The American Journal of Human Genetics, Volume *104*

Supplemental Data

Lessons Learned from Large-Scale, First-Tier Clinical Exome Sequencing in a Highly Consanguineous Population

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Figure S1. Flash WES protocol.

Summary of the steps and timing of FLASH WES resulting in an interval of 26 hours between consent and delivery of a provisional clinical report. Rapid DNA extraction was performed using the PureLink Genomic DNA kit (Thermo Fisher, Carlsbad, CA, USA) as recommended by manufacturer (https://www.thermofisher.com/document-connect/document-connect.html?url=https://assets.thermofisher.com/TFS-Assets/LSG/manuals/purelink_genomic_man.pdf). Library preparation, emulsion PCR, enrichment and sequencing were performed using the Ion Torrent AmpliSeq Whole Exome Sequencing protocol (https://www.thermofisher.com/sa/en/home/life-science/sequencing/dna-sequencing/exome-sequencing/exome-sequencing-ion-torrent-next-generation-sequencing.html). Sequence alignment, indexing of the reference genome (hg19), variant calling and annotation used a pipeline based on BWA, Samtools, GATK (https://software.broadinstitute.org/gatk/) and Annovar, respectively. Essentially, variants were annotated using a combination of public knowledge databases available from the Annovar package and in-house databases which included collections of previously published Saudi disease causing variants.

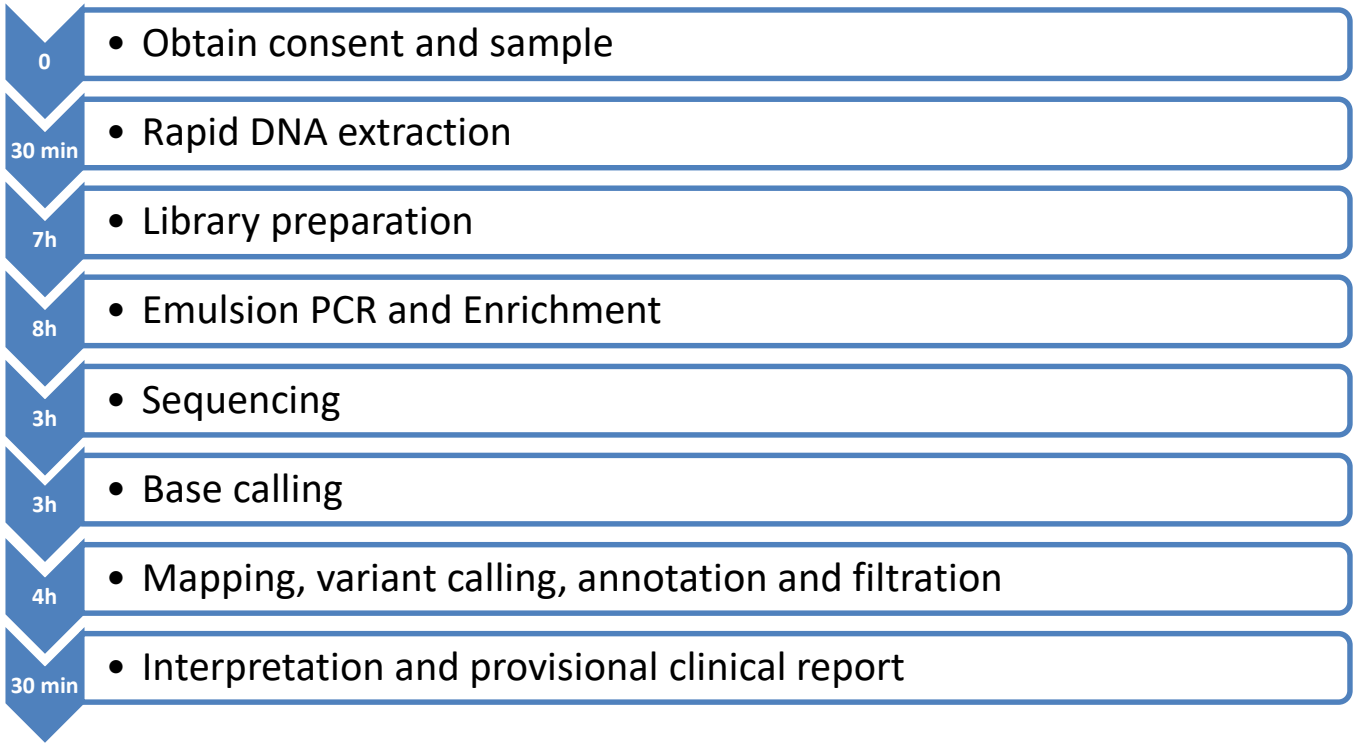

Figure S2. Carrier status for KSM (known Saudi mutations).

A) Distribution of KSM carrier status in the cohort. B) Distribution of shared KSM carrier status among couples.