**Supplementary Figure 2**

1. **Raw fastq files**
   - Alignment, trimming, deduplication, preliminary variant calling

2. **Inclusion of:**
   - Oncogenes
   - Drivers
   - Passengers with deleterious effect

3. **Exclusion of individual germline variants**

4. **FFPE**
   - Exclusion of:
     - Silent/synonymous
     - FFPE artefacts
     - Common SNPs (MAF > 0.02)
     - AF < 0.05
     - Total reads ≤ 30
     - Altered reads:
       - Single-read
       - (FWD x REV) < 8

5. **cfDNA & CTCs**
   - Exclusion of:
     - Silent/synonymous
     - Common SNPs (MAF > 0.02)
     - AF (cfDNA) < 0.05
     - Total reads ≤ 30
     - Altered reads:
       - Single-read
       - < 5

6. **VARIANT CALLING**
    - Identification of concordant and discordant variants

7. **ANALYSIS**
   - Manual inspection of discordant variants

**AGILENT SURECALL SOFTWARE**

**COSMIC & CGI DATABASES**