Methods: Publicly available databases were used to inferred copy number variation (RRBS with MethGo tool) and to analyze the transcriptome from trophoblast cells (DESeq2). RNAseq and SNP array from breast, stomach and esophagus carcinomas from TCGA were used for integrative and comparative *in silico* analyses in order to identify dysfunctional regulation on cancer HER2-signilaing pathway.

Results: Virtually all *ERBB2* amplified cancer samples exhibit a core amplification affecting *STARD3*, *TCAP*, *PNMT*, *PGAP3*, *ERBB2* and *GRB7* genes ($r > 0.99$). An additional 17 genes have a high copy number correlation ($r > 0.75$) with *ERBB2*. Five of them have high correlation with *ERBB2* expression (*PGAP3*, *STARD3*, *GRB7*, *ORMDL3*, *PSMD3* and *PNMT*) suggesting they may cooperate to *ERBB2* signaling. In trophoblastic cells, there is an amplification region at the long arm of chr17 affecting 58 genes including the *ERBB2*. Although all those genes are amplified in all trophoblast cells, the genes *GRB7*, *PGAP3*, *STARD3* and *PSMD3* are down regulated in EVT, suggesting the presence of regulatory mechanisms modulating the amplicon expression. Protein integration analysis identified a network connecting ERBB2, GRB7 and PSMD3 in association to STARD3 and PGAP3. GRB7 is known to interact with EGFRs and plays a role in the integrin signaling pathway and cell migration. PSMD3 has a post-translational role in stabilizing HER2, avoiding its degradation.

Conclusions: This integrative and comparative *in silico* analysis of physiologic/pathologic process is the first report suggesting the dysfunction on *ERBB2*, *GRB7*, *PGAP3*, *STARD3* and *PSMD3* network may be crucial for the lethal HER2-pathway in cancer.

Legal entity responsible for the study: Daniel G Tiezzi.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1299

1994P The tumour immune contexture and theranostic markers expression in patients with gastric carcinoma

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Background: Tumour immune microenvironment (TIME) assessment is thought to be effective tool for evaluation of tumour-host interplay and prognostication of different cancers development, including gastric carcinoma (GC). As inflammatory signaling is closely related with DNA-repair pathways, there could be the link between GC immune contexture and DNA-repair enzymes expression defining response to different therapies. This study aimed to assess the relations between TIME and theranostic markers expression in GC of different histological types.

Methods: In this retrospective study we assessed 50 cases (29 males and 21 females; 52.5±2.18 years old) of the locally advanced or metastatic GC naïve to preoperative chemotherapy and radiotherapy. Among enrolled cases there were 15 diffuse GC and 35 intestinal-type GC according to Lauren's classification. The number of CD8+, CD68+ and CD163+ cells as well as expression of ERCC1, TOPO2A and PD-L1 were assessed immunohistochemically.

Results: Intestinal-type GCs were associated with enhanced infiltration by CD8+ cells ($P=0.002$), high rate of PD-L1 expression ($P=0.03$) and CD163+ cells number. In contrast, diffuse GCs demonstrated mostly immune desert phenotype and CD68+ macrophages were the most prevalent within tumour nests and stroma ($P<0.001$). The lowest rate of ERCC1 expression was found in GC with high CD8+ infiltration ($P=0.047$) regardless histological type. Whereas high TOPO2A expression was mostly related with highly CD8-infiltrated GCs of intestinal type ($P=0.018$). Notably, PD-L1 expression was more often in intestinal type GCs rich in CD163+ macrophages ($P=0.03$).

Conclusions: Various histological types of GC demonstrated distinct immunogenisity and were related with different expression of theranostic biomarkers that could affect both immune escape mechanisms and resistance to therapies.

Legal entity responsible for the study: Laboratory of Pathology "CSD Health Care".

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1300

1995P Clinical significance of cannabinoid receptor CB2 expression in non-small cell lung cancer (NSCLC)

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Background: Cannabinoid receptor CB2 expression has been identified to be high in various malignant neoplasms and it is involved in the pathophysiological mechanisms related to carcinogenesis. Lung cancer is an important health problem and new biomarkers are needed for better patients' stratification. This study was conducted to elucidate the clinical significance of cannabinoid receptor CB2 expression in NSCLC.

Methods: Cannabinoid receptor CB2 expression was evaluated immunohistochemically on Tissue MicroArrays (TMAs) of 79 tissue samples from NSCLC patients and it was correlated to clinicopathological parameters and overall survival (OS).

Results: 79 NSCLC patients (48 adenocarcnomas and 31 squamous carcinomas) were studied. Enhanced cannabinoid receptor CB2 expression was observed in 20/79 (25.3%) NSCLC patients. In particular, enhanced cannabinoid receptor CB2 expression was found in 9 out of 48 (18.8%) adenocarcinomas and in 11 out of 31 (35.5%) of squamous cell carcinomas. Cannabinoid receptor CB2 expression was significantly associated with sex, smoking history and histological type ($p=0.019$, $p=0.022$ and $p=0.032$, respectively). In adenocarcinomas, cannabinoid receptor CB2 expression was correlated with overall survival (log-rank test, $p=0.031$), while there was a trend for correlation with tumor size ($p=0.091$) and lymph node metastasis ($p=0.074$). However, in squamous carcinomas cannabinoid receptor CB2 expression was not found to be significantly correlated with any of clinicopathological parameters or survival.

Conclusions: Cannabinoid receptor CB2 receptor may be involved in NSCLC malignant tranformation and growth particularly in adenocarcinomas. Therefore, cannabinoid receptor CB2 receptor could be considered as a potential biomarker or a therapeutic target in NSCLC. More studies needed to elucidate the role of this molecule in NSCLC.

Legal entity responsible for the study: First Department of Pathology, Medical School, National and Kapodistrian University of Athens, Athens, Greece.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1301

1996P Clinical significance of ephrin receptor (EPH)-B1, -B2, -B4 and -B6 expression in thymic epithelial tumours

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Background: Thymic epithelial tumours (TET) are classified according to WHO 2015 subtype and Masaoka stage. Ephrins (ephs) and their receptors (EPHs) −members of the receptor tyrosine kinases (RTKs) superfamily- are implicated in tissue development and homeostasis and aberrantly expressed in tumors. Several preclinical studies have reported safety of EPH-targeting factors. In EPH-B-deficient thymi the epithelial network is disrupted, but thymocyte development is spared. Hence, inhibition of EPH-Bs may constitute a strategy against TETs, without producing immune deficits. To our knowledge EPH-B expression has not been previously studied in TETs.

Methods: EPH-B1, -B2, -B4 and -B6 immunohistochemistry was examined in 98 TETs, (12 type A, 22 AB, 17 B1, 18 B2, 14 B3, 2 micronodular thymomas and 13 thymic carcinomas) and immunoreactivity scoring system (IRS) was used in clinicopathological correlations. Pearson's x^2 test was applied for association analysis.

Results: EPH-B1 nuclear and cytoplasmic expression pattern was noted in the epithelial compartment of all TET, with variations in their lymphocytic component. EPH-B2 was weakly and focally expressed in the cytoplasm of the epithelial cells and mostly weakly in lymphocytic nuclei in half of the cases. EPH-B6 nuclear expression pattern was variable, more common in lymphocytes, and present in about 2/3 of the tumours. EPH-B4 was not expressed. Lymphocytes in thymomas presented higher EPH-B6 IRS compared to thymic carcinomas ($p<.001$), where they probably represent antitumoral immune reaction; conversely, lymphocytic EPH-B1 expression was higher in carcinomas ($p=0.026$). Thymomas of early Masaoka stages presented higher lymphocytic ($p=0.043$) and lower epithelial ($p=0.010$) EPH-B6 IRS. Lymphocytic EPH-B1 expression was less strongly correlated with stage ($p=0.059$).

Conclusions: EPH-B1, -B2 and -B6 are expressed in both the epithelial and lymphocytic component of TETs. The expression level of EPH-B1 and -B6 correlates with established prognostic parameters, i.e. tumour subtype and Masaoka stage,