Project title: Novel liquid biopsies to guide treatment in recurrent head and neck cancer.

Project Summary: The prognosis for patients with recurrent head and neck quamous cell carcinoma (rmHNSCC) prognoses are bleak - even with optimal treatment, the survival rate at a year after disease recurrence is approximately one year. The integration of PD-1 checkpoint inhibitors for advanced HNSCC has enhanced outcomes, with a subset of patients experience durable responses, but no way of identifying who will respond to therapy prior to the start of treatment. Liquid biopsies, most notably circulating tumour DNA (ctDNA), can allow tumour profiling less invasively than with a tissue biopsy, and has shown promise in several clinical applications.

In this project, the candidate will investigate predicting response to immunotherapy in rmHNSCC, through analysis of clinical samples collected in the Dynamic Assessment of Response to Treatment (DART) Study. DART involves the longitudinal collection of tumour, plasma, saliva and peripheral blood mononuclear cells from patients with rmHNSCC receiving immunotherapy, and is open and recruiting at The Royal Marsden Hospital. The candidate will evaluate different, complementary liquid biopsy approaches to develop candidate biomarkers and explore the biology of resistance to immunotherapy in rmHNSCC.

Aim 1 – Establish the optimum approach for tumour-agnostic assessment of early ctDNA dynamics in rmHNSCC.

Using custom sequencing workflows for genomics and methylation, along with droplet digital PCR, the candidate will develop a ctDNA metric for prediction of response to immunotherapy.

Aim 2 – Assess early peripheral T cell receptor dynamics as a complementary early predictor of response to immunotherapy.

The candidate will examine whether changes in the T cell receptor repertoire over treatment can be used to predict clinical outcomes on immunotherapy for rmHNSCC using a novel TCR sequencing workflow developed in the Graham lab. This analysis will be extended to include both baseline tumour and pre-radiotherapy tumour, for patients who have relapsed following radiotherapy.

Aim 3 – Explore changes in plasma proteomics on treatment with immunotherapy. The Choudhary lab has developed a novel proteomic technique that is feasible for use in small volumes of human plasma. The candidate will perform longitudinal plasma proteomic analysis and integrate this with the data generated in aims 1 and 2, to explore whether this approach could inform candidate biomarker selection or

disease resistance biology.

Supervisory Team: Dr Ben O'Leary, Prof Jyoti Choudhary, Dr Annie Baker, Prof Trevor Graham

Clinical Specialities: all considered.