**Supplementary Methods**

**Library preparation, target capture and sequencing**

**SOLID 5500XL Genetic Analysis System (Life Technologies)**

The library preparation of samples to be sequenced in SOLID started by shearing three micrograms genomic DNA into 160 bp fragments on a S220 Focused-ultrasonicator (Covaris). The water temperature of the sonicator was set to 5oC before starting and then six cycles at 175 W peak power, 10 duty factor and 100 cycles/burst were performed. The water was let cooling down to 5ºC after each sample was sonicated. The fragments size was assessed using the High Sensitivity DNA kit (Agilent Technologies). Next steps of size-selection, end-polish, adenylation and ligation of adaptors were performed using the 5500 SOLiD Fragment Library Enzyme Module kit (Life Technologies). Manufacturer’s instructions were followed, but using half of the volume indicated in the protocol. The exome capture was performed using 62.5 ng from each of the eight purified barcoded ligated-libraries, which gave rise to 500 ng of pooled barcoded library. This pool was then amplified with 10 cycles of PCR and purified using the Agencourt AMPure XP magnetic beads in 25 µl of Low TE buffer. The exome pooled library was then clonally amplified by emulsion PCR following the SOLiD EZ bead E120 protocols (Life Technologies). A volume of 300 µl of emPCR beads were 3’ modified and deposited on 3 lanes of a FlowChip. The paired-end 50-35 bp reads chemistry was used for the sequencing.

The mapping and variant calling were performed using LifeScope™‘s low frequency variant detection (LFVD) workflows with the default parameters: 1) the color space reads generated by the SOLiD5500XL were mapped against the human genome reference version hg19 generating bam files which were then enriched for targets and good quality reads, 2) single-nucleotide variants (SNVs) were called on enriched bam. The Variant Call Format (VCF) output files were annotated and non-somatic variants filtered as described in the Materials and Methods section for the HiSeq2500 data.