AMLGlobalPortal

General AML

Serum miR-223 expression in patients with acute myeloid leukemia

| Nov 29, 2019

MicroRNAs (miRNAs) are single stranded, small, non-coding RNAs which are known to play an important role in many biological processes and are detectable in serum and plasma samples. Aberrant expression of several miRNAs (miR-155, miR-210, miR-126-5p, miR-370, miR-328, and miR-204) have been associated with outcome in acute myeloid leukemia (AML).[1-6] Recently, low serum expression of miR-223 has been implicated in the development of AML.[7-9]

Guopan Yu, Nanfang Hospital, Guangzhou, CN, and team compared serum levels of miR-223 in 131 patients with AML and 70 healthy controls who had no cancer symptoms or clinical signs of any other disease.[10] RNA was extracted from serum and reverse transcribed prior to quantitative real time polymerase chain reaction (qPCR) being performed for both miR-223 and for a control miRNA that had been spiked into the sample at a known concentration during RNA purification.

Key findings

- There was a significant reduction in expression of miR-223 in the AML group compared with the control group ($p< 0.05$)
- Receiver operating characteristic curve analysis demonstrated that miR-223 levels could differentiate AML from the controls with a sensitivity of 83.2% and a specificity of 81.4%
- Serum miR-223 levels were higher in the favorable than in the intermediate/unfavorable cytogenetic risk groups and in patients in who achieved complete remission (CR), whereas low miR-223 was more often associated with higher risk cytogenetics and blasts in bone marrow (**Table 1**)
- miR-223 expression levels pre- and post-induction chemotherapy were compared and the levels of miR-223 post-induction were higher than they had been at pre-induction in both the patients who had achieved CR ($p< 0.01$) and those who had not ($p< 0.05$)
- Overall survival (OS) and relapse-free survival at 5 years were significantly shorter for those patients who had lower miR-223 expression levels ($p= 0.021$ and $p= 0.003$, respectively)
- Univariate and multivariate analysis showed that miR-223 is an independent predictor of OS in patients with AML (risk ratio [RR] 3.54; 95% confidence interval [CI], 1.47–5.79; $p= 0.016$ and RR 4.25; 95% CI, 1.29–7.38; $p= 0.011$, respectively)
- There was no association between miR-223 expression and age, gender, white blood cells, or platelets

Table 1: Serum miR-223 expression in AML cases

	Patients (n= 131)	Low miR-223 (n= 69)	High miR-223 (n= 62)	p value
Cytogenetics				
Favorable	52	16	36	< 0.0001
Intermediate	61	38	23	
Unfavorable	18	15	3	
Complete remission				
Yes	55	20	35	0.0015
No	76	49	27	
Blasts in bone marrow				
< 50%	54	21	33	0.0081
≥ 50%	77	48	29	

Guopan Yu and colleagues state that their work is in agreement with previous work on miR-223 in AML.[7-9] miR-223 regulates the equilibrium between expansion and differentiation in hematopoietic stem and progenitor cells, and expression of miR-223 leads to the production of red blood cells, T cells and B cells. Expression of miR-223 inhibits cell proliferation and increases apoptosis in AML cell lines, and knocking down miR-223 increases the frequency of myeloid progenitors. The authors discussed how decreased expression of miR-223 seems to be associated with nasopharyngeal carcinoma, cervical cancer, gallbladder cancer, hepatocellular carcinoma, and breast cancer, yet increased expression is seen in gastric cancer, colon cancer, and non-small cell lung cancer.[10] The group conclude that miR-223 may be able to be used as diagnostic tool and as a predictor of poor patient outcome in patients with AML.

References

1. Xu L.H. *et al*. Overexpressed miR-155 is associated with initial presentation and poor outcome in Chinese pediatric acute myeloid leukemia. Eur Rev Med Pharmaco. 2015 Dec; 19(24):4841–4850
2. Tang X. *et al*. Overexpression of miR-210 is associated with poor prognosis of acute myeloid leukemia. Med Sci Monitor. 2015 Nov 09; 21:3427–3433. DOI: 10.12659/MSM.894812

3. Shibayama Y. *et al*. Upregulation of microRNA-126-5p is associated with drug resistance to cytarabine and poor prognosis in AML patients. Oncol Rep. 2015 May; 33(5):2176–2182. DOI: 10.3892/or.2015.3839

4. Lin X. *et al*. Serum MicroRNA-370 as a potential diagnostic and prognostic biomarker for pediatric acute myeloid leukemia. Int J Clin Exp Pathol. 2015 Nov; 8(11):14658–14666

5. Liu L. *et al*. Low expression of circulating microRNA-328 is associated with poor prognosis in patients with acute myeloid leukemia. Diagn Pathol. 2015 Jul 17; 10:109. DOI: 10.1186/s13000-015-0345-6

6. Butrym A. *et al*. Low expression of microRNA-204 (miR-204) is associated with poor clinical outcome of acute myeloid leukemia (AML) patients. J Exp Clin Canc Res. 2015 Jul 01; 34:68. DOI: 10.1186/s13046-015-0184-z

7. Xiao Y. *et al*. MiR-223 decreases cell proliferation and enhances cell apoptosis in acute myeloid leukemia via targeting FBXW7. Oncol Lett. 2016 Nov; 12(5):3531–3536. DOI: 10.3892/ol.2016.5115

8. Pulikkan J.A. *et al*. Cell-cycle regulator E2F1 and microRNA-223 comprise an autoregulatory negative feedback loop in acute myeloid leukemia. Blood. 2010 Mar 04; 115(9):1768–1778. DOI: 10.1182/blood-2009-08-240101

9. Gentner B. *et al*. MicroRNA-223 dose levels fine tune proliferation and differentiation in human cord blood progenitors and acute myeloid leukemia. Exp Hematol. 2015 Oct; 43(10):858–868.e7. DOI: 10.1016/j.exphem.2015.05.018

0. Yu G. *et al*. Low serum miR-223 expression predicts poor outcome in patients with acute myeloid leukemia. J Clin Lab Anal. 2019 Nov 6:e23096. DOI: 10.1002/jcla.23096. [Epub ahead of print]