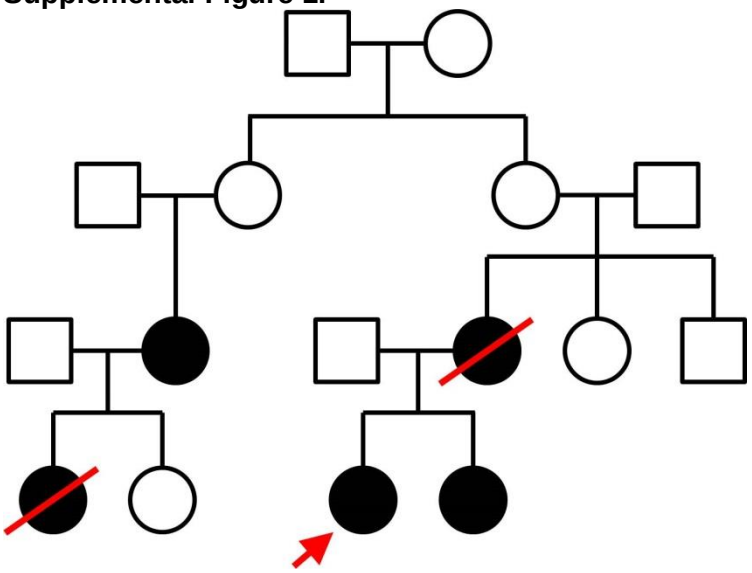
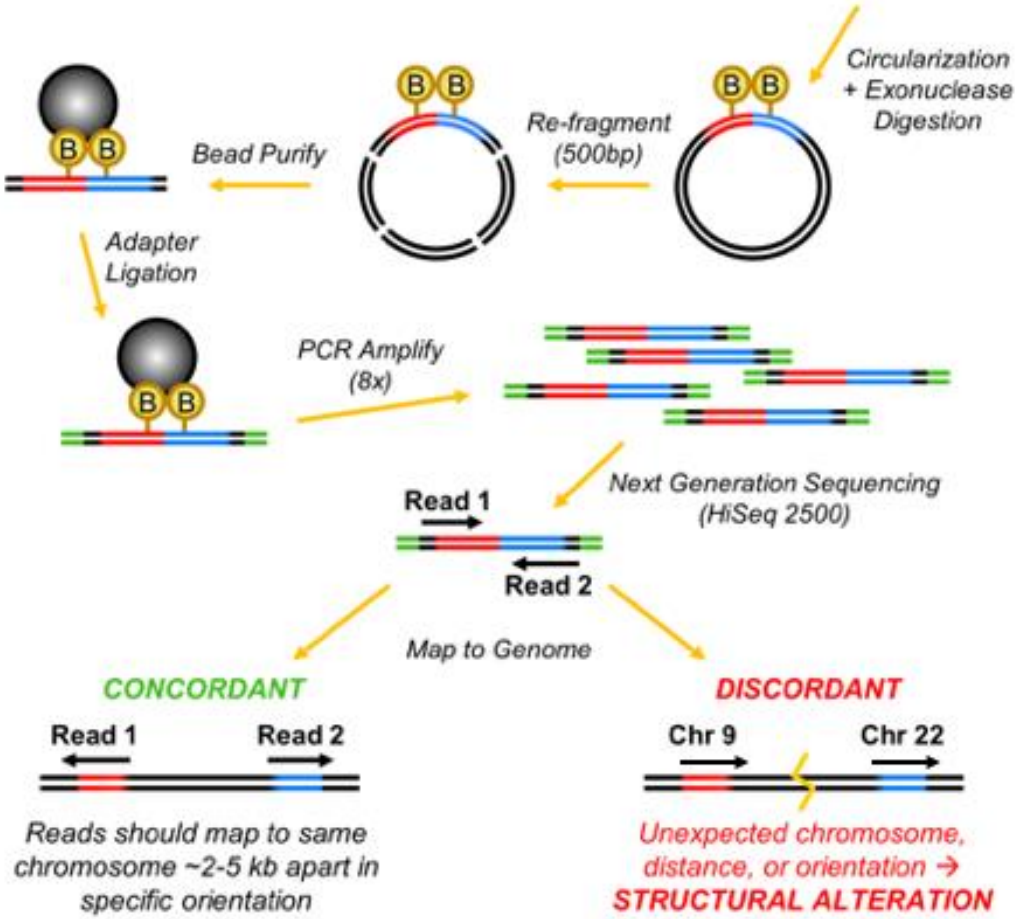
Supplementary material

Supplemental Figure 1.



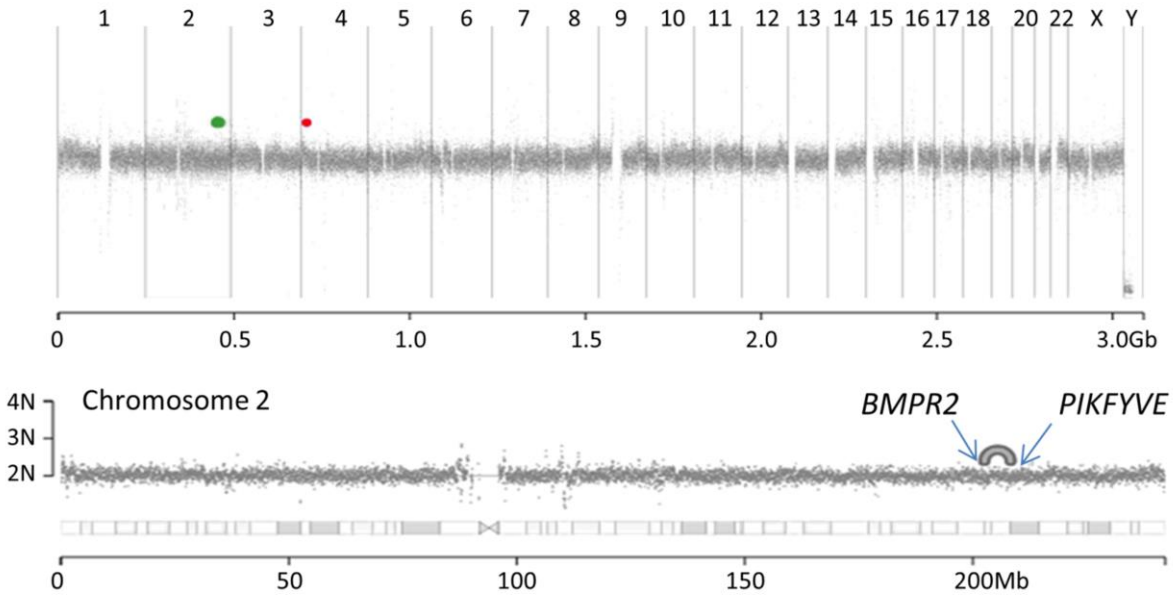
Family pedigree indicating autosomal dominant, sex-influenced inheritance of pulmonary arterial hypertension (black). Proband is indicated by the red arrow. History indicates an affected sister, mother (now deceased [red line]), first cousin once removed, and second cousin (now deceased [red line]).

Supplemental Figure S2.



MPseq fragment circularization. A) To make mate-pair libraries, DNA is fragmented to 2–5 kb pieces and the terminal ends are labeled with biotin. These fragments are circularized and re-fragmented to smaller 500 bps pieces. A capture step selects the biotin labeled fragments and these ends are then sequenced. B) The red and blue represents the 101 bps reads that are sequenced, and the mapped strand orientation of that read, red for reverse strand, blue for forward strand. This long insert size gives MPseq the ability to detect structural variants with less sequencing (cheaper) than traditional whole-genome sequencing with paired-end sequencing.

Supplemental Figure S3.



Linear genome plot from MPseq of patient germline DNA. Read coverage in 30kb window sizes (grey dots) across genome displayed horizontally and sequentially for chromosomes 1-22, X and Y. Normal diploid 2N level predicted across the genome. A structural variant is predicted on chromosome 2 (green marker) which is expanded in the lower image to reveal a genomic rearrangement with junctions hitting the *BMP2R* and *PIKYVE* genes. An additional unique germline structural variant which passes algorithmic filters is observed on chromosome 4p15.32 (red marker) involving a tandem duplication of 30kb of DNA in a non-coding region of the genome.