

# Sinai Health System

## Rhinology/Skull Base Research

**Ian Witterick, Allan Vescan, John de Almeida**

There are ongoing clinical research projects in rhinology and the skull base program. These include:

- Development of quality indicators for chronic rhinosinusitis
- Virtual reality simulators (Neurotouch) with validation trials
- Virtual reality sinus simulators to establish learning curves
- Clinical research in skull base surgery including juvenile nasopharyngeal angiofibroma experience and validation of the skull base inventory quality-of-life instrument
- Ongoing prospective clinical trial comparing patients on medical therapy versus surgical therapy for chronic rhinosinusitis
- A ten year outcomes study of non-squamous cell sinonasal malignancies

Education research continues with the OtoSim™ in undergraduate medical education as well as the development of quality and safety measures for our specialty.

## Head & Neck Oncology Research

**Ranju Ralhan, Ian Witterick, Paul Walfish, Jeremy Freeman, Allan Vescan and John de Almeida**

Our head and neck oncology group has focused on preclinical research for translation of proteomic biomarkers for improved diagnosis and prognosis of disease. Our major thrusts are to gain insight into the molecular basis of development of oral pre-cancer and its progression to frank cancer as well as

identifying new drugs for personalized patient care. The major themes are:

1. Preclinical validation of protein biomarkers for predicting oral pre-malignant lesions at high risk of cancer development and prognostic molecular signatures for stratifying oral cancer patients at risk of disease recurrence.
2. Two novel anticancer agents identified in high-throughput chemical libraries screens were tested for *in vitro* and *in vivo* pre-clinical efficacy using indigenously established experimental models of oral cancer for potential use for molecular therapeutics.
3. Validation of novel potential therapeutic molecular targets for head and neck cancer identified by proteomics.
4. Understanding the molecular mechanisms involved in malignant transformation of oral epithelial dysplasia.

Our laboratory successfully verified the potential of a panel of five protein biomarkers for predicting the risk of oral cancer development in patients with oral dysplasia. Identification of the disease in early stages will reduce cost and co-morbidity related to cancer treatment. The protein expression based risk model developed for prediction of recurrence risk in oral cancer patients was validated in an independent external cohort. External validation of the prognostic signature also confirmed our biomarkers panel for identifying aggressive cancer cases at high risk of recurrence as a step forward towards personalized medicine. The indigenous experimental models provide a unique opportunity for unraveling the molecular mechanisms underlying malignant transformation of oral dysplasia. Two novel small molecule inhibitors identified in chemical screens were validated for *in vitro* and *in vivo* pre-clinical efficacy and the mechanism of action of these drugs is under investigation.

## Endocrine Oncology Research

### Ongoing basic science studies (Ranju Ralhan, Paul Walfish, Jeremy Freeman, Ian Witterick, Allan Vescan)

We are developing quality indicators for well-differentiated thyroid cancer and medullary cancer. We are also evaluating our experience with thyroglobulin levels obtained from lymph node fine needle aspiration biopsies and looking at the utility of serial ultrasound imaging of thyroid nodules followed over an extended period of time.

We are developing clinically integrated diagnostics for thyroid cancer with two major themes:

1. Use of protein biomarkers for predicting aggressive thyroid cancers and molecular signature for distinguishing benign from malignant thyroid nodules in ultrasound guided fine needle aspiration biopsies to improve surgical selection.
2. Reference clinical database set up for cataloging the clinical course in different subtypes of thyroid cancer and correlating pre-operative FNA cytology with final surgical pathology.

Accurate identification of benign from malignant thyroid tumours prior to surgery poses a major challenge. Our research focused on identification of a biomarker signature based on alterations in expression analyses of a panel of proteins identified by secretome proteomics that will have the potential to more accurately distinguish between thyroid benign nodules and cancers in needle biopsies prior to surgery than the currently used cytology. A panel of protein biomarkers identified using proteomics and immunohistochemistry in our laboratory can accurately distinguish between thyroid benign nodules and cancers. We are evaluating the potential of these protein biomarkers in thyroid fine needle aspiration biopsies (FNAB) to strengthen the cytopathologic evaluation for diagnosing cancer with minimal invasive procedures. The ultimate goal is accurate stratification of benign thyroid nodules that will spare these patients from surgery.

In our laboratory, we are also developing novel methods of serum thyroglobulin quantification in

thyroid cancer patients with elevated thyroglobulin auto-antibodies using mass spectrometry.

We have established one of the largest clinical databases that have been developed for cataloging the clinical course in different subtypes of thyroid cancer. This database will also be useful for comparing the current pre-operative ultrasound and FNAB cytology based diagnosis with the final surgical pathology. It will therefore serve as a unique invaluable resource for comparative evaluation of new molecular diagnostic techniques with the current cytology based diagnostics to improve future surgical selection of patients for hemi-thyroidectomy vs total thyroidectomy and distinguishing benign from malignant thyroid nodules by pre-operative FNAB techniques.