anti-tumor immunity play a major role in carcinogenesis of NSCLC. $CD8^+CD28^-$ cytotoxic T (Tc) cells and $CD4^+CD25^+FoxP3^+$ regulatory T (Treg) cells known as suppresor CD4+ T cells, have been shown to exist in tumor tissues and inhibits the anti-tumoral immune responses. Natural killer (NK) cells are cytokine producing innate lymphoid cells having cytotoxic capacity to kill tumor cells. In this study the prevalence of Treg cells and CD28 expressing Tc cells and cytotoxic functions were analyzed. **Method:** The study groups comprised patients with newly-diagnosed non-small cell lung cancer (NSCLC) (n=46) with T1-3N0M0 NSCLC, none of whom had received preoperative chemotherapy and/or radiotherapy, and healthy subjects (n=46). The prevalence of $CD3^-CD16^+CD56^+$ NK cells, $CD4^+CD25^+Foxp3^+$ regulatory (Treg) and $CD8^+CD28^-$ T cells were analyzed by flow cytometry. Cytotoxic capacity of NK and $CD8^+$ T cells were analyzed by CD107a degranulation assay. **Result:** NK and $CD8^+CD28^-$ suppressor T cells were increased however percentage of activator $CD8^+CD28^+$T lymphocytes were significantly decreased in patients with NSCLC compared to healthy subjects (p=0.002, p=0.005, p=0.000, p=0.001, p=0.001, p=0.02 and p=0.02, respectively). Although the cytotoxic activity of NK cells did not differ between the groups, CD107a expression was found increased in total $CD8^+$ T cells in unstimulated and K562 stimulation (p=0.001). Although the number of Treg cells are decreased in the NSCLC group but this is not statistically significant. No statistically signficant difference was found in terms of lymphocyte subsets and NK cells between the patients with early(T1) and late stages(T2-3). **Conclusion:** Our findings showed that suppressor $CD8^+CD28^-$ T cell subset as well as NK cells were increased in patients with operable NSCLC. Increased $CD8^+CD28^-$ T cells might cause supression of antitumour immunity and their prevalence might be useful to assess immunotherapy outcomes in patients. Although the number of NK cells increased significantly, the activity of NK cells did not show difference. Functional evaluation of cells has been found to be more important than cell populations. **Keywords:** non-small cell lung cancer, anti-tumor immunity, Treg cells

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Exploring the Germ-Line Contribution to Exceptional Response to PD-1/PD-L1 Inhibition in Patients with NSCLC by Whole Genome Sequencing

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Background: Responses to immune checkpoint inhibitors (CPI) may vary between individuals because of somatic mutation differences in the tumour and/or germ-line differences in immunological tolerance. To explore the latter, this ongoing study evaluates patients with metastatic non-small cell lung cancer (NSCLC) treated with single agent PD-1 or PD-L1 inhibitors recruited from a treatment pool of 420 patients (total) / 137 (active since 1 August 2017). **Method:** Rare and common germ-line DNA variants are analysed in exceptional responders and non-responders by whole genome sequencing (WGS) (Illumina HiSeqX Ten). Exceptional responders are defined as patients with complete or partial response of more than 12 months or stable disease of more than 24 months (per RECIST), and a concurrent immune-related adverse event of any grade. Non-responders are defined as patients with best response of progressive disease, having received at least 4 cycles or 2 months of treatment. In these individuals, the burden of rare and common variants in immune tolerance genes is analysed and compared to the Medical Genome Reference Bank (MGRB), comprising WGS of 1144 well-elderly individuals. Comparisons are made with Fisher Exact test. Genetic risk scores for auto-immune conditions are calculated for these cohorts, MGRB and NSCLC patients included in The Cancer Genome Atlas. Scores are calculated using curated risk alleles and OR weightings derived from the NHGRI-EBI GWAS catalogue. **Result:** Recurrent rare variants (Exome Aggregation Consortium (ExAC) frequency $< 1\%$) were found within responders sequenced to date (n=20), including variant A, a frameshift mutation in a protein kinase not present in ExAC, with allelic frequency (AF) of 1.27% in MGRB and 17.5% of our cohort ($p<0.0001$). Multiple common variants (ExAC $\geq 1\%$) were more frequent within the cohort compared with population standard. Among these, three functional variants within gene B, encoding a protein involved in modulating immune-responsiveness, (variant B.1, B.2 and B.3, ExAC AF: 1.3%, 0.99% and 2.3%), were found seven times (total) across six individuals (one compound heterozygous B.2/B.3). The exceptional responders cohort was enriched for subjects with higher genetic risk for Disease A, psoriasis and psoriatic arthritis compared with control groups. **Conclusion:** Preliminary findings suggest individuals harbouring functional variants in genes promoting immune tolerance may be more responsive to PD-1/PD-L1 inhibitors. This may be due to higher basal immune activation, requiring greater reliance on inhibitory checkpoints to maintain homeostasis. Ordinarily, this would be clinically undetectable, however the addition of a pharmacological CPI may more effectively break immune tolerance in this primed environment. **Keywords:** Immunogenomics, Immunotherapy, whole genome sequencing

P1.04-12
Mass Spectrometry-Based Serum Proteomic Signature as a Potential Biomarker for Survival in NSCLC Patients with Immunotherapy

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Background: The Veristrat test is a serum biomarker using a mass spectrometry (MS)-based proteomic signature derived from machine learning. It is used as a prognostic marker for patients with NSCLC undergoing platinum-based chemotherapy. However, its role in patients undergoing immunotherapy has not been investigated. **Method:** 47 patients with advanced stage NSCLC and no activating EGFR mutation underwent VeriStrat testing from 2016 to 2017. Patients were grouped into Veristrat 'Good' risk group (VS-G) or Veristrat 'Indeterminate' and Veristrat 'Poor' risk group (VS-IP). Kaplan-Meier survival analyses with log rank test were performed to compare the progression-free survival (PFS) and overall survival (OS) between the two groups. PFS of NSCLC patients treated with immunotherapy was derived from the time of the immunotherapy to disease progression or death. **Result:** 47 patients had a mean age of 65.6 (range: 30 to 91). 26 patients were female (55%). 26 patients had diagnosis of adenocarcinoma (55%), while 18 patients had squamous cell carcinoma (38%). 32