Cancer biomarkers

Franco M Buonaguro^{*1}, Maria Lina Tornesello¹ & Luigi Buonaguro¹

Cancer biomarkers still represent a relevant topic of cancer research. Actually in the last decade they have acquired a further relevance given that biomarkers can contribute to a better identification and characterization of cancer subclasses and staging and to a more appropriate implementation of therapeutic protocols, as well as to the discovery of new therapeutic targets with the final goal of the individual tailoring of treatments. The omics revolution along with the next-generation sequencing has recently opened the possibility to identify molecular changes and metabolic pathways specific for each cancer with the resulting possibility of further molecular subclassification of each cancer histotype and identification of a more reliable prognostic tools and appropriate treatments. A further result of such studies is the possibility of identifying specific cancer targets, with higher effectiveness of chemotherapy and much lower general toxicity, along with the reduction of overtreatment of those with higher responsivity and better prognosis. Furthermore, the whole field is currently very active in search for determinants and biomarkers of cancer susceptibility

to etiological agents (including those for pathogen-related cancers) and cancer progression linked to genetic, epigenetic and microenvironmental components (including the immune response). New biomarker classes (i.e., miRNA) have been recently identified, relevant for their potential as therapeutic targets and their detection in plasma/serum samples, for easy clinical diagnosis and follow-up monitoring [1]. Moreover, several groups are focused on the clinical validation of newly identified biomarkers, in order to bridge molecular mechanisms with clinical diagnosis and therapeutic responsivity [2].

This special focus issue on 'Cancer biomarkers' includes a series of in-depth reviews written by leading scientists of each field, covering current critical issues. It is mostly dedicated to biomarkers in the developmental stage not yet fully established and validated in human clinical studies.

In the editorial by Ballotti, titled 'Identification of melanoma initiating cells', the author inquires on the future application of the CD271 biomarker [3]. CD271-positive melanoma cells have been

KEYWORDS

• cancer biomarkers • cancer determinants • cancer pathways • HCC • lung cancer • melanoma • SUMO pathway

"It is likely that the new season of cancer biomarkers is only at the beginning and will definitely contribute to the imminent tailored anticancer treatment and their expected success."

¹Laboratory of Molecular Biology & Viral Oncology, Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori – IRCCS 'Fondazione Pascale', Via Mariano Semmola 142, 80131 Napoli, Italy

^{*}Author for correspondence: fmbuonaguro@tin.it

shown with higher tumorigenic potential when injected into nude mice. However, CD271-positive cells can be dichotomized in two subpopulations with the slow-growing characterized by higher tumorigenic potential than the fast-growing. A further biomarker (i.e., MITF) is needed to complement a CD271 imperfect initiating marker.

Buonaguro *et al.* present a special report on 'Cellular prognostic markers in hepatocellular carcinoma', the fifth most prevalent cancer type worldwide and the third cause of cancer deaths [4]. A strong correlation between HCC clinical prognosis and intratumoral infiltration of cells affecting tumor growth, invasion, angiogenesis and metastasis has been accumulating in the recent years. Evaluation of such studies aims to the identification/validation of new biomarker for diagnostic and/or prognostic use.

In the review presented by Felizia *et al.* 'EGFR mutations in lung cancer: from tissue testing to liquid biopsy', the authors describe the relevance of EGFR mutations in non-small-cell lung cancer as prognostic biomarker and predictive marker of therapeutic responsivity to EGFR-tyrosine kinase inhibitors [5]. The current challenge is to move from not-always available tissue biopsies to blood, serum and plasma samples, as a new strategy for genotyping circulating tumor cells or cell-free tumor DNA.

In the article 'SUMO pathway components as possible cancer biomarkers', Mattoscio and Chiocca review the most recent data on the subject [6]. Sumoylation of proteins, a specific ubiquitination performed by small ubiquitin-related modifier, is a post-translational event critical in the cell cycle. Alterations of SUMO

pathway components, being frequent in cancer cells, represent a potential cancer biomarker, as for the sumoylation of the histone deacetylase 1.

Tornesello *et al.* present 'An overview of new biomolecular pathways in cancer', which is relevant for the appropriate classification of cancers and their molecular staging [7]. Characterization of the biomolecular pathways is crucial for the identification of the etiopathogenetic mechanisms, assessment of the prognosis and prediction of therapeutic responsivity. Moreover, evaluation of cancer stemness and their pathways will contribute to selection of appropriate therapeutic treatment.

In conclusion, the identification of innovative cancer biomarkers is still a very relevant ongoing quest. Moreover, their role in cancer diagnosis and clinical management has been radically changed in the last few years with the major emphasis on cancer molecular classification, therapeutic target identification and therapeutic protocol responsivity. It is likely that the new season of cancer biomarkers is only at the beginning and will definitely contribute to the imminent tailored anticancer treatment and their expected success.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

- Chen X, Ba Y, Ma L *et al.* Characterization of microRNAs in serum: a novel class of biomarkers for diagnosis of cancer and other diseases. *Cell Res.* 18(10), 997–1006 (2008).
- De Giorgi V, Buonaguro L, Worschech A *et al.* Molecular signatures associated with HCV-induced hepatocellular carcinoma and liver metastasis. *PLoS ONE* 8(2), e56153 (2013).
- Ballotti R. Identification of melanoma initiating cells: does CD271 have a future? *Future Oncol.* 11(11), 1587–1590 (2015).
- Buonaguro L, Tagliamonte M, Petrizzo A, Damiano E, Tornesello M, Buonaguro F. Cellular prognostic markers in hepatocellular carcinoma. *Future Oncol.* 11(11), 1591–1598 (2015).
- Fenizia F, De Luca A, Pasquale R *et al.* EGFR mutations in lung cancer: from tissue testing to liquid biopsy. *Future Oncol.* 11(11), 1611–1623 (2015).
- Mattoscio D, Chiocca S. SUMO pathway components as possible cancer biomarkers. *Future Oncol.* 11(11), 1599–1610 (2015).
- Tornesello M, Buonaguro L, Buonaguro FM. An overview of new biomolecular pathways in cancer. *Future Oncol.* 11(11), 1625–1639 (2015).