Reviewer's report

Title: P-glycoprotein and breast cancer resistance protein in acute myeloid leukaemia cells treated with the Aurora-B kinase inhibitor barasertib-hQPA

Version: 2 Date: 1 April 2011

Reviewer: Gareth Gerrard

Reviewer's report:

1. Major Compulsory Revisions

1.1. The authors must conduct an appropriate statistical analysis for all data reported; to say, 'The ABC transporter positive cell lines were all much more resistant to pHH3 inhibition,' as typified on p.6 is not acceptable. Appropriate statistical tests must be employed to ascertain whether differences between data sets are significant or not. Factors such as data normality, independence and multiple comparisons should be considered.

Where statistical tests have been employed by the authors (Fig.5a&b), no information about the type of test used has been given; again, this is unacceptable; please state what test was used (i.e., t-test, Mann-Whitney, etc).

2. Minor Essential Revisions

2.1. p.14 Methodology is given for a real-time PCR assay, which is not referred to elsewhere in the paper; please either remove this section or include the qPCR data (guidelines for the reporting of qPCR data are given in the MIQE Guidelines: http://www.clinchem.org/cgi/content/abstract/55/4/611 ).

2.2. No indication is given as to what the error bars on figure histograms denote; please supply this information, bearing in mind that SEM is not an acceptable metric since it does not describe the spread of the data. SD, CI or range should be used and clearly referred to in the figure legend.

2.3. The authors must ensure that they define the meaning of an abbreviation or acronym the first time they use it in the text. (e.g., R123 & CSA on p.6)

2.4. p.3. Although AURKC is highly expressed in testis tissue, it also expressed elsewhere and can be readily detected in PBMCs and its expression in known to be perturbed in certain cancers; please amend the sentence on p.3 to reflect this.

2.5. p.5, para.2, last sentence; are the authors implying that the genes themselves confer the resistance? The referenced paper refers to gene amplification and transcriptional up-regulation. Please rephrase.

2.6. p.7 & Fig 3c. Why has the corresponding OCI-AML3 +modulator data been excluded? This must be included as an appropriate control, even if the cell line is
MDR negative.

2.7. p.8 & p.13. The level of AML patient sample detail given is unacceptable. Please provide all pertinent data where available; not least: a breakdown of patient age & sex; type of disease (FAB type, inclusion of M3, karyotype, etc); sample type; type of anticoagulant used; single or multi-centre acquisition and time from sample extraction to processing.

2.8. p.8 & p.13 cont. Please state clearly whether ‘primary samples’ refers to ‘diagnosis/presentation’ patient samples, and if so, whether they were all pre-treatment. If not, please give the disease stage (diagnosis, remission (CR1, CR2), relapse), and if whether multiple sequential samples from the same patient were used in the analysis.

2.9. p.8. & p.13 cont. Please state whether PB and BM samples, since used synonymously, give equivalent background MDR profiles?

2.10. p.8, The meaning of last two sentences on p.8 (and the recapitulation on p.10) is unclear; please rephrase to ensure clarity.

2.11. p.8. Please indicate which cytokines were used in the cocktail and whether any of the substances used are known to affect MRD expression or function? Also, much of the exposition given in the corresponding figure legend (fig 5) would be better placed in the methods section.

2.12. p.11. The first sentence of the conclusions does not make grammatical sense; please rephrase.


2.14. p.14. Please state clearly in the text whether the arithmetic or geometric mean was used for the determination of MFI? The distinction is important given that the FL1 scale is logarithmic.

2.15. p.14. and elsewhere. Much of the methodology referred to in the text is too brief; please add at least a sentence or two of exposition in addition to a reference to a previously published paper.

3. Discretionary Revisions

3.1. p.7, para.1. Why was the UIC2 shift assay data not included? Please consider including it, especially as its result is referred to.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests