

06 October 2025

Dear Egon Álvarez,

Thank you for your successful participation in the *TP53* Analysis Certification Program (Round 15). Each participating laboratory received five DNA samples from patients with chronic lymphocytic leukemia (CLL) for *TP53* mutation analysis and result reporting. Individual samples and variants described according to HGVS nomenclature are depicted below.

Sample overview

| Sample | Variants | VAF* |
|----------|--------------------------------------|-------|
| ERIC15-1 | c.742C>T p.(Arg248Trp) | 14.0% |
| ERIC15-2 | c.314del p.(Gly105AlafsTer18) | 73.1% |
| | c.375+5G>T p.? | 26.1% |
| ERIC15-3 | c.559+1G>T p.? | 99.5% |
| ERIC15-4 | <i>Wild-type</i> | |
| ERIC15-5 | c.614A>G p.(Tyr205Cys) | 57.6% |
| | c.400T>C p.(Phe134Leu) | 5.0% |
| | c.517G>A p.(Val173Met) | 3.9% |
| | c.716A>T p.(Asn239Ile) | 2.7% |
| | c.742C>T p.(Arg248Trp) | 2.8% |
| | c.818G>A p.(Arg273His) | 2.5% |
| | c.537_539dup p.(His179_Glu180insAsp) | 1.4% |
| | c.537T>A p.(His179Gln) | 1.0% |
| | c.524G>A p.(Arg175His) | 0.3% |

Common polymorphisms c.215C>G p.(Pro72Arg) and c.639A>G p.(Arg213=) are not depicted.

Variants detected by the reference laboratory and at least one participant of Round 15 are shown.

*Variant allele frequencies (VAF) represent median values reported by participants using next-generation sequencing.

Your results

Below you find your individual results along with comments on specific samples and your performance. A detailed summary of all samples and an anonymized comparison of results from all participating laboratories are included in the supplementary section of this letter.

| | Your result | Minimal requirements |
|---|-------------|----------------------|
| Correct identification of all TP53 variants above your limit used for reporting (excluding common SNPs) | ✓ | ✓ |
| Correct result interpretation | ✓ | ✓ |
| Providing lab specific report | ✓ | ✓ |
| Covering at least exon 4-10 | ✓ | ✓ |
| Correct variant description | ✓ | X |

Comments

Sample 2: Please note that according to HGVS nomenclature, the recommended format of deletion is "prefix" "position(s)_deleted" "del", e.g., c.314del. It is not recommended to describe the deleted sequence; it is redundant information.

General comment: The missense variants in Samples 1 and 5 were described as "activating". Although many pathogenic missense variants in TP53 gene gain additional oncogenic functions ("gain-of-function") their most important effect is the loss of function, particularly the loss of ability to activate transcription of target genes. We do not recommend to use term "activating mutations" in case of TP53 gene.



Prof. Paolo Ghia



Dr. Sarka Pavlova



Dr. Jitka Malcikova