Background
Pancreatic ductal adenocarcinoma (PDAC) has an environment characterized by heterogeneity in cancer associated fibroblasts (CAF) as well as an immune desert phenotype. It is well-established that dendritic cells (DCs) which are often dysfunctional in the PDAC tumor microenvironment (TME), are crucial in priming and sustaining T cell immunity. It is speculated that this immune dysfunction is potentially caused by crosstalk between DCs or their progenitors with tumor or CAF, but this mechanism is not well characterized. Flt3L is known to drive expansion and mobilization of DCs, in particular, the cross-presenting DC1s into the tumor.

Methods
We utilized a magnetic bead-based method to capture the tumor, immune and stromal components of the KPCY (Pdx-1-Cre, KRASG12D, p53-/-, YFP+) TME in response to Flt3L injection followed by scRNAseq profiling to examine overall changes.

Results
As expected, Flt3L injection induced increased DC numbers in the TME. Interestingly we observed several genes downregulated in tumor cells and a change in the CAF subpopulation upon Flt3L treatment. Because tumor and CAF cells do not express Flt3, our observation suggests this change results from the cross-talk between Flt3-induced DC lineage with tumor and/or CAF subpopulations. Using differential expression of gene (DEG), pathway and ligand-receptor analysis, we characterized molecular interactions between Flt3L-responsive DC lineage with tumors and CAF cells in the TME.

Conclusions
Our results highlight the impact of these DCs on tumors and TME stroma as an additional function to shape immune response, thereby providing a rationale to modify TME with Flt3 agonism.