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 al1 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 myocardial infarction. 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 al2 suggested miR-208 as a candidate biomarker for AMI in humans (present in 90% of the patients). Adachi et al3 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 AMI5 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.

Yuri D’Alessandra, PhD
Giulio Pompilio, MD, PhD
Laboratorio di Biologia Vascolare e Medicina Rigenerativa
Centro Cardiologico Monzino–IRCCS
Milan, Italy

Maurizio C. Capogrossi, MD
Laboratorio di Patologia Vascolare
Istituto Dermopatico dell’Immacolata
ID1–IRCCS
Rome, Italy

References

Letter by D'Alessandra et al Regarding Article, "Circulating MicroRNA-208b and MicroRNA-499 Reflect Myocardial Damage in Cardiovascular Disease"
Yuri D'Alessandra, Giulio Pompilio and Maurizio C. Capogrossi

Circ Cardiovasc Genet. 2011;4:e7
doi: 10.1161/CIRCGENETICS.110.958769
Circulation: Cardiovascular Genetics is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 1942-325X. Online ISSN: 1942-3268

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circgenetics.ahajournals.org/content/4/1/e7

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Genetics can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Genetics is online at:
http://circgenetics.ahajournals.org/subscriptions/