exchanges Glutamic Acid by Lysine and K is greater than E, which can disrupt interactions with other molecules or other parts of the protein. Finally, rs145530358 SNV exchanges Arginine for Histidine at position 123, with H being smaller and neutral; R has a positive charge, which can interfere with salt and hydrogen bond interactions, in addition to being in a conserved region. To validate the SNVs predicted as deleterious, we searched the Gnomad database that unfortunately does not register data on their clinical significance, but confirmed their low MAF, making epidemiological confirmation difficult. In conclusion, 4 SNVs of the IL17A gene produce significant changes in the protein and may have an important role in thyroid tumors aggressiveness.

LATE BREAKING POSTER 549

Thyroid Cancer Translational Poster

IMPROVED RISK STRATIFICATION FOR PAPILLARY THYROID CANCER (PTC) USING A GENOMIC CLASSIFIER INFORMED BY CLINICAL FEATURES

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Background: Thyroid GuidePx® is a new genomic classifier for PTC. The test classifies PTCs into three distinct molecular subgroups based on expression of 82 prognostic genes. While the test reliably identifies a molecular subtype with a poor prognosis, the capability of the test to identify a very good prognosis sub-group may be improved by incorporating clinical features that are easily identifiable prior to surgery.

Methods: RNASeq data were acquired from The Cancer Genome Atlas, and cohorts from Korea and Canada (total N = 742). The algorithm for the genomic classifier was used to determine molecular subtype. Cases were dichotomized to early PTC (tumor size 1- 4 cm and absence of lymph node disease) and advanced PTC. Structural recurrences only were considered for calculation of progression free survival (PFS).

Results: The 5-year recurrence rate for early Type 1 PTC (enriched with Ras-like follicular variants) was significantly lower in early PTC in comparison to advanced PTC (3.7% vs. 12%). Similarly, early Type 2 PTC had a much lower recurrence rate in comparison to advanced cancers (1.2% vs. 11.4%). In contrast, in Type 3 PTCs (clinically indistinguishable from Type 2), recurrence rate was high in early as well as advanced tumors (20.0 vs. 18.0%). The PFS for low risk PTCs (early Type 1 and Type 2) was significantly better compared to the higher risk classes (log-rank $p < 0.0001$), and time-related AUROC performed better than the ATA risk stratification (AUROC 0.77 vs. 0.71).

Conclusion. Thyroid GuidePxÒ in conjunction with two simple clinical factors improves recurrence risk stratification for PTC. These clinical factors are easily identifiable prior to surgery, and therefore Thyroid GuidePx® could be applied in the preoperative setting using FNA specimens to improve selection of candidates for thyroid lobectomy.

LATE BREAKING POSTER 550

Thyroid Cancer Translational Poster

DIFFUSE SCLEROSING PAPILLARY THYROID CANCER: PATHOLOGICAL FEATURES, MOLECULAR GENETICS AND OUTCOME

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Introduction: Diffuse Sclerosing variant papillary thyroid cancer (DSVPTC) is a rare subtype of PTC. We studied clinicopathological features and molecular genetics of a cohort of DSVPTC seen over a 20-year period (January 1999-January 2019).

Methods: Clinical and pathological data were reviewed and DNA was isolated from FFPE. PCR and Sanger sequencing was done for common somatic point mutations (*BRAFV600E, HRAS, NRAS, KRAS, TERT* promotor, *PTEN* exons 5, 6, 7, and 8, *PIK3CA* exons 9 and 20) followed by Next Generation Sequencing to confirm Sanger sequencing findings and search for fusion genes and other genetic alterations using a cancer gene panel (Oncomine Comprehensive Assay v3, Catalog No. A35806, Thermo Fisher Scientific). We classified molecular findings to definite and probable. Definite are those genetic alterations that are well known to be associated with PTC (e.g. $BRAF^{V600E}$). Probably pathogenic are alterations in genes that are known to be important in cancer pathogenesis (e.g., *TP53*) and were reported in the TCGA [1] or poorly differentiated and anaplastic cancer [2] databases.

Results: A total of 23 patients (16 females, 7 males, median age 18 years, range 8-81) were studied. All patients had total thyroidectomy and received I-131. Central ± lateral lymph node dissection was performed in 20 cases (87%) and was positive in all of them. Distant metastases were diagnosed in 9 patients (39%). Fifteen patients (65%) received one or more additional surgical or I-131 therapies. Ten pts (43.5%) achieved an excellent response, 3 (13%) indeterminate responses, 1 (4.3%) biochemically incomplete, 5 (21.7%) structurally incomplete, 3 (13%) unclear statuses and 1 (4.3%) died. The median duration of follow-up was 8.75 years (2.8-19).

Definite genetic alterations occurred in 8 patients (34.8%) as follows: 1 (4.3%) had $BRAF^{V600E}$, 5 (21.7%) *RET-PTC1*, 1 (4.3%) *RET-PTC3* and 1 (4.3%) *STRN-ALK* fusions. Probably pathogenic alterations included mutations in *FGFR4* (34.8%), *POLE* (30.4%), *TSC2* (21.7%), *CDKN2A* (21.7%), *ERBB2* (17.4%), *NF1* (17.4%), *BRCA2* (13%), *TP53* (8.7%), *SETD2* (4.3%), *ATM* (4.3%), *FLT3* (4.3%), and *ROS1* (4.3%). No mutations were found in *RAS*, *PTEN*, *PIK3CA,* or *TERT* promotor.

Conclusions: DSVPTC is an aggressive type of PTC affecting mostly young patients and is characterized by frequent lymph node and distant metastases. Fusion genes especially *RET-PTC1* are the most common genetic alterations. $BRAF^{V600E}$ and other usual somatic point mutations are rare to absent. However, there are high rates of mutations in *FGFR4*, *POLE, TSC2, NF1, CDKN2A, BRCA2,* and *TP53*. There is no clear genotype/phenotype correlation.

LATE BREAKING POSTER 551

Thyroid Cancer Clinical Poster

DRIVERS OF THYROID ULTRASOUND USE: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Excessive use of thyroid ultrasound (US) fuels thyroid nodule and cancer overdiagnosis. The drivers of US are unknown. Understanding the drivers of US use could help identify when it is misused and further inform the development of interventions to decrease the overdiagnosis of thyroid nodules and thyroid cancer.

Objectives: To determine the drivers of US use and to describe the outcomes of its use.