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Editorial Open Access

For Novel Disease Diagnostic Markers in Blood RNA

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Editorial

For early detection of cancer or other serious diseases, we continue to develop diagnosis approach as a major clinical duty. Diagnosis using bodily fluids such as blood, urine, saliva is low and non-invasive and can be the first option. Especially, blood is accepted as clinical diagnostics and contains huge kinds of disease markers. While we use proteins and metabolites as those markers, RNA also can be those for next generations. RNA contains a huge amount of information on messenger RNA and non-coding functional RNAs which regulate gene expressions. The latter is now strongly counted on.

In recent years, microRNAs (miRNAs) have been a focus of various specimens and diseases. miRNAs are small, single-stranded RNA molecules that bind to complementary mRNAs. Binding of miRNAs to mRNAs leads to regulate the target mRNA, either to silencing, or translational inhibition. Thus, miRNAs contains information that will not be translated to proteins. We must be aware of next generation information for different types of disease and cancer. A prediction model based on four-plasma miRNA signature (miRs-126, 145, 210, and 205-5p) was developed for distinguishing lung cancer patients from cancer-free smokers by cohort included 92 lung cancer patients and 88 cancer-free smokers. A four-plasma miRNA signature could accurately differentiate early stage NSCLC patients from cancer-free smokers [1]. miRNAs are known to be out of regulation in different types of cancer, including breast cancer. Thus, it has been demonstrated that deregulation of several miRNAs can be used as biological markers in cancer [2]. Isolated RNA from serum was profiled for over 2500 human miRNAs. The miRNA expression data were input into a stepwise linear regression model to discover a multivariable miRNA signature that predicts long-term risk of breast cancer. As a result, a refined 6-miRNA risk-signature was discovered following regression modelling that distinguishes cases and controls (AUC0.896, CI 0.804-0.988) in this cohort [3]. Studies using not only blood but other body fluids have been done. Only limited knowledge exists regarding ascites, the potential of miRNAs as biomarkers of ascites were systematically evaluated. Schindler et al. prospectively analysed samples from patients with peritoneal carcinomatosis (PCA), spontaneous bacterial peritonitis (SBP), and portal hypertension (no SBP/PCA). As a result, a simple proportion score between miR-21 and miR-223 allowed to discriminate between the patients with PCA and those with SBP with an area under the curve of 0.982 (95% confidence interval, 0.943-1.022) [4]. Circulating miRNAs are also proposed as a biomarker of heart disease. The cardiac function of patients with childhood dilated cardiomyopathy (CDCM) was characterized by echocardiography and serum miRNA profiles of all participants were assessed by miRNA sequencing. As a result, a unique signature comprising mir-142-5p, mir-143-3p, mir-27b-3p, and mir-126-3p differentiated patients with CDCM from healthy subjects [5]. Thus, circulating microRNAs (C-miRNAs) have emerged as measurable biomarkers (liquid biopsies) for not only various cancer detection but other diseases.

To detect target RNA, we have to develop the protocol to get high quality RNA samples and quality control methods first of all. The measurement of mRNA using microarray or real-time RT-PCR studies were significantly influenced by RNA integrity [6,7]. Classically, the method of agarose gel electrophoresis stained with ethidium bromide is used for RNA quality. The ratio of 28S:18S bands near to 2.0 or higher RNA is considered of high quality. While the ratio has been shown to be inconsistent. Recently, the RIN evaluation method was developed using the algorithm accounting 5S region, fast region, 18S fragment, inter region, 28S fragment and post region [8,9]. RIN is considered more reliable to evaluate RNA quality than that base on the 28S/18S ratio [10].

Recently, we proposed the new method to employ the standard RNA of refRNA1000 [11]. The refRNA1000 was developed for spike-in microarray control RNA as certificated reference materials (CRM), which has the length of 1000 base pairs without homology to natural RNA sequences (http://www.ncbi.nlm.nih.gov/nuccore/AB610945). We studied the evaluation methods based on RIN and the amount of refRNA1000 in various condition of degradation, and we found the significant correlation among those. We also found the benefits of reference RNA, as we can grasp the degradation of the whole process by adding different kinds of standard RNA after blood sampling, before storage, before extraction, and before measurement.

Blood RNA diagnosis has the possibility to diagnose various unprecedented diseases at an early stage. In order to conduct a more accurate diagnosis, progress of comprehensive research such as extraction method, conservation method, evaluation method, verification method in addition to searching for biomarkers is desired. We just now gain the quality control protocol.

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