Genomics Education Programme

NHS
Health Education England

Niamh Appleby

Niamh is an Irish clinical haematology doctor based in the Oxford Molecular Diagnostics Centre. She graduated from the School of Medicine at Trinity College Dublin and completed postgraduate training in haematology in Ireland before completing additional training in diagnostic haematopathology in the UK. Her career interests include molecular diagnostics and the application of genomic technologies to direct and personalise therapy for patients with haematological cancers.

While settling into Oxford life by learning to punt on the river, Niamh has been getting involved with the Oxford Genomic Medicine Centre and the Haematological Malignancy programme in particular. Her project examines sequencing technologies for plasma circulating tumour DNA and how circulating tumour DNA might be applied in to examine genomic changes in the lymphatic tissue, to predict treatment response and identify impending relapse.

Outline of Research (Full Time, PhD)

Development and Evaluation of the clinical utility of plasma-based ultra-sensitive detection methods for high risk chronic lymphocytic leukaemia and lymphoma.

Chronic lymphocytic leukaemia (CLL) is the commonest adult leukaemia and while treatable, patients relapse after chemo-immunotherapy. In a minority, CLL transforms to high-grade lymphoma; Richter's syndrome (RS).

New, costly drugs based on understanding how leukaemia cells survive offer effective alternatives to chemo-immunotherapy for selected patients, making it important to identify before treatment, which patient will benefit.

Specific changes in the leukaemia DNA (somatic mutations) predict clinical outcomes and help decide which therapy is suitable for each patient. CLL affects white cells, marrow and lymph nodes but previous studies concentrated on blood or marrow DNA, not lymph nodes. Somatic mutations arising in lymph nodes are thought responsible for relapse, treatment-resistance and RS.

Cancers release fragments of tumour DNA into blood plasma. Studying plasma circulating tumour DNA (ctDNA) offers a biopsy-free method to detect somatic mutations. Plasma ctDNA from lymph node, marrow and leukocytes will be detectable, providing a complete picture of CLL somatic mutations.

Niamh's study will identify how best to detect CLL somatic mutations in ctDNA. Then, I will compare ctDNA with mutations identified from CLL/RS cells to learn how ctDNA

mutations impact on response to different therapies in patients enrolled in the Genomics England programme and CLL/RS clinical trials.