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The role of germline and somatic DNA mutations in oral and oropharyngeal cancers

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Scientific Outline

Summary

The overall aim of our project is to improve understanding of the role of genetic factors in risk and prognosis of oral cancer (OC) and oropharyngeal cancer (OPC). Our project has three specific aims.

Aim 1: Evaluate the relationship between germline variants and risk of HPV-related OPC.

We will determine the HPV status all OPC cases in our study population for whom existing serum or plasma samples are available (~2400) using HPV16 E6 serology. Subsequently, we will conduct GWA analysis of OPC stratified by HPV status to evaluate the relationship between germline variants and risk of HPV-related OPC. Modifying effects of tobacco use and alcohol consumption will be explored.

Aim 2: Assess associations between germline variants, environmental exposures, and the presence of somatic driver alterations in tumor DNA.

We will use targeted sequencing to determine the presence of previously reported somatic driver mutations in 1000 tumors (including 500 OCs and 500 OPCs). The tumours will be selected from among the 3300 cases successfully genotyped with the OncoArray for whom tumour tissue is available. Associations between germline variants, environmental exposures such as smoking, and somatic driver mutations will be evaluated.

Aim 3: Examine the role of genetic markers, HPV and smoking history in OC and OPC outcome.

We will examine the role of germline variants in OC and OPC relapse and survival, and characterize the clinical relevance of recently catalogued somatic driver mutations. We will also explore the potential modifying role of HPV status and smoking on disease outcome.

KEYWORDS

Oral cancer, oropharyngeal cancer, human papillomavirus, germline mutations, somatic mutations