**IG Report Examples file** 

[Report of a mutated case]

Name of the Hospital/Lab

## **Determination of IGHV gene SHM status**

Date of result: Date of sample collection: 22/01/2022 09/01/2022

Patient name: \*\*\* Diagnosis: CLL Tissue type: blood Molecule type: genomic DNA

#### Utilized methodology

PCR amplification of IGHV-IGHD-IGHJ gene rearrangements with leader primers. Genescan analysis Bidirectional Sanger sequencing Immunoinformatics analysis: IMGT/V-QUEST

**Result:** a productive IGHV3-30\*01/IGHD6-13\*01/IGHJ4\*02 gene was detected. The rearranged IGHV gene had 96.82% nucleotide identity with the germline sequence of the IGHV3-30\*01 gene.

**Interpretation:** following the 98% germline identity cut-off value which is used for discriminating CLL cases into the IG-mutated or IG-unmutated category, this case belongs to the IG-mutated category which is generally associated with favorable prognosis.

[Report of an unmutated case]

Name of the Hospital/Lab

## **Determination of IGHV gene SHM status**

Date of result: Date of sample collection: 22/01/2022 09/01/2022

Patient name: \*\*\* Diagnosis: CLL Tissue type: blood Molecule type: genomic DNA

### Utilized methodology

PCR amplification of IGHV-IGHD-IGHJ gene rearrangements with leader primers. Genescan analysis Bidirectional Sanger sequencing Immunoinformatics analysis: IMGT/V-QUEST

**Result:** a productive IGHV1-69\*01/IGHD1-2\*01/IGHJ6\*01 gene was detected. The rearranged IGHV gene had 99.56% nucleotide identity with the germline sequence of the IGHV1-69\*01 gene.

**Interpretation:** following the 98% germline identity cut-off value which is used for discriminating CLL cases into the IG-mutated or IG-unmutated category, this case belongs to the IG-unmutated category which is generally associated with adverse prognosis and poor response to chemo(immuno)therapy.

[Report of a borderline unmutated case]

Name of the Hospital/Lab

# **Determination of IGHV gene SHM status**

Date of result: Date of sample collection: 22/01/2022 09/01/2022

Patient name: \*\*\* Diagnosis: CLL Tissue type: blood Molecule type: genomic DNA

### Utilized methodology

PCR amplification of IGHV-IGHD-IGHJ gene rearrangements with leader primers. Genescan analysis Bidirectional Sanger sequencing Immunoinformatics analysis: IMGT/V-QUEST

**Result:** a productive IGHV3-33\*01/IGHD3-22\*01/IGHJ4\*02 gene was detected. The rearranged IGHV gene had 97.3% nucleotide identity with the germline sequence of the IGHV3-33\*01 gene.

**Interpretation:** following the 98% germline identity cut-off value which is used for discriminating CLL cases into the IG-mutated or IG-unmutated category, this case belongs to the IG-mutated category. However, the identity percentage is close to the 98% cut-off and, thus, the case can be considered as borderline-mutated. In such cases, caution is warranted regarding the precise prognostic implications.

[Report of a subset #2 case]

Name of the Hospital/Lab

## **Determination of IGHV gene SHM status**

Date of result: Date of sample collection: 22/01/2022 09/01/2022

Patient name: \*\*\* Diagnosis: CLL Tissue type: blood Molecule type: genomic DNA

#### Utilized methodology

PCR amplification of IGHV-IGHD-IGHJ gene rearrangements with leader primers. Genescan analysis Bidirectional Sanger sequencing Immunoinformatics analysis: IMGT/V-QUEST

**Result:** a productive IGHV3-21\*01/IGHD: not determined/IGHJ6\*02 gene was detected. The rearranged IGHV gene had 96.12% nucleotide identity with the germline sequence of the IGHV3-21\*01 gene.

**Interpretation:** following the 98% germline identity cut-off value which is used for discriminating CLL cases into the IG-mutated or IG-unmutated category, this case belongs to the IG-mutated category. However, this particular rearrangement belongs to stereotyped subset #2 which is associated with adverse prognosis and poor response to chemo(immuno)therapy regardless of the somatic hypermutation status (Baliakas et al. Blood 2015; Jaramillo et al. Haematologica 2020).

[Report of a subset #8 case]

Name of the Hospital/Lab

## **Determination of IGHV gene SHM status**

Date of result: Date of sample collection: 22/01/2022 09/01/2022

Patient name: \*\*\* Diagnosis: CLL Tissue type: blood Molecule type: genomic DNA

### Utilized methodology

PCR amplification of IGHV-IGHD-IGHJ gene rearrangements with leader primers. Genescan analysis Bidirectional Sanger sequencing Immunoinformatics analysis: IMGT/V-QUEST

**Result:** a productive IGHV4-39\*01/IGHD6-13\*01/IGHJ5\*02 gene was detected. The rearranged IGHV gene had 100% nucleotide identity with the germline sequence of the IGHV4-39\*01 gene.

**Interpretation:** following the 98% germline identity cut-off value which is used for discriminating CLL cases into the IG-mutated or IG-unmutated category, this case belongs to the IG-unmutated category. Furthermore, this particular rearrangement belongs to stereotyped subset #8 which is associated with the highest risk for Richter's transformation among all CLL (Rossi et al. Clinical Cancer Research 2009).