Author's response to reviews

Title: The Colorectal cancer disease-specific transcriptome facilitates the discovery of more biologically and clinically relevant information

Authors:

Wendy L Allen (w.l.allen@qub.ac.uk)
Puthen V Jithesh (p.jithesh@qub.ac.uk)
Gavin R Oliver (gavin.oliver@almacgroup.com)
Daniel B Longley (d.longley@qub.ac.uk)
Heniz-Josef Lenz (Lenz_h@ccnt.norccc.usc.edu)
Vitali Proutski (vitali.proutski@almacgroup.com)
Dennis Paul Harkin (paul.harkin@almacgroup.com)
Patrick G Johnston (p.johnston@qub.ac.uk)

Version: 2 Date: 8 December 2009

Author's response to reviews: see over
Dear Editor,

Please find enclosed our research article ‘The Colorectal cancer disease-specific transcriptome facilitates the discovery of more biologically and clinically relevant information’, which we would like to submit to Molecular Cancer for consideration.

The aim of this study was to assess the biological and clinical relevance of disease-specific transcriptome-based profiling in advanced colorectal cancer. Within this study we compared transcriptional profiling data from drug treated HCT116 colorectal cancer cells (both sensitive and drug-resistant) from a leading generic array, the Affymetrix HG U133 Plus2.0 array, with a disease-specific transcriptome-based array, the Almac Diagnostics colorectal cancer specific array (DSA). The Colorectal DSA is based on the colorectal transcriptome and shares 60% common information with the Affymetrix Plus2.0 array, however, it also contains 40% unique information. A subset of genes from each microarray platform was validated by quantitative RT-PCR and we have demonstrated a strong correlation between microarray and QRT-PCR results. We demonstrated that the Colorectal DSA outperformed the Affymetrix Plus2.0 array based on detection and differential expression filtering. We also demonstrated that, when studying colorectal cancer, more biologically relevant information is gained when using the Colorectal DSA, specifically relating to pathway analysis. Additional analysis revealed that the unique content contained within the Colorectal DSA contains a high percentage of transcripts that are in the reverse or antisense orientation and furthermore, that a number of these transcripts exist in sense:antisense pairs. We have further demonstrated that these sense:antisense pairs are clinically relevant by examining transcriptional profiling data from pre-treatment metastatic colorectal cancer biopsies. Overall, our study demonstrates that if the colorectal transcriptome was not examined in this setting important biologically relevant information may be lost.

All microarray data is available within the ArrayExpress repository (http://www.ebi.ac.uk/microarray-as/ae/). For access to the microarray data, reviewers should use the following details: E-MEXP-390 and E-MEXP-1691 for in vitro analysis and E-MEXP-1692 for clinical analysis.

Statement of conflict of interest: Professor Patrick Johnston and Prof Paul Harkin are the Founders and Directors of Almac Diagnostics, Craigavon, UK. Gavin Oliver and Vitali Proutski are employees of Almac Diagnostics, Craigavon, UK.
Two leading experts in colorectal cancer research that would be suitable reviewers are:

1. Prof Timothy Kinsella tkinsella@notes.cc.sunysb.edu
2. Prof Elaine Kay elaine.kay@beaumont.ie

All authors of this research paper have directly participated in the planning, execution, or analysis of the study. All authors of this paper have read and approved the final version submitted. The manuscript is original and has not been published or accepted for publication in any other journal, nor is it currently under consideration for publication elsewhere. The contents of this manuscript will not be copyrighted, submitted, or published elsewhere while acceptance by the Journal is under consideration.

Yours faithfully,

Wendy Allen, PhD.