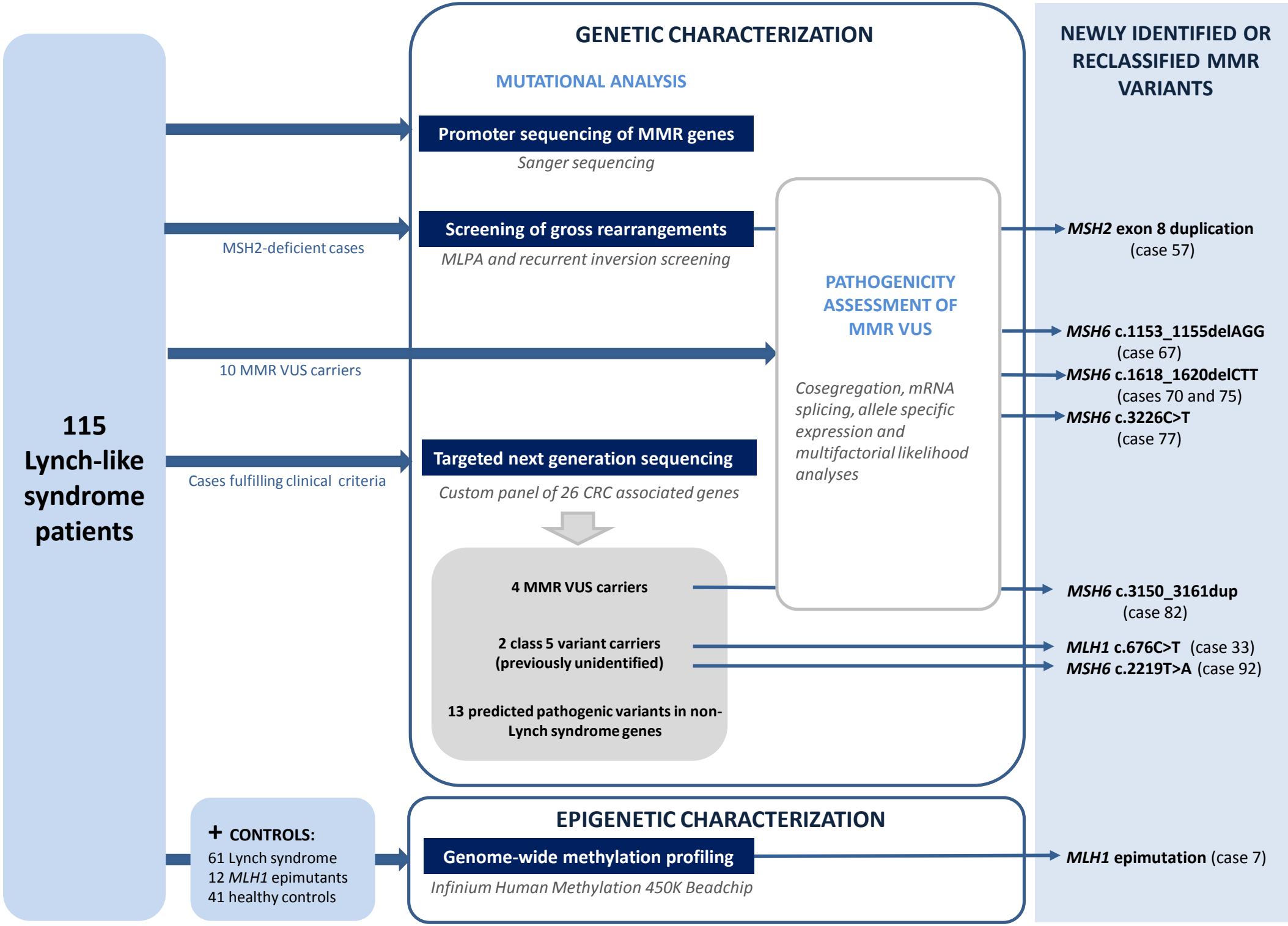
115 Lynch-like syndrome patients
GENETIC CHARACTERIZATION
MUTATIONAL ANALYSIS
Promoter sequencing of MMR genes
Sanger sequencing
MSH2-deficient cases
Screening of gross rearrangements
MLPA and recurrent inversion screening
10 MMR VUS carriers
Cases fulfilling clinical criteria
Targeted next generation sequencing
Custom panel of 26 CRC associated genes
4 MMR VUS carriers
2 class 5 variant carriers (previously unidentified)
13 predicted pathogenic variants in non-Lynch syndrome genes
PATHOGENICITY ASSESSMENT OF MMR VUS
Cosegregation, mRNA splicing, allele specific expression and multifactorial likelihood analyses
NEWLY IDENTIFIED OR RECLASSIFIED MMR VARIANTS
MSH2 exon 8 duplication (case 57)
MSH6 c.1153_1155delAGG (case 67)
MSH6 c.1618_1620delCTT (cases 70 and 75)
MSH6 c.3226C>T (case 77)
MSH6 c.3150_3161dup (case 82)
MLH1 c.676C>T (case 33)
MSH6 c.2219T>A (case 92)
+ CONTROLS:
61 Lynch syndrome
12 MLH1 epimutants
41 healthy controls
EPIGENETIC CHARACTERIZATION
Genome-wide methylation profiling
Infinium Human Methylation 450K Beadchip
MLH1 epimutation (case 7)