MON-491

Introduction: Most thyroid cancers (TC) are due to mutually exclusive somatic driver mutations. *NTRK* fusions are rare oncogenic drivers in papillary TC (PTC), poorly differentiated TC (PDTC) and anaplastic TC (ATC), estimated to be in 2.3% of all TC. However, the clinical presentation and behavior of TRK-fusion TC remains largely unknown. **Methods / Case Presentation:** Using institutional databases, we identified all TC patients (pts) with an NTRK fusion reported on somatic testing performed by a CLIA-certified laboratory. Data from the medical records were collected. The objective of this study was to investigate the clinical and pathological features of TC pts whose tumors harbored an NTRK fusion. **Results / Discussion:** We identified 36 TC pts with somatic *NTRK* fusions. Fusion testing was generally done in pts with advanced or radioactive iodine refractory (RAI-R) disease. Median age at diagnosis was 27.4 years (range 4–75 years), 21 (58%) were female and 16 (44%) were pediatric. 28/36 (78%) pts had PTC, 2/36 (5%) PDTC and 6/36 (17%) ATC. There were a total of 12 (33%) *NTRK1*, 24 (67%) *NTRK3*, and no *NTRK2* fusions. In ATC and PDTC pts *NTRK3* was the most common *NTRK* fusion 7/8 (87%). In PTC pts, 11 (39%) had *NTRK1* and 17 (61%) had *NTRK3*. In the adult pts *NTRK3* was more common 17/20 (85%) (Odds Ratio 7.2, P=0.013), however, in pediatric pts rate of *NTRK1* and *NTRK3* were similar. One pt had additional mutations along with the *NTRK* fusion, an ATC pt with multiple mutations including *BRAF* V600*E*. Of the 30 PTC/PDTC pts, 23 (77%) had distant metastases (mets). 14 (38%) pts had distant mets at diagnosis and 11 (69%) pediatric pts had distant mets. Lung 21 (70%) and bone 9 (30%) were the most common distant mets sites. In the PTC pts with distant mets, 9 (41%) had RAI-avid and 11 (50%) had RAI-R disease. In the entire cohort of 36 pts, 17 (53%) were on a systemic therapy of whom 11 pts were PTC. *NTRK* directed was the most common systemic therapy 16 (94%). All PTC pts were alive with a median time from diagnosis of 46 months (Interquartile 1–3: 25–118 months). Four ATC and one PDTC pts had died at the time of the analysis. **Conclusions**: In this study we confirmed that *NTRK* fusions occur primarily in PTC but also in less differentiated tumors. Most were young pts but *NTRK* fusions were identified in tumors from adults as old as 75 years. *NTRK1* and *NTRK3* were the most common *NTRK* fusions with *NTRK3* being more common in adults. In thyrocyte-derived TC pts, *NTRK* fusions are mutually exclusive genetic events that occur in pts of all ages and varying histologies. Given the availability of NTRK targeted therapy, consideration should be given to testing for *NTRK* fusions in advanced thyroid cancer pts, especially those in whom prior genetic testing did not identify an oncogenic driver.

Adipose Tissue, Appetite, and Obesity

NEURAL MECHANISMS OF OBESITY

Characterization of Dual Projection Patterns of Refeeding-Activated Neurons in the Parasubthalamic Nucleus

Gabor Wittmann, PhD, Nicholas Cosentino, BS, Ronald M. Lechan, MD,PHD.
Tufts Medical Center, Boston, MA, USA.

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We have observed that following a fast, animals terminate their food intake within 2h after refeeding accompanied by a pattern of neuronal activation as identified by c-fos immunostaining that involves a number of brain regions associated with the regulation of food intake including the nucleus tractus solitarius (NTS), parabrachial nucleus (PBN), central nucleus of the amygdala (CEA), hypothalamic arcuate and paraventricular nuclei, and bed nucleus of the stria terminalis. We also observed striking c-fos activation in the posterior-lateral hypothalamus called the parasubthalamic nucleus or PSTN, raising the possibility that it may also be an important anorectic center in the brain. To establish how the PSTN is integrated into the CNS, we performed dual-label retrograde tract tracing studies to characterize whether refeeding-activated PSTN neurons project to one, or more than one target area in the CNS. Adult, Sprague-Dawley rats received dual stereotaxic injections of Alexa Fluor 488- and Alexa Fluor 555-conjugated cholera toxin β subunit (CTB; 0.1%, 0.5–1 μl volume) into the 1) PBN and NTS, 2) PBN and CEA and 3) NTS and CEA. After 7–12 days, the animals were fasted for 24 h and then given free access to food for 2 h before euthanasia by transcardial perfusion with 4% paraformaldehyde. Brains with successful dual injections were further processed for c-fos immunohistochemistry. The results showed that 26.5±3.8% of PSTN neurons projecting to the PBN also project to the CEA, and 34.6±7.6% of PSTN neurons that project to the CEA also project to the PBN. In addition, 20.2±2.7% of PSTN neurons that project to the PBN also project to the NTS, and 38.1±9.7% of PSTN neurons that project to the NTS also project to the PBN. Furthermore, 35.0±12.5% of PSTN neurons that project to the CEA project to the NTS and 37.1±4.0% of PSTN neurons that project to the NTS project to the CEA. Finally, up to 15% of the neurons with dual projections to the PBN and CEA contained c-fos after refeeding; up to 18% of the neurons with dual projections to the PBN and NTS contained c-fos; and up to 30% of neurons with dual projections to the NTS and CEA contained c-fos. We conclude that a large number of PSTN neurons have more than one projection site within the brain, thus the PSTN appears to have the capability of simultaneously communicating information about appetite to several, major feeding-related sites within the brain, presumably to terminate feeding.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Chronic Treatment Of Juvenile Hypothalamic Pomc-deficient Mice With RM-493 Prevents The Development Of Obesity

Zoe Thompson, PhD[1], Bhavik P. Shah, PhD[2], Malcolm J. Low, MD, PhD[1].
[1]University of Michigan Medical School, Ann Arbor, MI, USA, [2]Rhythm Pharmaceuticals, Boston, MA, USA.

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Arc-*Pomc* knockout mice have a disruption of the two neural enhancers for the *Pomc* (proopiomelanocortin) gene, resulting in selective loss of *Pomc* gene expression in the