Results and discussions We observed systemically elevated levels of Tregs prior to metastatic disease. These tumor-educated Tregs display a distinct phenotype and specifically accumulate in the lung and lymph node metastases that arise in our metastasis models, perhaps indicating their possible importance for metastasis formation and progression. In addition to these systemic changes, within primary tumors and metastases a large population of PD1high Tregs is found. Preliminary data suggest that tumor-associated myeloid cells influence this population. Conclusion We are currently setting out to dissect the mechanism behind this interplay of intra-tumoral immune cells and the role of distinct Tregs found prior to metastatic disease.

PO-387 ABSTRACT WITHDRAWN

PO-388 THE GASTROINTESTINAL TRACT TUMOUR MICROENVIRONMENT DIFFERENTIALLY INFLUENCES MATURATION OF AND CYTOKINE SECRETION FROM DENDRITIC CELLS

1M Morrissey*, 1R Byrne, 1N Lynam-Lennon, 2C Butler, 2C Nuhy, 2K Kennedy, 1M Dunne, 1N McCabe, 1N Reynolds, 1O Sullivan. 1Trinity Translational Medicine Institute TTM, Department of Surgery- St James's Hospital- Trinity College Dublin, Dublin, Ireland; 2University College Dublin, School of Biomolecular and Biomedical Sciences- UCD Conway Institute, Dublin, Ireland; 3Oesophageal Unit, St. James's Hospital- Trinity College Dublin, Dublin, Ireland

Introduction Oesophageal adenocarcinoma (OAC) and rectal adenocarcinoma are treated with neoadjuvant chemoradiotherapy in order to reduce tumour size prior to surgery however only 10%–30% of patients have a complete pathological response. Inflammatory and angiogenic mediators in the tumour microenvironment (TME) have many functions, such as enabling evasion of anti-tumour immune responses by disabling infiltrating dendritic cells (DCs) and have been linked with radioresistance. Tumour Conditioned Media (TCM) from colonic cancer has been shown to strongly inhibit DC maturation. Our aim was to understand if this DC inhibition extends to other cancers of the gastrointestinal tract, to investigate if radiotherapy influences this and to profile constituents of TCM that may influence DC maturation. Material and methods TCM from 0Gy or 2Gy-irradiated cell lines or tumour biopsy explants, was used to pre-treat monocyte-derived DCs prior to stimulation with LPS to measure DC maturation based on DC cell surface markers (HLA-DR, CD86, CD54, CD80, CD83 and PD-L1) and two cytokine levels (IL12 p70 and TNF alpha). Inflammatory and angiogenic mediator multiplex ELISAs were used to profile the TCM of oesophageal and rectal adenocarcinoma. Results and discussions DCs remained responsive to LPS following pre-treatment with OAC cell line TCM, whereas extensive inhibition was induced by CRC cell line TCM. ex vivo TCM from different gastrointestinal adenocarcinoma types induced different effects on DC maturation with oesophageal inducing DC activation, rectal inducing minor activation and colonic inducing inhibition of DC maturation markers. Interestingly, all cancer types induced DC inhibition of secreted TNF alpha. It was also found that 2Gy-irradiated TME induced significant inhibition of DC maturation for irradiated rectal adenocarcinoma and no effect with irradiated oesophageal cancer. Differential levels of inflammatory (IL2) and angiogenic mediators (Ang2 and bFGF) in TCM of GI tumours correlated with DC maturation. Conclusion Overal, this study offers new evidence that there are differences in the human TME from different gastrointestinal (GI) cancers which can directly induce varying levels of inhibition of LPS-induced DC maturation markers, whilst all inhibit secreted TNF alpha.

PO-389 THE ROLE OF IMMUNE MICROENVIRONMENT IN DETERMINING THE ORGAN-SPECIFIC HOMING OF METASTASES

1A García Mulero*, 1JM Piulats, 2V Moreno, 2R Sanz-Pampolona. 1Bellvitge Biomedical Research Institute IDIBELL, Clinical Research in Solid Tumors Group, Hospital de Llobregat, Spain; 2Catalan Institute of Oncology ICO- Bellvitge Biomedical Research Institute IDIBELL and CIBER-ESP, Unit of Biomarkers and Susceptibility, Hospital de Llobregat, Spain

Introduction Metastasis to different organs or tissues may require distinct sets of regulators which may influence the homing and growth of tumour cells to specific secondary sites. Under the hypothesis that the immune microenvironment of the different niches may play an important role in this process, we have categorised metastatic samples from different primary tumours based on their immune profile. Material and methods Gene expression data from metastatic samples with different primary tumour origin (n=342) were downloaded from open repository GEO. Samples were scored using different gene expression profiles and characterised on the basis of their immune and stromal infiltration and activation of immune response pathways (Immunophenoscore, MCPcounter, ESTIMATE; among others). Resultant scores were analysed for statistical differences with ANOVA test. Multivariate analysis was used for clustering the samples based in their immune-features. Results and discussions As expected, significant differences were found between the immune profiles of samples metastasizing in distinct organs. For instance, breast cancer metastasis in lung showed a much higher immunogenic score than breast metastasis in brain (p=5e-4), suggesting a different immune microenvironment modulation. Also in breast, significant differences have been found in cell lineages infiltration, lung metastasis being the ones with the highest T cell component (p=0.002) and liver metastasis the ones with the lowest infiltration of endothelial cells (p=0.005). Moreover, in other cancer types like melanoma, samples showed differences among different metastatic locations. Interestingly, when comparing metastatic samples originating from different primary tumour, a high concordance among secondary tumours in immune scores were found; specifically in brain metastasis. These results suggest that cells needs to share similar molecular profiles to evade the immune surveillance and growth in a specific niche, independently of their origin. Conclusion Metastases from the same primary tumour growing in different organs show differences in their immune profile. However, those samples from different primary origin but growing in the same secondary organ shared a characteristic immune profile. These results suggest that immune system plays a role in determining the organ-specific homing of metastasis.