Cancer-Associated Fibroblasts correlates with immune phenotypes in human tumors

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Background
Cancer associated fibroblast (CAFs) are key players in immune regulation that shapes the tumor microenvironment. Data related to their contribution to infiltrated, deserted, and excluded immune phenotypes in human tumor samples are lacking.

Methods
Colorectal cancer, non-small cell lung cancer, ovarian cancer, pancreatic cancer, triple-negative breast cancer, leiomyosarcoma, and undifferentiated pleomorphic sarcoma samples from the IMMUCAN institutional profiling program (Institut Bergonié, Bordeaux, France) were evaluated. Adjacent slides were stained with H&E and a multiplex immunofluorescence panel staining for CD8 and collagen 1 (COL1). Slides were evaluated by two pathologists who characterized the tumors as immune deserted, immune excluded, or immune infiltrated using the following criteria: deserted: characterized by a paucity/absence of CD8+ T cells; excluded: characterized by the presence of CD8+ T cells that do not penetrate the tumor parenchyma; and infiltrated: characterized by the presence within the tumor parenchyma of CD8+ T cells. Image analysis was used to quantify fibroblasts (nucleated, COL1+ cells in the TME) and immune infiltrate in the TME.

Results
In 143 samples evaluated, 67 (47.9%) were excluded, 27 (18.9%) deserted, and 49 (34.4%) infiltrated. Median CD8+ density increased in excluded (209 (40-1309) cells/mm2) and infiltrated (184 (25-1472) cells/mm2) compared to deserted (47 (4-307) cells/mm2) tumors ($p<0.001$). Fibroblast density was elevated in excluded (2937 (43-6616) cells/mm2) and deserted (2908 (467-7987) cells/mm2) tumors compared to infiltrated (1877 (581-6742) cells/mm2). CD8+ cell density directly correlated with fibroblast density in excluded ($r=0.87$), deserted ($r=0.67$), and infiltrated ($r=0.79$) tumors (all $p<0.001$).

Conclusion
Immune excluded tumors have high levels of CD8+ lymphocytes in the TME, albeit without penetration into the tumor parenchyma. Higher CD8+ lymphocyte infiltration in the TME is associated with increased CAFs density in all immune phenotypes. Additional data related to the spatial relationships of immune cells and fibroblast subsets in the TME of different cancer immune phenotypes will be presented at the meeting.