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Editorial

Protein-Coding Genes of the Cancer-Related Genomic Locus 19q13 and MicroRNAs as Emerging Tumor Biomarkers

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Editorial

Despite the clinical advances that have been noticed during the last decade, clinical practice is still missing reliable tumor biomarkers with increased sensitivity and specificity for particular malignancies. Early diagnosis is the key step for the management of cancer. Furthermore, early detection of tumor recurrence and monitoring of treatment response or relapse of cancer patients is of high importance. Thus, there is a huge need for novel diagnostic, prognostic, and predictive tumor biomarkers [1]. Quantitative real-time PCR (qPCR) is a cost-effective methodology that can be used to measure the concentration of such biomarkers at the RNA level.

The genomic locus 19q13 is a chromosomal region on which many cancer-related genes are located. One of these genes is KLK3, which encodes the most widely used cancer biomarker, namely the prostate-specific antigen (PSA). KLK3 is a member of the family of human tissue kallikrein (KLK1) and kallikrein-related peptidases (KLKs), are secreted serine proteases with trypsin- or chymothypsin-like activity, distinct expression patterns and physiological roles in different organs and systems. The involvement of KLKs in the development and growth of solid tumors, angiogenesis, invasion and metastasis of tumor cells, render these proteases potential cancer biomarkers. Expression analysis of KLKs has uncovered their association with various clinicopathological parameters of cancer patients. Furthermore, several KLKs are significant favorable or unfavorable prognosticators in specific cancer types [2].

Another important cancer-related gene of the same locus is protein arginine methyltransferase 1 (*PRMT1*). PRMTs are histone-arginine N-methyltransferases. These enzymes participate in protein complexes which repress the transcription of protein-coding genes. *PRMT1* plays an important role in carcinogenesis and its expression at the mRNA level possesses important clinical value. This gene constitutes a promising biomarker in colon and breast cancer. In more detail, *PRMT1* transcript variant 2 is an indicator of unfavorable prognosis in colon cancer patients, while *PRMT1* transcript variant 1 expression status predicts short-term relapse in breast cancer patients [3,4].

Carcinoembryonic antigen-related cell adhesion molecule 19 (*CEACAM19*) is a member of the carcinoembryonic antigen (CEA) family. CEA is a glycoprotein involved in cell adhesion. CEA protein concentration in serum is mainly used as a tumor biomarker to monitor colorectal cancer treatment, to identify relapse after surgical resection, and for tumor staging. CEA is elevated more in gastrointestinal cancer patients presenting lymph node and distant metastases than in those with organ-restricted tumors [5]. *CEACAM19* mRNA expression has recently been shown to be associated with breast cancer progression. In addition, *CEACAM19* mRNA expression is also associated with clinicopathological factors that are indicative of aggressive behavior and poor prognosis in this malignancy [6].

The genomic locus 19q13 includes also SR-related CTD-associated factor 1 (*SCAF1*), which encodes an Arg/Ser-rich splicing factor. The mRNA levels of *SCAF1* have been shown to increase in cancer cells treated with various steroid hormones, including estrogens, androgens and glucocorticoids, and to a lesser extent with progestins [7]. *SCAF1* mRNA expression was demonstrated to constitute a new unfavorable prognostic marker in breast and ovarian cancer. Expression of the *SCAF1* gene in cancerous breast tissues is influenced by the tumor size and the existence of regional lymph node metastases. With regard to *SCAF1* mRNA expression in ovarian carcinoma, it is associated with low tumor differentiation, advanced disease stage, and debulking success [8,9].

The BCL2-like 12 (*BCL2L12*) gene, a member of the BCL2 family located in the chromosomal region 19q13, is an apoptosis-related gene with significant prognostic potential. Some *BCL2L12* protein isoforms are proapopotic, while others are antiapoptotic [10]. The prognostic value of *BCL2L12* mRNA expression has already been examined in several solid tumors, such as colon cancer, breast cancer, bladder cancer, nasopharyngeal carcinoma, as well as in hematological malignancies such as chronic lymphocytic leukemia and acute myeloid leukemia. The *BCL2L12* gene is aberrantly transcribed in colon cancer specimens compared to their paired non-cancerous colonic tissues. *BCL2L12* overexpression predicts significantly longer DFS and OS in colon cancer patients. Increased expression of *BCL2L12* has also been linked to longer survival intervals of gastric adenocarcinoma patients. Furthermore, *BCL2L12* mRNA expression has been suggested as a novel, useful tissue biomarker in nasopharyngeal carcinoma for the prediction of patient relapse [11]. Thus, this apoptosis-related gene is a valuable tissue cancer biomarker.

MicroRNAs (miRNAs) are small non-coding RNAs that post-

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transcriptionally regulate the expression of protein-coding genes. miRNAs act mainly by repressing translation or destabilizing targeted mRNA molecules. microRNAs are associated with many normal cellular functions, including cell proliferation, differentiation, and programmed cell death. Moreover, they can act both as oncogenes - probably by reducing the expression of tumor-suppressor proteins – and as tumor-suppressor genes by downregulating oncoproteins. Their aberrant expression has been associated with pathogenesis of several diseases, the most prominent being cancer. Thus, patients with solid tumors or hematopoietic malignancies present distinct signatures of expression of miRNAs [12]. For instance, miR-15a and miR-16-1 are frequently downregulated or even lost in chronic lymphocytic leukemia [13]. Furthermore, several miRNAs possess significant prognostic and/or predictive value in cancer. miR-224 is such an example, as its overexpression constitutes a strong and independent prognosticator of short-term relapse and poor overall survival in colorectal cancer patients [14]. Moreover, miR-17-5p and miR-20a are indicators of favorable prognosis in myelodysplastic syndromes, as their expression predicts increased overall survival of patients. Thus, this class of tiny RNA molecules provides very promising cancer biomarkers [15].

Identification of novel diagnostic, prognostic, and predictive biomarkers will highly assist the clinical decision-making, as early diagnosis of primary cancer and recurrence following surgery are crucial for an effective treatment and a favorable clinical outcome. Since single biomarkers do not provide enough sensitivity and/or specificity, reliable diagnosis, prognosis, and prediction of therapy response will be achieved through the development of multiparametric panels of biomarkers originating from families of cancer-related molecules. The first attempts have already proven to be fruitful; nevertheless, there is still much work to be done.

References

1. Sturgeon C. Practice guidelines for tumor marker use in the clinic. Clin Chem. 2002; 48: 1151-1159.
2. Kontos CK, Scorilas A. Kallikrein-related peptidases (KLKs): a gene family of novel cancer biomarkers. Clin Chem Lab Med. 2012; 50: 1877-1891.
3. Mathioudaki K, Papadokostopoulou A, Scorilas A, Xynopoulos D, Agnanti N. The PRMT1 gene expression pattern in colon cancer. Br J Cancer. 2008; 99: 2094-2099.
4. Mathioudaki K, Scorilas A, Ardavanis A, Lymberi P, Tsiambas E. Clinical evaluation of PRMT1 gene expression in breast cancer. Tumour Biol. 2011; 32: 575-582.
5. Duffy MJ. Carcinoembryonic antigen as a marker for colorectal cancer: is it clinically useful?. Clin Chem 2001; 47: 624-630.
6. Michaelidou K, Tzovaras A, Missitzis I, Ardavanis A, Scorilas A. The expression of the CEACAM19 gene, a novel member of the CEA family, is associated with breast cancer progression. Int J Oncol. 2013; 42: 1770-1777.
7. Scorilas A, Kyriakopoulou L, Katsaros D, Diamandis EP. Cloning of a gene (SR-A1), encoding for a new member of the human Ser/Arg-rich family of pre-mRNA splicing factors: overexpression in aggressive ovarian cancer. Br J Cancer. 2001; 85: 190-198.
8. Leoutsakou T, Talieri M, Scorilas A. Prognostic significance of the expression of SR-A1, encoding a novel SR-related CTD-associated factor, in breast cancer. Biol Chem. 2006; 387: 1613-1618.
9. Leoutsakou T, Talieri M, Scorilas A. Expression analysis and prognostic significance of the SRA1 gene, in ovarian cancer. Biochem Biophys Res Commun. 2006; 344: 667-674.
10. Kontos CK, Scorilas A. Molecular cloning of novel alternatively spliced variants of BCL2L12, a new member of the BCL2 gene family, and their expression analysis in cancer cells. Gene. 2012; 505: 153-166.
11. Kontos C, Thomadaki H, Scorilas A. BCL2L12 (BCL2-like 12 (proline-rich)) (19q13.3). Atlas Genet Cytogenet Oncol Haematol. 2009; 13: 467-468.
12. Calin GA, Croce CM. MicroRNA signatures in human cancers. Nat Rev Cancer. 2006; 6: 857-866.
13. Calin GA, Cimmino A, Fabbri M, Ferracin M, Wojcik SE. MiR-15a and miR-16-1 cluster functions in human leukemia. Proc Natl Acad Sci. 2008; 105: 5166-5171.
14. Adamopoulos PG, Kontos CK, Rapti SM, Papadopoulos IN, Scorilas A. miR-224 over expression is a strong and independent prognosticator of short-term relapse and poor overall survival in colorectal adenocarcinoma. Int J Oncol, 2014, (in press).
15. Vasilatou D, Papageorgiou S, Pappa V, Papageorgiou E, Dervenoulas J. The role of microRNAs in normal and malignant hematopoiesis. Eur J Haematol. 2010; 84: 1-16.

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