

PROJECT PROPOSAL

2025/6 Academic Entry Year – Cohort 4

Supervisory Team

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Project Details

Title: Investigating the role of microbiomes and socioeconomic factors in oral cancer outcomes among South Asian and Caucasian populations in England

Summary: Socioeconomic and ethnic disparities in oral cancer (OC) in England have been documented for decades, with worse outcomes reported in Black populations [1]. However, there is limited data on outcomes for South Asian populations, despite a rising incidence of OC and poor five-year survival rates [2]. Recognized risk factors include income deprivation, health behaviours, and age. The COVID-19 pandemic has further exacerbated socioeconomic inequalities in cancer outcomes, disproportionately affecting patients in deprived areas [3]. Leicester has a significantly higher

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incidence of OC than the national average, especially in Asian/Asian British groups, with local data indicating worse treatment outcomes in these populations [2]. This project will explore the impact of race and ethnicity, and the gut and oral microbiome in OC patients and how this correlates with immunotherapy outcomes. An exploratory pilot study will be performed involving at least 20 patients (10 Caucasian and 10 British South Asian), with matched samples from their gut and oral microbiomes. Dietary and lifestyle factors will be assessed through questionnaires, and whole exome sequencing of tumours will be conducted alongside 16S sequencing of tumours, mouth rinses, and stool samples to analyze microbiome differences. Samples will also be collected at three months and one year into the study

Aim: This pilot study aims to explore the intersection of ethnicity, microbiomes, and oral cancer (OC) treatment outcomes. Leicester, with a higher-than-average incidence of OC, particularly among its South Asian population, provides a unique setting to investigate these disparities.

Background: Oral cancer is a significant public health concern in England, with disparities in incidence and outcomes shaped by socioeconomic status, ethnicity, and race. While Black populations have been studied, data on South Asians remains limited, despite a rising incidence and poor survival rates [2]. Leicester's local data indicates worse immunotherapy and radiotherapy outcomes for British South Asians. Increasing evidence suggests that the gut and oral microbiomes play a key role in cancer treatment outcomes by influencing immune responses and drug metabolism [4]. In addition, no data exists regarding whether there are somatic mutational differences that drive oral cancers in underrepresented patients. **We hypothesise that gut and oral microbiomes, along with diet, lifestyle and genetic factors may affect treatment outcomes, with the aim to identify microbial and mutational biomarkers that may predict immunotherapy success**

Research Plan:

Objective 1: Investigating the Impact of Ethnicity, Microbiome, and Immunotherapy Outcomes

This objective involves recruiting at least 20 patients, 10 Caucasian and 10 British South Asian individuals diagnosed with oral cancer and undergoing treatment with immunotherapy (pembrolizumab), to explore microbiome and somatic mutational variations between these groups. Whole exome sequencing (WES) of tumours and matched white blood cells will be performed to uncover potential genetic disparities that may influence immunotherapy responses. WES can provide insights into personalized medicine and targeted treatments.

Additionally, 16S sequencing of oral rinses and stool samples will be used to analyze the gut and oral microbiomes. Emerging evidence suggests that these microbiomes can affect cancer development, immune regulation, inflammation, and treatment outcomes [4]. By comparing microbiomes across ethnic groups, we aim to identify distinct microbial compositions or imbalances that could inform tailored treatment strategies for oral cancer. Samples will be collected at three time points: baseline, three months, and one year, enabling the study of dynamic microbiome changes over time, especially during treatment.

Objective 2: Assessing Dietary and Lifestyle Factors

The second objective will assess dietary and lifestyle factors through questionnaires given to each participant. This assessment will examine nutrition, exercise, tobacco use, alcohol consumption, and other lifestyle factors influencing oral cancer outcomes, particularly in conjunction with socioeconomic status. Lifestyle factors such as diet and physical activity vary significantly across ethnic groups, contributing to health disparities [5]. For example, betel nut consumption, more prevalent among South

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Asians, is linked to a higher incidence of oral cancer [6]. Income deprivation and educational disparities can also contribute to poor diet and unhealthy behaviors, worsening cancer outcomes.

Recruited patients will be provided with questionnaires about their dietary habits and lifestyle, with responses standardized (e.g., smoking frequency, daily fruit/vegetable servings, exercise hours per week), and basic descriptive statistics calculated for both ethnic groups. T-tests for continuous variables (e.g., calorie intake, exercise hours) and chi-square tests for categorical variables (e.g., smoker/non-smoker) will be conducted. Regression models will control for confounders such as age, income, and education, which could influence both diet and lifestyle.

Expected outcomes and impact: This study will provide a holistic understanding of how lifestyle and socioeconomic disparities, as well as genetics and the microbiome influence cancer prognosis and treatment response. The results (published in peer-reviewed papers) will form the basis of future studies to identify microbiome factors that are associated with treatment outcomes in underrepresented populations and will also guide the development of screening strategies and interventions to reduce risk of oral cancer. This cross-disciplinary project will stimulate a new collaboration between the Leicester Cancer Research Centre and Leicester Diabetes Centre, with data generated from the project informing future grant applications to CRUK and the MRC

References:

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6. Hernandez, B.Y., et al., *Betel nut chewing, oral premalignant lesions, and the oral microbiome*. PLoS One, 2017. **12**(2): p. e0172196.