Reviewer’s report

Title: Expression of centromere protein F (CENP-F) associated with higher FDG uptake on PET/CT, detected by cDNA microarray, predicts high-risk patients with primary breast cancer

Version: 3 Date: 3 September 2008

Reviewer: Donal Brennan

Reviewer’s report:

The authors have presented a study whereby they evaluated used PET imaging to identify tumours with a high SUV which they believe to be a good prognostic tool. They followed on to identify a number of genes associated with a high SUV and then validate these using rtPCR and IHC.

Major Compulsory Revisions

1. There are a number of misrepresentations in the introduction mainly around the phrase "primary systemic chemotherapy" and the use of the Mammaprint and Oncotype DX assays. For example the authors say these are "sufficiently established" which is wrong. In general the introduction is poorly written and needs to be completely revised.

2. As there are three cohorts used in the it is hard to follow. They need to be outlined in detail in the materials and methods section and a table needs to be provided to allow reviewers to examine them for differences between the cohorts.

3. My major issue regarding this paper is regarding the cDNA microarrays. The bioinformatic approach outlined in the paper is fundamentally flawed and needs to be addressed. Initially the groups are made up of different numbers of tumours 14 versus 24. No clinical data is given regarding the nuclear grade, tumour size or nodal status in the two groups. There is no information about how the tumours were stored following surgery - were they snap frozen or stored in RNA later? If the SUV high group has a larger number of high grade T2 tumours obviously cell cycle related genes such as CENPF. Additionally no information is given about the approach used to identify the top 20 genes - were the data normalised, why was a cut off of 1.7 fold used?

4. The TMAs used in this study were constructed using a single 2mm core from tumour blocks. It is debatable how well this approach accounts for tumour heterogeneity given that current recommendations are to take a minimum of 3 1mm cores.

I can’t see the benefit of this paper in predicting the need for or response to adjuvant chemotherapy. My own opinion is that CENPF is probably a marker of high grade aggressive tumours, however I don't understand what SUV adds to it as these patients will all have surgery prior to any chemotherapy. My own feeling
is that PET imaging may help to identify that small number of patients who will show a complete pathological response following neoadjuvant therapy.

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests