ESPS Peer-review Report
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Title: Gene Expression Profiles of Peripheral Blood in Colorectal Cancer
Reviewer code: 02854680
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D (Fair)		BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

This paper is very well written and examines the possibility of using a panel of genes as a potential biomarker of CRC. Peripheral leucocyte gene expression was quantified using PCR. The authors used a pooled multivariate analysis to select genes of interest from a list of CRC candidate genes. The authors then compared their own panel of genes from peripheral blood, to microarray data sets from colonic tissue (CRC and control).   Major limitations.   - Was a microarray used to identify the initial list of CRC genes of interest from peripheral blood? Or were these candidate genes described in previous studies, and were these genes differentially expressed in blood or colonic tissue. - Surely a better study design would be to perform a meta-analysis of public microarray datasets, find a the best performing panel of genes, and validate these genes in peripheral blood -Were statistics corrected for multiple testing? -For what reason should gene expression from peripheral blood leucocytes be similar to gene expression from colonic tissue?(i.e. microarray datasets) - It appears the accuracy of the 5 gene model is largely driven by the results of one gene (DUSP6), what happens to results when this gene is removed from analyses   Overall it is a laudable concept to develop biomarkers from peripheral blood as this would be useful for national screening programmes, and a PCR assay for a panel of 5 or so genes would be a feasible methodology for widespread utilisation.   If the authors (as may be interpreted from the introduction) suggest that changes evident in peripheral blood arise from tumour cells metastasising prior to presentation, this would invalidate the method as a screening method, as patients with metastatic disease would be picked up, and would not be useful for early detection and prevention of metastasis. May be worthy of touching on this point in the discussion.