CRUK Cambridge Centre Clinical PhD project

PhD Project Title	**Early Lung Cancer – detection and intervention**
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Programme	Aerodigestive
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Laboratory Location	Departments of Biochemistry and Medicine

Project Outline	**Aims and objectives** Lung cancer was responsible for 6 % of all UK deaths in 2013. It accounts for 21% of all cancer deaths, more than double any other common cancers. There is an urgent need to improve strategies for early detection and early intervention in lung cancer. There are two key aims for this project which address these unmet needs: **Aim 1**. To define a parsimonious multiparametric molecular biomarker to classify high-risk patients with CT detected lung nodules into cancer and non-cancer. **Aim 2**. Refine a plausible strategy for the targeted chemoprevention of squamous lung cancer. We seek to recruit an enthusiastic physician for this project that combines clinical and translational laboratory science. The recruit will be embedded in a multidisciplinary team (clinicians/scientists/biotechnologists/biostatistics) already working on early lung cancer.
Experimental plan	**Aim 1** 1) Recruitment of patients with: • High-risk indeterminate pulmonary nodules (IPNs) undergoing standard-of-care pathway 2) Analysis of the following non-invasive biomarkers in all recruits • cfDNA – targeted amplicon next generation sequencing (1) • sputum – assessment of aneuploidy in epithelial cells, targeted amplicon next generation sequencing • +/- breath – "biopsy" 3) Patients will undergo biopsy procedures to establish a histological diagnosis. 4) Individual and multiparametric analysis, processing and integration of biomarkers **Aim 2** We have developed an entirely novel *in vitro* system of human bronchial dysplasia (early squamous lung cancer) (2) that we have now used to test the ability of a range of compounds to ***reverse*** established bronchial dysplasia. We have *in vitro* evidence of efficacy of a specific therapeutic already in Phase 3 trials for other indications. Separately we have developed a novel *in vivo* model of squamous cancer. The candidate will test the efficacy of this and related compounds *in vivo,* both in the new model and in established xenograft models of squamous cancer. If efficacy is confirmed *in vivo*, the candidate will help lead on the development of a pilot/early phase clinical trial already supported in principle by the relevant Pharma company. The aim of the pilot clinical trial will be to demonstrate efficacy and boost confidence in the potential to repurpose the compound for lung cancer chemoprevention.

Main Techniques	• Clinical trials • Patient recruitment • Standard and navigational bronchoscopy • Specimen collection/processing/analysis • Mouse models of squamous lung cancer (CRISPR Cas9 dependent) • Cell culture/imaging/histology • Early phase intervention study design and development
Key References	1. Murtaza M et al. Nature. 2013 May 2;497(7447):108-12. 2. Correia et al. Am J Respir Crit Care Med. 2017 Jun 1;195(11):1494-1508.