

Analysis of *DNMT3A* Epimutation

Mutations in AML

Acute myeloid leukemia (AML) is frequently associated with genomic mutations in the DNA-methyltransferase 3A gene (*DNMT3A*), which encodes a major modifier of the DNA-methylation pattern. This mutation is usually associated with poor prognosis indicating that mutations in *DNMT3A* contribute to the progression of this type of cancer.

Epimutations in *DNMT3A*

Recent findings reveal that AML often reveals aberrant hypermethylation within *DNMT3A* (Figure 1). These epimutations seem to mimic genomic mutations of *DNMT3A*. In analogy to the genomic mutations it is also associated with an elevated cytogenetic risk score and poor prognosis (Figure 2). Thus, analysis of *DNMT3A* epimutations is useful for risk stratification in AML - and it may also be relevant in other types of leukemia.

Cygenia offers analysis of *DNMT3A* epimutations (patent pending). This method is based on DNA-methylation analysis at a unique CpG site - it is therefore relatively simple and cost-effective.

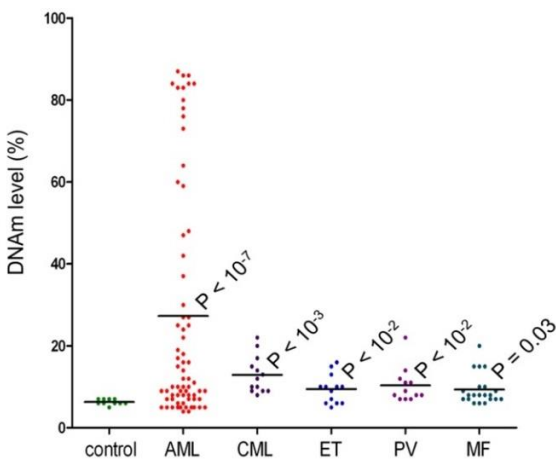


Figure 1: DNA-methylation level in *DNMT3A*.

Samples of normal blood (control), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), and myeloproliferative disorders (ET, PV, and MF) were analyzed by pyrosequencing. Particularly AML samples often reveal aberrant hypermethylation at the relevant region within *DNMT3A*.

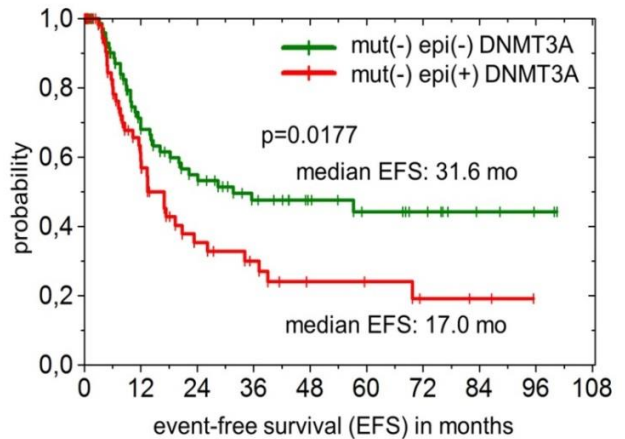


Figure 2: Epimutations entail poor prognosis.

Patients with aberrant hypermethylation in *DNMT3A* (epi+) have shorter EFS than those without epimutation (epi-; samples with genomic mutations in *DNMT3A* are excluded).

Our service for you:

- You provide either 1 mL of freshly/frozen blood (bone marrow aspirate or peripheral blood) or 200 ng of genomic DNA.
- We perform DNA isolation (optionally) and bisulfite conversion of genomic DNA
- We analyze the DNA-methylation at the relevant CpG site by pyrosequencing
- Results - including pyrograms, raw data, and graphical presentation - are provided by Email
- You can then easily correlate the results with clinical outcome or other parameters.

Publication:

- Jost E*, Lin Q*, *et al.* Epimutations mimic genomic mutations of *DNMT3A* in acute myeloid leukemia. *Leukemia*. 2014; 28(6):1227-34.
- Patent application: 2013; EP 13167411.1

Further Information

Please visit us at www.cygenia.com.