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headandneck 5000

Is there a shared genetic predisposition to both cleft lip and palate and head and neck cancer?

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Scientific Outline

Summary

Orofacial clefts, which include cleft lip and or cleft palate are among the most common birth defects occurring in around 1 in 700 live births. Around 30% of children are found to have a syndrome with other congenital abnormalities. Many of these syndromic cases will have associated chromosomal anomalies or genetic mutations. However, it is a heterogeneous condition and many genes have been implicated as well as some environmental factors, such as anti-epileptic drug use, smoking and alcohol intake during pregnancy.

To date more than 40 genes have been implicated in the risk of orofacial clefts (Setó-Salvia et al, 2014). Many of these genes also control cell signalling, proliferation, migration and survival (processes that may influence cancer risk) and some have also been linked to cancer risk, for example MYC and NTN1. Some small studies have reported an increased risk of cancer among 1st degree relatives of cleft cases and vice versa, and a Danish study found an excess risk of cancers of the breast, and lung and brain tumours among those with oral clefts (Bille et al, 2005). Recently, a study has looked at the association between genome wide association study hits for various cancer with cleft and vice versa (Dunkhasea et al, 2016). This study found that although a small number of single nucleotide polymorphisms (SNPs) were common to both cancer and cleft, there was not a great deal of overlap. However, possibly owing to the fact that both oral clefts and head and neck cancer are uncommon, no association between the two has been reported to date.

The aim of this project is to determine whether genes known to be implicated in oral clefts are associated with head and neck cancer risk in genome wide association studies and vice versa. This project would make use of publically available dataset on cleft lip and palate as well as the Head and Neck 5000 study, we would also use biobank data as a control group. We plan to look at known (reported in genome wide association or other studies) SNPs and also to adopt a whole genome approach.

If a shared genetic risk between the two is found this would advance the understanding of both conditions as well as highlighting whether those with oral clefts are at increased risk of head and neck cancer later in life.

References:

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