# Germline susceptibility variants impact clinical outcome and therapeutic strategies for stage III colorectal cancer

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**Supplementary information**

**Supplementary Figure S1.** Workflow for variant discovery and ClinVar annotations. Detailed description in Materials and Methods.

**Supplementary Figure S2.** Patients with or without cancer-associated genetic variants and their family cancer history pedigrees.

**Supplementary Figure S3.** Mutational signature in patients with cancer-associated genetic variants (CAG(+)) or without cancer associated genetic variants (CAG(-)).

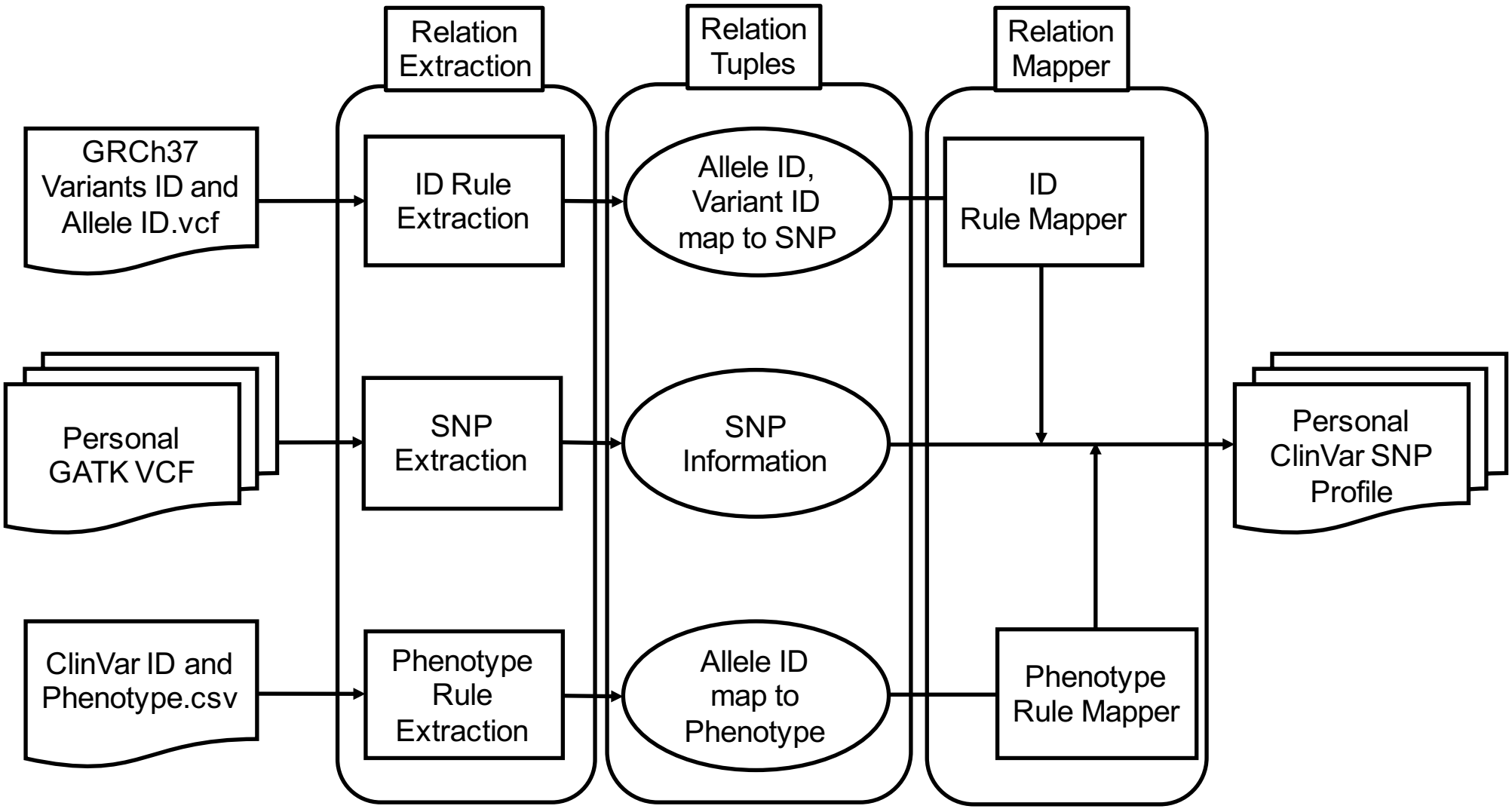
**Supplementary Table 1.** Patients' clinical characteristics.

**Supplementary Table 2.** ACMG SF v2.0 genetic variants in cancer patients and normal subjects.

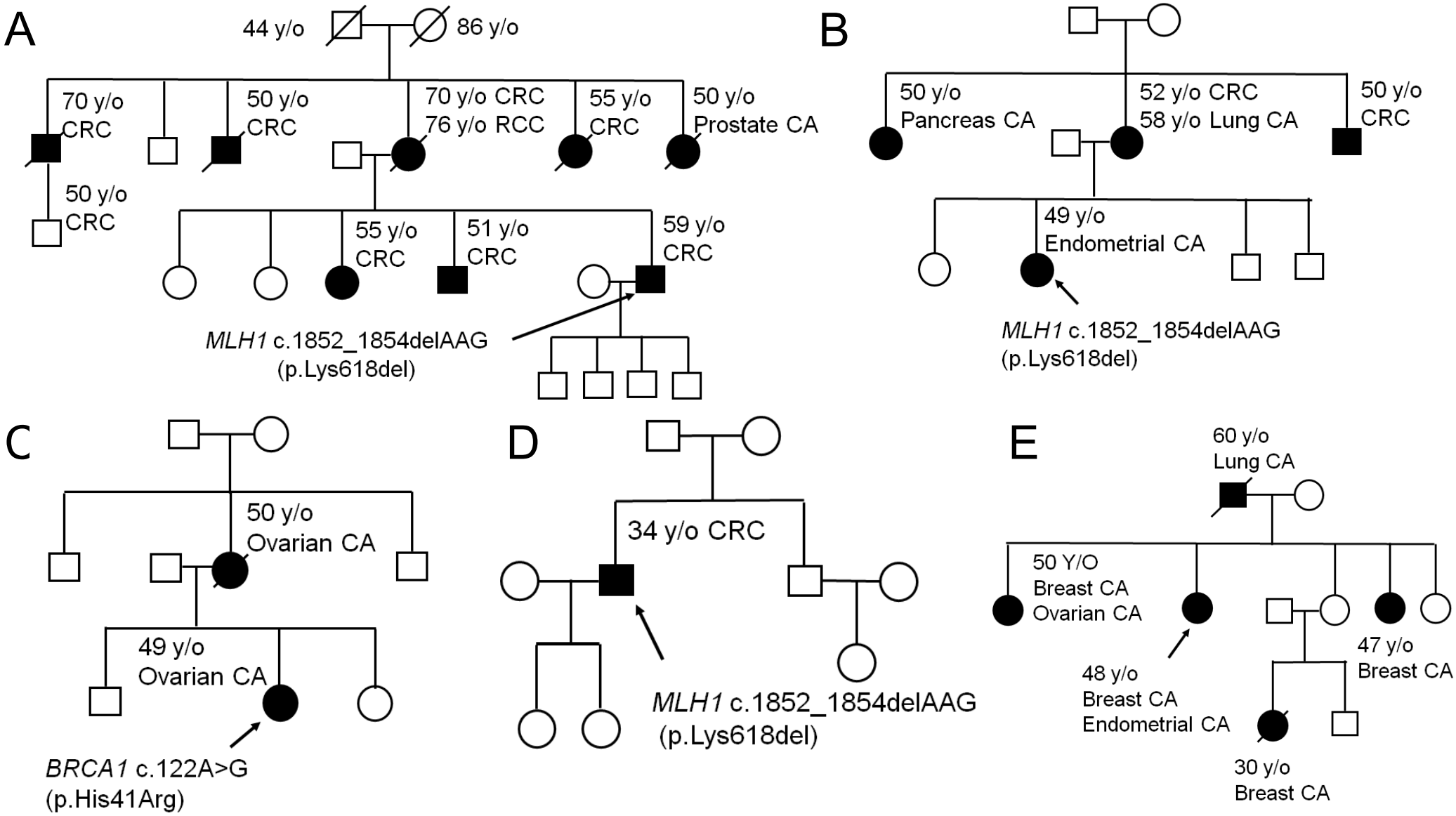
**Supplementary Table 3.** Ethnic-specific genetic variants in cancer patients and normal subjects.

**Supplementary Table 4.** Germline cancer-associated genetic variants in cancer patients.

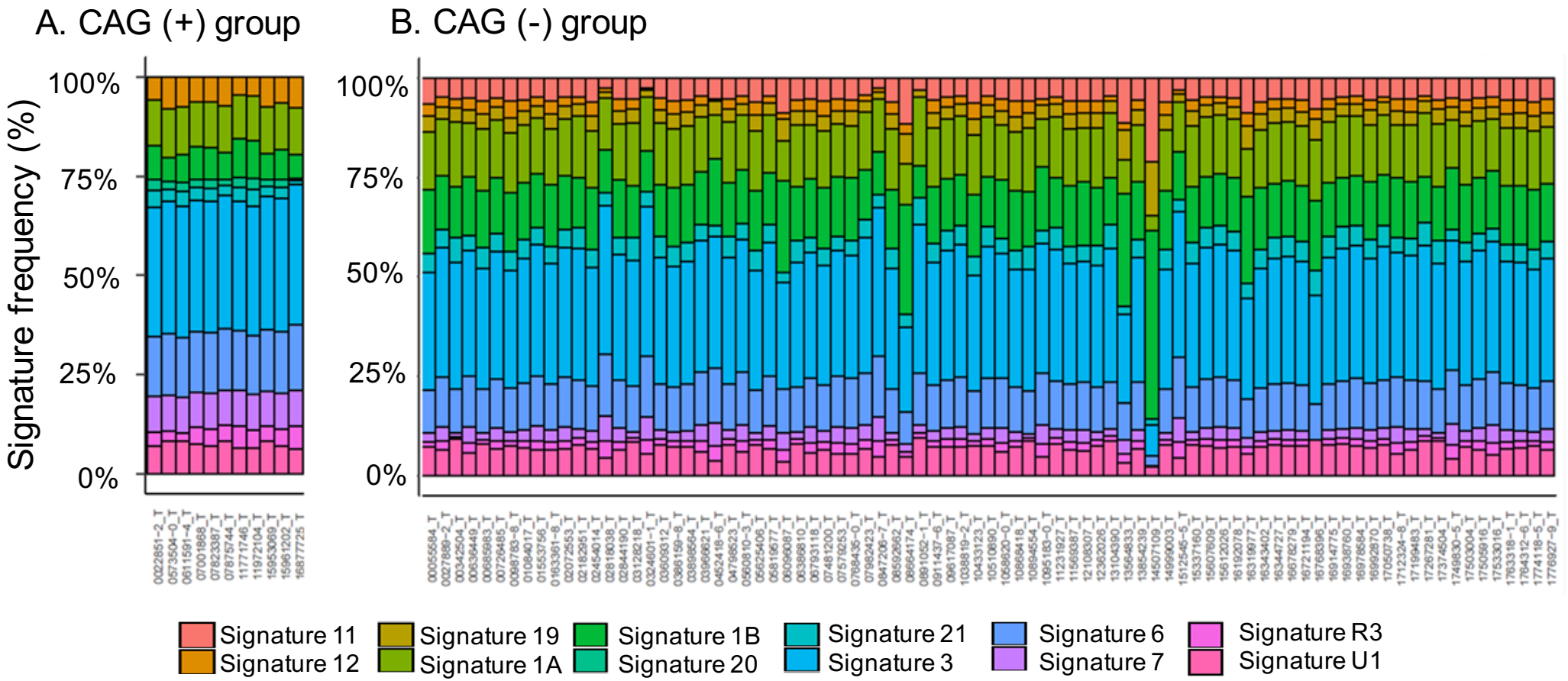
**Supplementary Table 5.** Primary and recurrent tumor mutation variant allele frequency (VAF) and clusters.




**Supplementary Figure S1.** Workflow for variant discovery and ClinVar annotations. Detailed description in Materials and Methods.




**Supplementary Figure S2**. Patients with or without cancer-associated genetic variants and their family cancer history pedigrees. Lynch syndrome was diagnosed in (A) one CRC patient and (B) one endometrial cancer patient. Both patients had a germline pathogenic variant of MLH1 c.1852_1854delAAG. (C) A germline pathogenic variant of BRCA1 c.122A>G was detected in one ovarian cancer patient. (D). A MLH1 pathogenic variant was detected in one CRC patient without cancer family history. (E) No well-known cancer-associated genetic variants is identified. Arrows indicate the patients enrolled in this study. A square represents a male and a circle represents a female. A solid square or circle indicates the person has cancer.




**Supplementary Figure S3**. Mutational signature in patients with cancer-associated genetic variants (CAG(+)) or without cancer associated genetic variants (CAG(-)). Mutational signature frequency (y-axis) in individual cancer patients (x-axis). Each color indicates a different mutational signature. Signatures 1B, 11, and 19 are predominant in patients without cancer-associated genetic variants.

**Supplementary table 1. Patients' clinical characteristics**

| Characteristics | Patients number (%) |
|---|---|
| Total | 159 (100) |
| Median age, y/o (range) | 57 (23-82) |
| Gender | |
| Male | 54 (34) |
| Female | 105 (66) |
| Tumor type | |
| Colorectal | 104 (65.4) |
| Ovarian | 31 (19.5) |
| Endometrial | 24 (15.1) |
| Cancer family history | |
| No relatives | 77 (48.4) |
| First-degree relatives | 63 (39.6) |
| Second-degree relatives | 19 (11.9) |