CCL19-producing fibroblastic stromal cells restrain lung carcinoma growth by promoting local antitumor T-cell responses

Hung-Wei Cheng, Lucas Onder, Jovana Cupovic, Maximilian Bösch, Mario Novkovic, Natalia Pikor, Ignazio Tarantino, Regulo Rodriguez, Tino Schneider, Wolfram Jochum, Martin Brutsche & Burkhard Ludewig

BACKGROUND
A particular characteristic of non-small cell lung cancer is the composition of the tumor microenvironment with a very high proportion of fibroblastic stromal cells (FSCs).

OBJECTIVE
Lapses in our basic knowledge of fibroblast phenotype and function in the tumor microenvironment make it difficult to define whether FSC subsets exist that exhibit either tumor-promoting or tumor-suppressive properties.

METHODS
We used gene expression profiling of lung versus tumor FSCs from patients with non-small cell lung cancer. Moreover, CCL19-expressing FSCs were studied in transgenic mouse models by using a lung cancer metastasis model.

RESULTS
CCL19 mRNA expression in human tumor FSCs correlates with immune cell infiltration and intratumoral accumulation of CD8 T cells. Mechanistic dissection in murine lung carcinoma models revealed that CCL19-expressing FSCs form perivascular niches to promote accumulation of CD8 T cells in the tumor. Targeted ablation of CCL19-expressing tumor FSCs reduced immune cell recruitment and resulted in unleashed tumor growth.

CONCLUSION
These data suggest that a distinct population of CCL19-producing FSCs fosters the development of an immune-stimulating intratumoral niche for immune cells to control cancer growth.

type: journal paper/review (English)
date of publishing: 31-01-2018
journal title: J Allergy Clin Immunol
ISSN electronic: 1097-6825