Gene Expression Profiling for Discovery of Novel Markers of Minimal Disease

To the Editor: As Cheung et al. (1) report, accurate assessment of minimal disease is essential to inform the fight to cure children with neuroblastoma. Cheung et al. have exploited gene expression profiling to identify and prioritize targets for the detection of this disease using quantitative reverse transcriptase-PCR (RT-PCR). Eight of 34 genes are prioritized for investigation.

Using a similar approach, we and others have previously identified three key mRNA targets (2); one of these targets (Phox2B) has also been prioritized by Cheung et al. Interestingly, the sensitivity and specificity of Phox2B as a target for the detection of minimal disease by quantitative RT-PCR in children with neuroblastoma has been corroborated (3, 4). However, differences in the remaining putative targets for optimal detection of minimal disease may lead to skepticism about the value of genome-wide expression data to inform candidate selection. Unfortunately, a direct comparison of data from the two Affymetrix array minimal disease studies in neuroblastoma (1, 2) is limited due to several differences in methods. First, the study of Cheung et al. (1) used the Affymetrix human U95 platform, in contrast to the U133 Plus 2.0 array used in our study (2). Using the U95 platform, Cheung et al. identified MEG3 and MLLT11 as specific sequences, although these probe sets also match to an additional five and two potential targets, respectively. This reinforces the importance of careful verification of probe-set gene annotation (2). Cheung et al. (1) report that they have excluded targets known to be expressed in bone marrow from healthy volunteers, although they do not describe the steps taken to identify such genes. Searching the National Center for Biotechnology Information expressed sequence database for the 34 potential markers of minimal disease identified by Cheung et al., we found that six of these genes have previously been described in bone marrow (CCND1, KIF21A, MLLT11, PFN2, UCHL1, and MAOA) and 11 in peripheral blood (CCND1, KIF21A, MLLT11, PFN2, KIF5C, MEG3, GRIA2, DDC, RGS5, KIF1A, and GABRB3) from healthy volunteers. Not surprisingly then, all but DDC were subsequently detected in normal blood using quantitative RT-PCR (1). The selection of eight targets for detection of minimal disease by Cheung et al. (1) is therefore questionable. The precision of minimal disease detection using quantitative RT-PCR will be facilitated by standardized assays for selected candidate genes not expressed in the normal hemopoietic compartments (2, 5).

The clinical significance of minimal disease detected by quantitative RT-PCR for individual mRNAs emphasizes the importance of this disease and the studies by Cheung et al. (1), although it is unfortunate that they did not investigate the independent prognostic significance of detecting disease using individual and multiple marker sets (4).

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Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

References

Published OnlineFirst October 27, 2009; DOI: 10.1158/1078-0432.CCR-09-1601

© 2009 American Association for Cancer Research. doi:10.1158/1078-0432.CCR-09-1601
Correction: Gene Expression Profiling for Discovery of Novel Markers of Minimal Disease

In this article (Clin Cancer Res 2009;15:6742), which was published in the November 1, 2009, issue of Clinical Cancer Research (1), there was an error in the spelling of the second author's name in the online article. It should read Susan A. Burchill. The online article has been changed to reflect this correction and to match the print.

Reference

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