Letter to the Editor

Eleftherios P. Diamandis* and Mario Plebani

Glypican-1 as a highly sensitive and specific pancreatic cancer biomarker

DOI 10.1515/cclm-2015-0773
Received August 10, 2015; accepted August 28, 2015; previously published online September 19, 2015

Keywords: biomarker; glypican-1; pancreatic cancer.

To the Editor,

Melo et al. recently described a new and exciting way for the highly sensitive and specific diagnosis of pancreatic cancer by using exosomes carrying the protein glypican-1 (GPC1) [1]. The most impressive finding is the diagnosis of early stage pancreatic cancer in comparison to other benign pancreatic diseases, with a claimed 100% sensitivity, specificity, positive and negative predictive value. We have the following comments:

1. Although seemingly performing to perfection, the method would not be practical at present due to the difficulty in isolating GPC1-positive exosomes by flow cytometry; the serum ELISA for GPC1 was no better than the classical pancreatic cancer biomarker CA19-9.
2. In the history of cancer biomarker identification and validation, there is no biomarker that performs with 100% sensitivity and specificity, especially for early stage disease.
3. Previous papers reporting such outstanding sensitivities/specificities/predictive values, were subsequently shown to be associated with various shortcomings, such as preanalytical, analytical, postanalytical and bioinformatic biases. Some examples of initially exciting and later failed cancer biomarkers, and the reasons for the failures, have been summarized elsewhere [2–4].
4. It is known in the cancer biomarker literature that the enthusiasm for new biomarkers is exponentially decaying over time. We hope that this newly identified biomarker will be an exception.
5. For relatively rare diseases, such as pancreatic cancer (lifetime risk ~1:70), it is known that under a screening scenario, even with high assay specificities, such as 99%, that there will still be many false positives, diminishing the positive predictive value of the test to <2%. It remains to be seen if GPC1-carrying exosomes will retain in subsequent validations, perfect specificity for pancreatic cancer.

The best way to confirm the claims of this interesting report is an independent validation by other research groups, or through the Early Detection Research Network of the National Institutes of Health (www.edrn.nci.nih.gov). If in such validation the near absolute specificity of this biomarker is not maintained, then, it will not be useful for screening for this lethal disease.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.
Research funding: None declared.
Employment or leadership: None declared.
Honorarium: None declared.
Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

***Corresponding author: Dr. Eleftherios P. Diamandis,** MD, PhD, FRCP(C), FRSC, FAAAS, Hold'em for Life Chair in Prostate Cancer Biomarkers, Division Head of Clinical Biochemistry, Mount Sinai Hospital and University Health Network; Professor and Head, Division of Clinical Biochemistry, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada, E-mail: ediamandis@mtsinai.on.ca
Mario Plebani: Department of Laboratory Medicine, University-Hospital of Padova, Padova, Italy.
http://orcid.org/0000-0002-0270-1711

References

1. Melo SA, Luecke LB, Kahlert C, Fernandez AF, Gammon ST, Kaye J, et al. Glypican-1 identifies cancer exosomes and detects early pancreatic cancer. Nature 2015;523:177–82.

2. Diamandis EP. Analysis of serum proteomic patterns for early cancer diagnosis: drawing attention to potential problems. J Natl Cancer Inst 2004:96;353–6.
3. Diamandis EP. Cancer biomarkers: can we turn recent failures into success? J Natl Cancer Inst 2010:102;1462–7.
4. Lippi G, Plebani M. Personalized medicine: moving from simple theory to daily practice. Clin Chem Lab Med 2015;53:959–60.