**Experimental Procedure of the Whole Exome Sequencing**

1. **DNA Extraction**
   * Extract DNA using the magnetic bead-based method (931236，QIAGEN QIAsymphony DNA Mini kit, Germany) with a nucleic acid extraction and purification analyzer (QIAsymphony SP, QIAGEN, Germany).
   * Measure the DNA concentration using a microplate reader (Infinite 200 pro, Tecan, Switzerland). Only use DNA samples with a concentration of ≥10 ng/μL for subsequent experiments.
2. **Library Construction**
   * Digest 100 ng of the qualified DNA using a DNA library construction kit (180479, QIAGEN QIAseq FX DNA Library Kit, Germany), followed by end-repair and addition of an A-base.
   * Add 2 μL of Index Adapter for ligation.
   * Purify the ligated products and perform fragment selection using 0.8×AMPure XP beads (A63882, Beckman, USA).
   * Conduct PCR amplification under the following conditions:

[98°C, 2 min]; [98°C, 20 s; 60°C, 30 s; 72°C, 30 s] for 10 cycles; [72°C, 1 min]; [10°C, ∞].

* + Purify the PCR products using 1×AMPure XP beads (A63882, Beckman, USA) to complete the library construction.
  + Ensure the library concentration is ≥10 ng/μL. Use an Agilent 2100 Bioanalyzer (DNA 1000 Kit) to verify that the library fragment size ranges from 300 to 500 bp.

1. **Target Region Capture**
   * Use the Nuoandachip capture magnetic beads and hybridization-elution kit (1005101, Nuoandachip, China) to capture the whole-exome target regions.
2. **Target Region Amplification**
   * Amplify the captured target regions by PCR using a high-fidelity DNA polymerase (KK2621, KAPA, USA) with a product concentration of ≥10 ng/μL.

The PCR amplification conditions are as follows:

[98°C, 45 s]; [98°C, 15 s; 65°C, 30 s; 72°C, 30 s] for 8 cycles; [72°C, 1 min]; [10°C, ∞].

1. **Sequencing**
   * Perform paired-end 150-bp (Pair End 150bp) sequencing in high-throughput mode on a Novaseq 6000 sequencer (Illumina, USA).
2. **Bioinformatics analysis**

After sequencing, the raw data were saved as a FASTQ format, then followed the bioinformatics analysis: First, Illumina sequencing adapters and low-quality reads (<80bp) were filtered by cutadapt. After quality control, the clean reads were mapped to the UCSC hg19 human reference genome using Burrows-Wheeler Aligner software. Duplicated reads were removed using picard tools and mapping reads were used for variation detection. Second, the variants of SNP and InDel were detected by GATK Haplotype Caller, then using GATK Variant Filtration to filter variant. After above two steps, the data would be transformed to VCF format, variants were further annotated by ANNOVAR and associated with multiple databases, such as,1000 genome, ESP6500, dbSNP , EXAC, Inhouse, HGMD, and predicted by SIFT, PolyPhen-2, MutationTaster, GERP++.