Published in final edited form as:

Ann Thorac Surg. 2014 March ; 97(3): 1045. doi:10.1016/j.athoracsur.2013.12.031.

INVITED COMMENTARY

David S. Schrump, MD, MBA

Thoracic and GI Oncology Branch, National Cancer Institute, Building 10; 4-3942, 10 Center Dr, Bethesda, MD 20892, david_schrump@nih.gov

MicroRNAs are critical mediators of stem cell pluripotency, differentiation, and malignancy. To date, more than 1,000 miRNAs (miRs) have been identified in humans, one third of which are located within large polycistronic clusters, in which a single transcript yields multiple distinct, yet functionally related, mature miRs. In the present study, Xu and colleagues [1] examined expression of the miR-17~92 cluster in 105 esophageal squamous cell carcinomas (ESCC) and paired normal esophageal tissues from a Chinese population. These authors observed overexpression of all six members of this cluster in ESCC, with the frequency of overexpression of individual miRs ranging from 25% to 67%. Importantly, none of the patients had received chemotherapy, which can alter the transcription of miR-17~92 in cancer cells [2]. Interestingly, activation of miR-17~92 did not appear to be related to tobacco or ethanol exposure. Overexpression of miR-18a, miR-17, and miR-19a (observed in 67%, 31%, and 25% of ESCC specimens, respectively) correlated with decreased overall survival.

One issue not addressed in the present study pertains to the frequency and relevance of simultaneous upregulation of miRs-18a, -17, and -19a in ESCC, and the prognostic significance of various combinations of miR-18a, -17, and -19a overexpression in these cancers. In all likelihood, such analysis will require a much larger sample size than was used in this study. Additionally, expression levels of miR-17~92 in tumor tissues were directly compared with paired noncancerous esophageal tissues; as such, it is possible that endogenous levels of individual miRs within the cluster varied considerably among the paired samples, thereby affecting the observed frequencies and relevance of miR-17~92 overexpression reported in this study. Normalizing miR-17~92 expression in all tissues to a "standard" miR preparation (ie, pooled esophageal microRNA from healthy nonsmoking individuals) may have demonstrated that more patients than reported had overexpression of miR-17~92 members, and possibly revealed an even more significant correlation between activation of miR-17~92 and prognosis in ESCC patients. Additionally, the study would have been more complete if expression levels of the predicted targets had been analyzed to further define the mechanisms by which miR-17~92 activation alters the phenotype of ESCC.

Overall, the findings of Xu and colleagues [1] are very intriguing, and consistent with recent observations that circulating miR-18a levels correlate with tumor burden and overall survival in patients with ESCC [3]. Interestingly, activation of miR-17~92 has also been observed recently in esophageal adenocarcinomas [4]. Collectively, these findings highlight the emerging roles of microRNAs in esophageal carcinomas, and the significance of miR-17~92 as a potential biomarker and therapeutic target in these malignancies.

References

1. Xu X-L, Jiang Y-H, Feng J-G, Su D, Chen P-C, Mao W-M. MicroRNA-17, microRNA-18a and microRNA-19a are prognostic indicators in esophageal squamous cell carcinoma. *Ann Thorac Surg* 2014;97:1037–45. [PubMed: 24360091]
2. Kim K, Chadalapaka G, Pathi SS, et al. Induction of the transcriptional repressor ZBTB4 in prostate cancer cells by drug-induced targeting of microRNA-17–92/106b-25 clusters. *Mol Cancer Ther* 2012;11:1852–62. [PubMed: 22752225]
3. Hirajima S, Komatsu S, Ichikawa D, et al. Clinical impact of circulating miR-18a in plasma of patients with oesophageal squamous cell carcinoma. *Br J Cancer* 2013;108:1822–9. [PubMed: 23579215]
4. Wu X, Ajani JA, Gu J, et al. MicroRNA expression signatures during malignant progression from Barrett's esophagus to esophageal adenocarcinoma. *Cancer Prev Res (Phila)* 2013;6: 196–205. [PubMed: 23466817]