Reviewer's report

Title: Genotyping Panel for Assessing Cancer Risk and Response to Chemotherapy

Version: 4  Date: 23 January 2008

Reviewer: Michael Gottesman

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Summary:
To date, no single approach can detect all genotypes due to the variety of polymorphism types (translocations, loss of heterozygosity, insertions, etc). This manuscript reports the adaptation of an existing platform, termed SNPlex, to a flexible high-throughput genotyping system for genes involved in drug response and cancer biology. While this approach can detect the majority of genetic variants, additional methods need to be applied to reveal all of the remaining polymorphisms. The authors applied their methodology to detect 432 SNPs in 160 genes through two cohorts of patients with chronic lymphocytic leukemia and colorectal cancer.

Minor Essential Revisions:
1. Supplemental table 1: Numerous SNPs failed to be detected by the SNPlex system for some technical reasons partially explained in Materials and Methods, in the SNPlex pools and reagents section. While some of the results obtained from the SNPlex platform were validated using other methods such as SNaPshot or PCR, few SNPs that failed to be detected by the adapted SNPlex method were studied using these methods. What is the reason for this choice? Is it related to a technical issue or their clinical irrelevance, which was previously demonstrated? Is their detection possible using these additional approaches? To be clear, it should also be mentioned in the table what SNPs that appear in bold type can be detected by alternative methods and which methods.

2. There is a discrepancy between the Materials and Methods section and the Results that brings confusion. In the M&M, the authors report that they used the SNaPshot approach to detect 3 SNPs analyzed using their SNPlex method. The authors should also mention that they used this alternative method and others as well to detect polymorphisms that failed to be detected by their platform.

3. The selection of genes was careful and well established. However, the number of selected uptake transporters, important actors in drug response, is extremely low. Is this choice related to the current lack of knowledge or scientifically unrelated?

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.