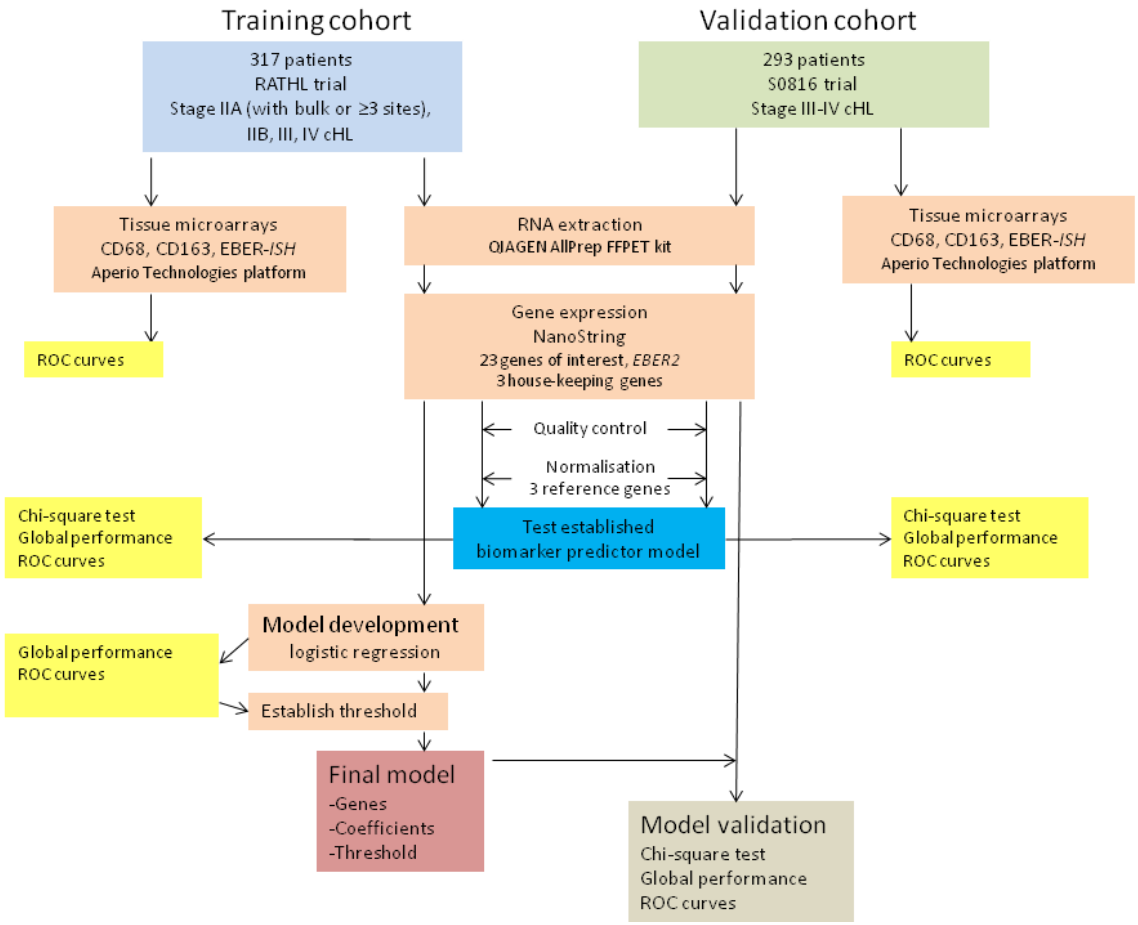
2014 Mike & Carole Ralston Travelling Fellowship- progress report: Yasmin Harvey

I gratefully received the above award, enabling me to undertake a research project at the Centre for Lymphoid Cancer Research at the BC Cancer Agency in Vancouver, Canada. The project I am working on commenced in January this year and is ongoing.

The aim of the project is to develop a gene expression-based model, utilising NanoString technology predictive of interim FDG-PET scan (PET2) results in patients with advanced-stage classical Hodgkin lymphoma (CHL) treated with response-adapted therapy. Patient samples from two independent cohorts drawn from international response-adapted therapy clinical trials, the "response-adapted therapy for Hodgkin lymphoma" (RATHL) trial and the S0816 US intergroup trial are being analysed. The overall study design is shown in the figure below. In both trials, patients received two cycles of therapy with ABVD prior to an interim FDG-PET scan (PET2). The PET2 scans were reviewed centrally using a standardised scoring system (Deauville criteria) which determined further management. Patients with a positive PET2 (Deauville score 4-5) were given intensified therapy with escBEACOPP or BEACOPP-14. Patients with a negative PET2 scan (Deauville score 1-3) continued with ABVD therapy, or in the RATHL trial were randomised to either ABVD or AVD treatment arms. Samples from the RATHL cohort have been processed thus far, with the S08016 trial cohort patient sample processing to occur in the next stage. The NanoString technology being used would enable this assay to be performed at diagnosis, with a 48-72 hour turn-around-time, using routinely prepared formalin-fixed paraffin embedded tissue. Thus, by identifying the approximately 20-30% of 'high risk' patients, unlikely to achieve cure with ABVD with or without radiotherapy, the results may inform upfront treatment decisions thus hopefully improve cure rates for high risk patients, and limit exposure to unnecessary toxicity for the majority of patients likely to be cured with standard therapy.

The opportunity to spend 12 months here has been an enriching experience. I have enjoyed learning new skills and gaining knowledge relating to my project specifically, but I have also been exposed to other research, technologies and educational opportunities available at the British Columbia Cancer Agency. I have enjoyed the weekly seminar series here, which is typically presented by an international expert and has included seminars relating to the 100 000 genomes project in the UK, the Cancer Genome Atlas project as well as projects by the many resident world-renowned experts in various disciplines. I attended a Personalised Medicine Summit at the University of British Columbia recently which had a very interesting, diverse range of speakers with a vision and roadmap to utilise genomic technologies to implement 'personalised medicine' in British Columbia. There are obviously significant challenges for this to be achieved, however appears to be in progress with the hope of improved outcomes possible for patients across a broad spectrum of pathologies.

Thank you for the financial support to undertake this research fellowship. I do feel it has significantly broadened my horizons and been a very worthwhile educational experience.


Training cohort
Validation cohort
317 patients
RATHL trial
Stage IIA (with bulk or ≥3 sites), IIB, III, IV cHL
293 patients
S0816 trial
Stage III-IV cHL
Tissue microarrays
CD68, CD163, EBER-ISH
Aperio Technologies platform
RNA extraction
QIAGEN AllPrep FFPET kit
Tissue microarrays
CD68, CD163, EBER-ISH
Aperio Technologies platform
ROC curves
Gene expression
NanoString
23 genes of interest, EBER2
3 house-keeping genes
ROC curves
Quality control
Normalisation
3 reference genes
Chi-square test
Global performance
ROC curves
Test established biomarker predictor model
Chi-square test
Global performance
ROC curves
Model development
logistic regression
Global performance
ROC curves
Establish threshold
Final model
-Genes
-Coefficients
-Threshold
Model validation
Chi-square test
Global performance
ROC curves