.** A) Three genomic DNA molecules, shown in different shades of green, are from different chromosomes or different locations of the same chromosome. B) By dsDNA fragmentase, these DNA molecules are fragmented into short double-stranded fragments with average length around 35 bp, as shown at right. C) The short DNA pieces are partially end-repaired and randomly combined into longer molecules of DNA with lengths ranging from 50 bp to 7 kb. Consequently, each DNA molecule contains several short DNA fragments from different regions of the genome. D) These DNA stretches are ligated with sequencing adaptors containing sample barcodes (shown as blue and red lines linked to the boxes labeled “barcode”). E) Size selection is carried out to enrich for DNA fragments from 250–700 bp. F) After a final PCR amplification, libraries are ready for sequencing. For the results shown at right, the x-axis represents the length of DNA fragments. “FU” in the Bioanalyzer plots refers to relative fluorescence units.