# HematoLogics

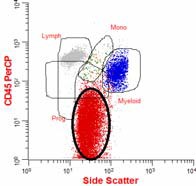
3161 Elliott Avenue, Suite 200, Seattle, WA 98121 Phone: (800) 860‐0934 Fax: (206) 223‐5550 [www.hematologics.com](http://www.hematologics.com/)

**Are you screening for RAM immunophenotype and CBFA2T3‐GLIS2 in pediatric AML?**

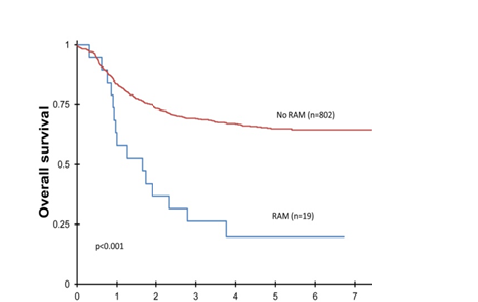
**HematoLogics has identified a unique recurrent Immunophenotype at diagnosis that identifies a high‐risk pediatric AML (RAM)1**

* **∆N:™** (Difference from Normal) **Flow Cytometry** provides a definitive diagnostic RAM phenotype, which is an independent predictor of poor outcome in pediatric AML

**RAM phenotype expresses high intensity CD56 expression, lack of HLA‐DR, dim to negative expression of both CD38 and CD45.**



* RAM phenotype can be identified rapidly at diagnosis, allowing clinicians to predict failure before initial therapy, thereby allowing more effective alternative therapies.
* Survival of patients with the RAM phenotype is like, or worse than those with high- risk molecular features and does not respond to standard therapy.

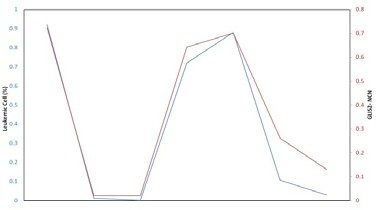


Patients with RAM AML have significantly worse overall survival compared to patients with non‐RAM AML.

No RAM (n=802)

RAM+ (n=19)

* Patients ≤ 5 years old or have AMKL (M7 megakaryoblastic) should be screened and monitored for RAM and CBFA2T3-GLIS22 (both have bad prognoses).



Tracking tumor percentage by both flow and GLIS2 fusion transcripts by RQ‐PCR shows tumor load. (Case Study)

Percent Leukemia by Flow

GLIS2 Normalized Copy Number

* The CBFA2T3 -GLIS2 fusion transcript is a common feature in pediatric AML (M7) in patients having normal cytogenetic findings and confers a poor prognosis.3
* FAB M7 classification might not be poor risk if RAM phenotype patients are considered independently.

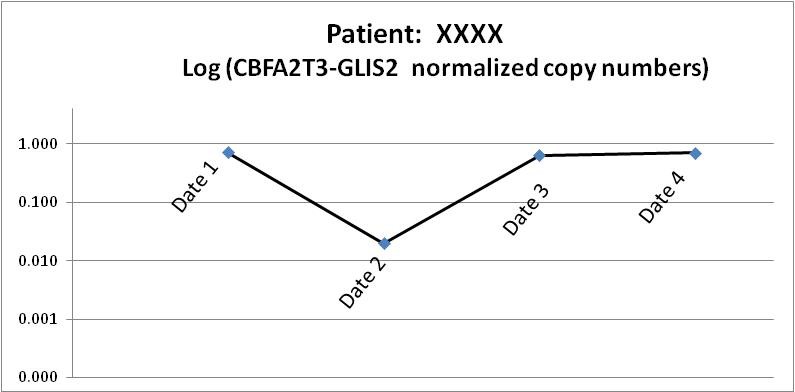
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**SAMPLE MOLECULAR ANALYSIS REPORT**

## CBFA2T3‐GLIS2 RT‐PCR Results: POSITIVE



|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Date** | **HLID#** | **Specimen** | **CBFA2T3‐**  **GLIS2 NCN** | **%**  **Reduction** | **Log Reduction** |
| Date 1 | HLID1 | BMA | 0.724 | Baseline | Baseline |
| Date 2 | HLID2 | BMA | 0.020 | 97.2 | 1.6 |
| Date 3 | HLID3 | BMA | 0.643 | 11.2 | 0.1 |
| Date 4 | HLID4 | BMA | 0.702 | 3.0 | 0.0 |

**NCN (normalized copy numbers): 0.702 ‐** Quantitative assay units: CBFA2T3‐GLIS2 transcript levels are reported as a ratio of fusion gene transcript to ABL reference gene transcript.

**Analysis/Conclusions:** The specimen tested positive for CBFA2T3 fusion transcripts, which are the molecular result of the cryptic chromosome 16 inversion [inv(16)(p13.3q24.3)], associated with a poor prognosis in AML.

## The quantitative CBFA2T3-GLIS2 NCN value of 0.702 is reduced by 3.0% (log reduction 0.0) in comparison to the patient’s baseline specimens.

This PCR test can detect the CBFA2T3‐GLIS2 transcript with sensitivity up to 1 in 10e5 transcripts (0.001%). Note: Control gene amplification indicated good RNA quality.

References:

**1.** Eidenschink Brodersen L. et al. “A Recurrent Immunophenotype at Diagnosis Independently Identifies High Risk Pediatric Acute Myeloid Leukemia: A report from Children’s Oncology Group.” Leukemia. 2016. 30(10):2077-2080.

**2.** Gruber, TA et al. An Inv(16)(p13.3q24.3)‐Encoded CBFA2T3‐GLIS2 Fusion Protein Defines an Aggressive Subtype of Pediatric Acute Megakaryoblastic Leukemia, Cancer Cell 22, 683‐697, November 13, 2012 Elsevier, Inc.

**3.** Masetti R. et al. CBFA2T3‐GLIS2 fusion transcript is a novel common feature in pediatric, cytogenetically normal AML, not restricted to FAB M7 subtype BLOOD, 25 APRIL 2013 x VOLUME 121, NUMBER 17

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