

Prognostic Biomarker for Acute Myeloid Leukemia

DNA methylation in AML

Epigenetic aberrations play a central role in the pathophysiology of acute myeloid leukemia (AML). It has been shown that molecular signatures based on DNA methylation (DNAm) patterns can be used for classification of the disease. Furthermore, DNA-methylation at a single CpG site in the gene of complement component 1 subcomponent R (*C1R*) is indicative for overall survival (OS) in AML.

Advantages:

- Simple assay based on one unique CpG site.
- Cost-effective and straightforward interpretation (no need for expensive and complicated microarray or sequencing technology).
- Only small amount of easily obtainable blood sample is needed.
- Important complementation to existing risk assessment assays from an epigenetic perspective.

Prognostic relevance

The genomic location with high prognostic relevance was first identified in a dataset of 194 patients from The Cancer Genome Atlas (TCGA): patients with higher methylation at this CpG site (>27% DNAm level) reveal significantly longer overall survival (53 months *versus* 11 months; adjusted $P < 0.0001$; Figure 1).

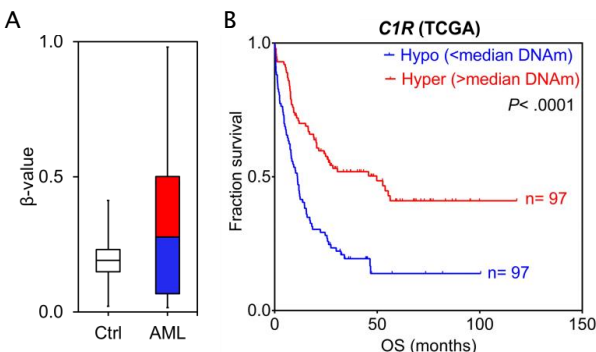


Figure 1: DNA-methylation at *C1R* has prognostic relevance in AML. (A) Beta-value distribution at the CpG site in *C1R* in healthy controls and AML samples (TCGA). (B) Kaplan-Meier estimation of overall survival in patients that were classified by median DNAm level of 27% at *C1R*.

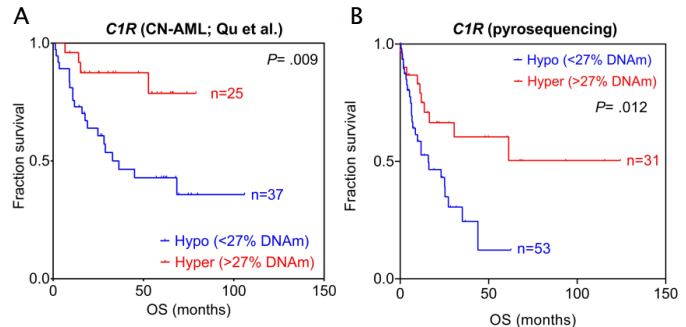


Figure 2: Validation in independent datasets.

Kaplan-Meier analysis of survival in (A) 62 cytogenetic normal AML patients or (B) 84 AMLs analyzed by pyrosequencing.

This finding was validated in an independent set of 62 DNAm profiles of cytogenetically normal AML patients ($P = 0.009$) and with a region-specific pyrosequencing assay in 84 AML samples ($P = 0.012$; Figure 2). DNA-methylation in *C1R* is associated with DNAm and gene expression patterns linked to developmental processes. Furthermore, it is associated with occurrence of specific genomic mutations in AML and correlates with overall survival also in several other types of cancer.

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:

- Božić T*, Lin Q*, *et al.* DNA-Methylation in *C1R* is a Prognostic Biomarker for Acute Myeloid Leukemia. *Clinical Epigenetics*. 2015; 7:116.
- Patent application: 2015; EP1519142.5

Further Information

Please visit us at www.cygenia.com.