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Acute myeloid leukaemia (AML)

The "AML" NGS panel includes the analysis of 41 genes: *ASXL1/BCOR/BCORL1/BRAF/CALR/CBL/CEBPA/CSF3R/DNMT3A/ETNK1/ETV6/EZH2/FLT3/GATA2/GNB1/HRAS/IDH1/IDH2/JAK2/KIT/KMT2A-MLL/KRAS/MPL/NF1/NPM1/NRAS/PHF6/PPM1D/PRPF8/PTPN11/RUNX1/SETBP1/SF3B1/SRSF2/STAG2/TET2/TP53/UBA1/U2AF1/WT1/ZRSR2.*

It can be used in the three areas of **diagnosis, prognosis** and **theranostics** and must be associated with a cytogenetic study to classify an AML and define its prognosis.

- Two classifications exist for an AML **diagnosis** with mutational data: the WHO 2022 classification and the ICC/ELN 2022 classification.
  - WHO 2022: the *NPM1* and *CEBPA* mutational status is used to define 2 entities of "AML with defining genetic abnormalities".

    Rq : for *CEBPA*, the concepts of biallelic mutations (whatever the type of mutation) (biCEBPA) or a monoallelic mutation of the bZIP domain (smbZIP-CEBPA) are retained.

  - ICC/ELN 2022: the *NPM1*, *CEBPA* and *TP53* mutational status is used to define 3 entities of "AML with defining genetic abnormalities".

    Rq : for CEBPA, it is exclusively a bZIP domain mutation (monoallelic or biallelic).

  For both classifications, in the context of "AML with defining genetic abnormalities", 10% of blasts are sufficient (and no longer 20%) to make the diagnosis of AML (exception: for WHO 2022: 20% for *CEBPA* and *BCR::ABL1* and whatever the percentage of blasts for NPM1 - for ICC/ELN 2022: 20% for *TP53* and *BCR::ABL1)*.

  For the entity "AML, myelodysplasia-related", in addition to the search for defined cytogenetic abnormalities, analysis of mutations in the following 8 genes must be performed according to WHO 2022: *ASXL1, BCOR, EZH2, STAG2, SF3B1, SRSF2, U2AF1* and *ZRSR2.* The ICC/ELN 2022 also includes a 9th gene: *RUNX1*.

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- The AML NGS panel also provides **prognostic** support (ICC/ELN 2022 recommendations) by allowing the definition of molecular factors for a favorable, intermediate or unfavorable prognosis:
  - Favorable :
    - *NMP1* mutation without *FLT3-ITD* mutation
    - monoallelic or biallelic mutation of the bZIP domain of *CEBPA*
  - Intermediate :
    - *FLT3-ITD* mutation (irrespective of allelic ratio) with or without *NPM1* mutation.
  - Unfavorable :
    - *TP53* mutation (VAF of at least 10%), frequently associated with a complex karyotype.
    - *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1* or *ZRSR2* mutations. These markers should not be used as an adverse prognostic marker if they co-occur with favorable-risk AML subtypes.

  Rq : FLT3-ITD/FLT3wt ratio is no longer used.

- In **theranostic**, testing for *FLT3* mutation is already a prerequisite for a targeted treatment. IDH1, IDH2 and TP53 mutations may also represent therapeutic targets.

The "AML" NGS panel therefore allows exhaustive analysis of somatic mutations reported in AML. It is not suitable for searching for germline mutations.

As a reminder, cellular haematology, cytogenetic and molecular biology data must be compared for a diagnosis and/or prognosis of haematological malignancy

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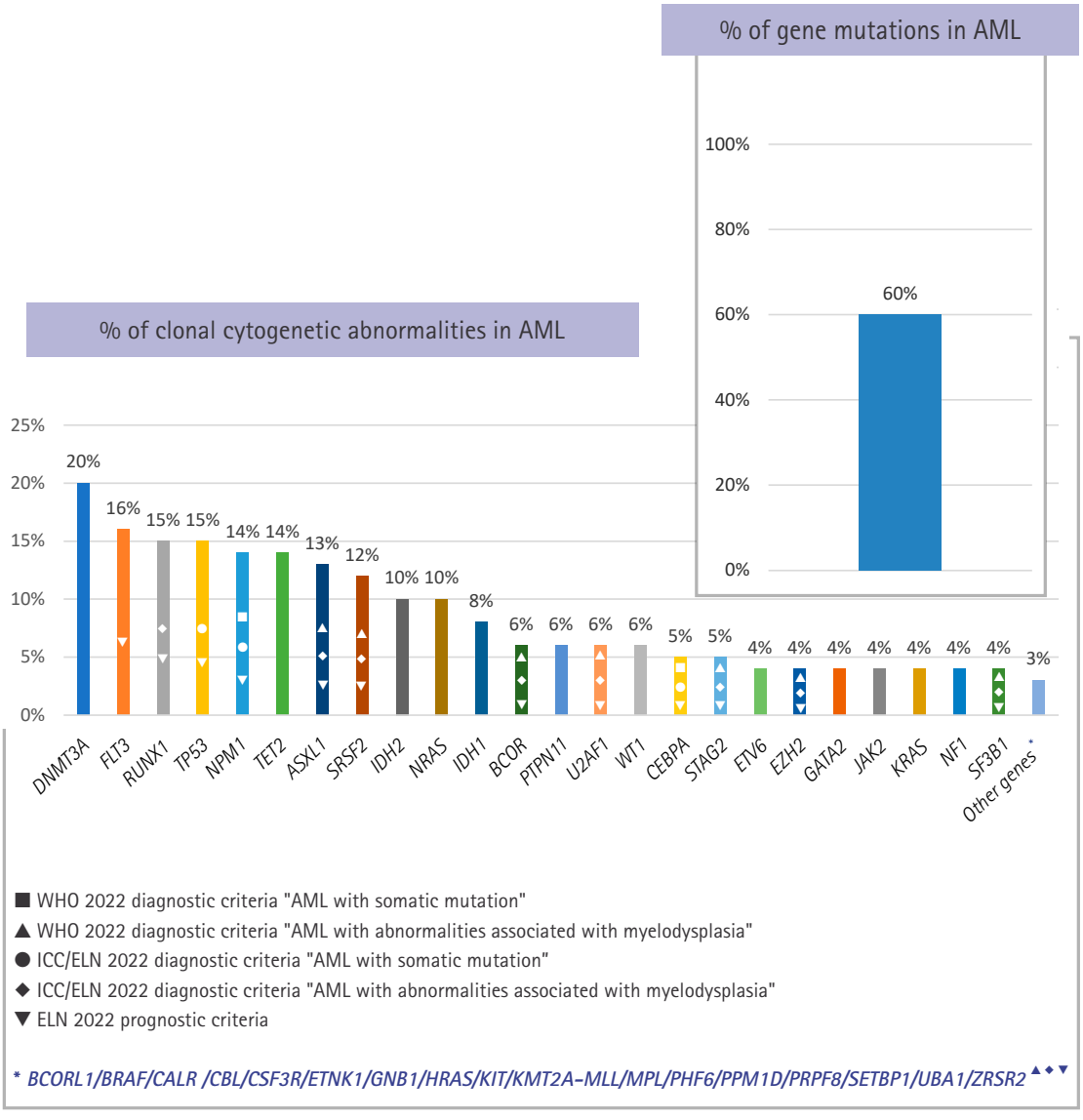
Gene mutations and clonal cytogenetic abnormalities in AML



Source : www.mycancergenome.org

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“AML” NGS Panel –Targeted genes

Gene	Transcript NM	Exon rank
ASXL1	NM_015338	Full coding region
BCOR	NM_017745	Full coding region
BCORL1	NM_021946	Full coding region
BRAF	NM_004333	Full coding region
CALR	NM_004343	Full coding region
CBL	NM_005188	Full coding region
CEBPA	NM_004364	Full coding region
CSF3R	NM_000760	Full coding region
DNMT3A	NM_022552	Full coding region
ETNK1	NM_018638	Full coding region
ETV6	NM_001987	Full coding region
EZH2	NM_004456	Full coding region
FLT3	NM_004119	Full coding region
GATA2	NM_032638	Full coding region
GNB1	NM_002074	Full coding region
HRAS	NM_176795	Full coding region
IDH1	NM_005896	Full coding region
IDH2	NM_002168	Full coding region
JAK2	NM_004972	Full coding region
KIT	NM_000222	Full coding region
KMT2A MLL	NM_001197104	Full coding region
KRAS	NM_033360	Full coding region
PHF6	NM_005373	Full coding region
PPM1D	NM_000267	Full coding region
PRPF8	NM_002520	Full coding region
PTPN11	NM_002524	Full coding region
RUNX1	NM_032458	Full coding region
SETBP1	NM_003620	Full coding region
SF3B1	NM_006445	Full coding region
SRSF2	NM_003016	Full coding region
STAG2	NM_001042749	Full coding region
TET2	NM_001127208	Full coding region
TP53	NM_000546	Full coding region
U2AF1	NM_006758	Full coding region
UBA1	NM_003334.4	Full coding region
WT1	NM_024426	Full coding region
ZRSR2	NM_005089	Full coding region

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Test code : MYSLA

Pre-analytical requirements : EDTA whole blood or bone marrow

Turnaround time : 10 days (Results may require an extended turnaround time of one week, depending on the confirmation tests required by Sanger sequencing).

Contact

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