Letter by D’Alessandra et al Regarding Article, “Circulating MicroRNA-208b and MicroRNA-499 Reflect Myocardial Damage in Cardiovascular Disease”

To the Editor:

In their recent article in Circulation: Cardiovascular Genetics, Corsten et al\(^1\) report that circulating mir-208b was elevated in nearly 90% of patients with acute myocardial infarction (AMI), whereas it was undetectable in 89% of control subjects and suggest that this miRNA may represent a good biomarker of AMI in humans. However, studies on circulating miRNAs and AMI have led to contrasting conclusions on miR-208 suitability as a biomarker of AMI in humans. Specifically, of 6 published studies on circulating miRNAs and AMI, 4 evaluated miR-208.\(^1\)\(^-\)\(^4\) Wang et al\(^2\) suggested miR-208 as a candidate biomarker for AMI in humans (present in 90% of the patients). Adachi et al\(^3\) found very low levels of miR-208a and miR-208b in human hearts and considered these miRNAs unsuitable as biomarkers of myocardial injury in humans. In our hands,\(^4\) circulating miR-208 was barely detectable, and only in 30% of AMI patients but never in healthy control subjects. In contrast, we found that miR-499-5p was detectable in all control subjects, it increased in all patients with AMI, and, in mice, it closely paralleled the increase in TnI after coronary artery ligation. Further, a recent report investigating patients with coronary artery disease without AMI\(^5\) shows that miR-208b was significantly upregulated in patients’ plasma but could be detected only using ten times the amount of RNA used for all other miRNAs. Since miR-208 is expressed at extremely low levels in the human heart and in the systemic circulation, its use as a biomarker poses at least 2 problems: (1) it requires a larger amount of RNA than other miRNAs to be identified and (2) expressing miR-208 level as fold-increase versus control is misleading since in control condition it may be undetectable.

We believe that as circulating and tissue miRNAs levels become increasingly attractive as clinically relevant biomarkers of a variety of diseases, there is a urgent need to develop standardized criteria for normalization (eg, the commonly used spike-in of a Caenorhabditis elegans miRNA reflects only the efficiency of RNA extraction) and, ultimately, to report the miRNA level not as a fold difference from control but as an absolute value.

Disclosures

None.

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References

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