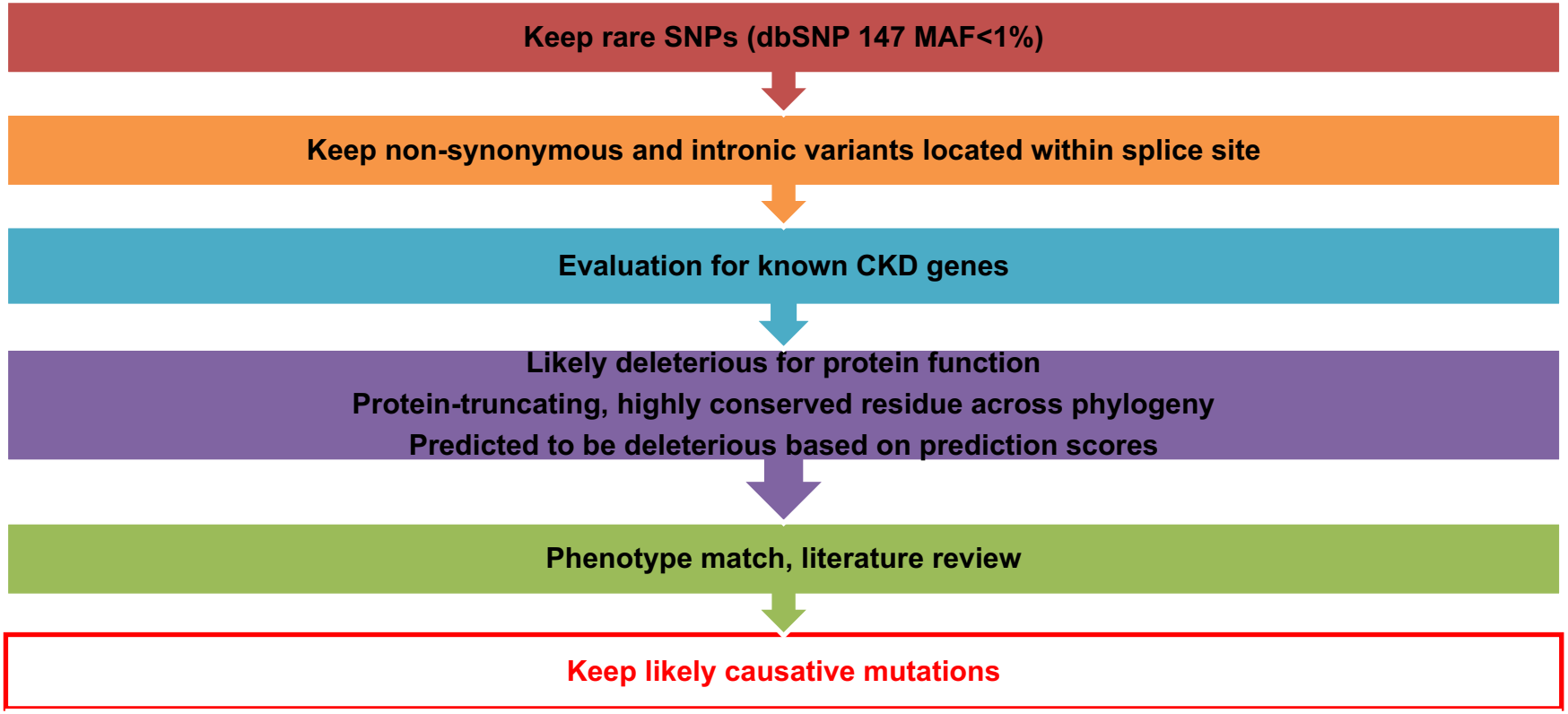

Supplementary Figure S3. Variant filtering process for the identification of pathogenic mutations in genes known to cause chronic kidney disease (CKD)

Schematic overview of the workflow used for filtering of WES data.

i. Keep rare variants present with a minor allele frequency (MAF) <1% in healthy control cohorts **dbSNP147** (https://www.ncbi.nlm.nih.gov/projects/SNP).
ii. Keep non-synonymous variants and intronic variants that are located within splice sites.
iii. Applying known gene approach by selecting all variants detected in known CKD genes (**Suppl. Table 6-13**).
iv. Ranking of remaining variants based on their predicted likelihood to be deleterious for the function of the encoded protein using **Polyphen 2** (http://genetics.bwh.harvard.edu/pph2, **SIFT** (http://sift.jcvi.org/) and **Mutation Taster** (http://www.mutationtaster.org)
v. Reviewing literature and review with referring physician delineating whether the detected mutation matches the phenotype.
vi. Cross reference with the ACMG guidelines to determine if pathogenic, likely pathogenic or a variant of uncertain significance.