Investigators

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Project Title

Molecular markers in Cutaneous SCC

Institutions Involved

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Summary of the Project

Cutaneous squamous cell carcinoma (cSCC) is the second most common malignancy in Australia and the most costly cancer to the Australian health system. Rates of cSCC in Australia are the highest in the world and continue to rise. Metastasis to regional lymph nodes occurs in < 5% of cases, but, when present, imparts significant mortality and morbidity. Most patients who develop metastases present with advanced disease that requires a combination of radical surgery and high dose adjuvant radiation. Many of these patients will die or suffer profound physical, functional and psychosocial side-effects as a result of their disease and its treatment.

Currently there are no reliable indicators to help identify primary cSCCs at high risk of developing metastases. This is a significant problem because most metastatic cSCCs are detected and treated too late.

We hypothesise that metastasis driver mutations exist in cSCC and that these could be used to more reliably predict metastasis risk in primary cSCC at the time of initial presentation. The molecular mechanisms underlying metastasis drivers in cSCC are not known. We intend to redress this severely under-researched cause of morbidity and death.

Goals/Aims and How it Aims to Benefit Head & Neck Patients with Cancer/Pathology

Our research is the first systematic and comprehensive effort to identify the genetic changes that occur in the different categories (low and high-risk) and stages (metastatic and non-metastatic) of cSCC, and to characterise the biological effect of these changes.

We have assembled the largest comprehensive clinicopathologic database of metastatic cSCC in the world and a globally unique biobank of specimens with cognate tumour, normal tissue, blood samples and cognate clinical and follow up data.

We have completed whole genome sequencing on metastases samples and are currently completing sequencing on cohorts of non-metastasising and metastasising primary cSCC tumours and coincident metastases from our biobank, representing the largest number of cSCC specimens to undergo whole genome sequencing. We have also completed targeted expression analyses (Nanostring) on these samples.

Aims

Transcriptional landscape: Undertake the first comprehensive transcriptional analysis of cSCC. Integrating Ribonucleic acid (RNA) sequencing with whole genome sequencing will facilitate the stratification of potential clinically important genes (biomarkers) and provide many valuable insights into the functional outcome of genetic variations.

Validation of biomarkers: We will use Nanostring technology to validate a subset of genes that potentially discriminate non-metastasising from metastasising tumours.

Benefit to patients

This project will not only establish the benchmarks for genomic analyses of cSCC but it will provide prognostic data that can be applied immediately. This is of great importance, because the current tools used to stage patients with cSCC are inaccurate and understanding prognosis is critical for both the clinician and patient deciding on whether to recommend or proceed with a particular treatment, especially therapies applied after initial treatment for cancer. In particular, to suppress secondary tumour formation.

Armed with the knowledge of the genetic drivers of metastatic SCC, we will be able to develop routine screening test of all cSCCs at the time they are first treated. This will enable us to identify patients at risk of their cancer spreading so they will undergo either close surveillance or pre-emptive treatment, avoiding the devastating consequences of late detection of metastatic disease.