BIOGRAPHICAL SKETCH

.

NAME: Jean Albrengues

POSITION TITLE: Post-doctoral fellow

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Nice, Sophia Antipolis, France.	B.Sc.	06/08	Biology
University of Nice, Sophia Antipolis, France.	M.Sc.	06/10	Cancer Biology
University of Nice, Sophia Antipolis, France.	Ph.D.	12/14	Cancer Biology

A. Personal Statement

During my Master's, Ph.D. degrees and post-doctoral training, I specialized in studying the role of inflammation and the tumor microenvironment in cancer progression. In particular, I studied how inflammatory cytokines can activate stromal fibroblasts in the early stages of carcinogenesis (as a Ph.D. student in Dr. Cedric Gaggioli's lab) and how inflammation can promote metastatic cancer recurrence (as a Post-doctoral fellow, in Mikala Egeblad's lab). A combination of three-dimensional cultures, biochemistry, molecular biology and *in vivo* modeling helped me characterize how inflammation can trigger fibroblasts and neutrophils activation to promote extracellular matrix remodeling and subsequent tumor progression. These training allowed me to understand the importance of microenvironmental cues during cancer progression. Indeed, it is now well accepted that cancer progression relies on the tumor microenvironment, and that these communications can be the foundation of new therapeutic strategies. In this context, my research aims to discover new signaling pathways within the tumor microenvironment that could be used as therapeutic targets to complement conventional chemotherapies.

B. Positions and Honors

Positions:
2015: Postdoctoral fellow at Cold Spring Harbor Laboratory (Mentor: Dr. Mikala Egeblad**)**

Awards and Honors:
2009*: Master I of Science in genetic, development and immunology, with honors* (University of Nice Sophia Antipolis (UNS), Nice, France). Mentor: Dr. Jean-François Peyron.
2010: *Master II of Science in genetic, development and immunology, with honors* (UNS, Nice, France). Mentor: Dr. Cedric Gaggioli.
2010: *French Ministry of Research Graduate Fellowship* (UNS, Nice, France) (3 years).
2013: Targeting the Tumor Stroma meeting (Beatson Institute, Glasgow, Scotland), *best poster presentation.*
2014: *Ligue Nationale Contre le Cancer, Graduate Fellowship* (Paris, France) (1 year).
2014: *Ph.D. in Cellular Biology, with honors* (UNS, Nice, France). Mentor: Dr. Cedric Gaggioli.
2015: *Fondation ARC pour la recherché sur le cancer, postdoctoral fellowship* (Paris, France) (1 year).
2016: *European Molecular Biology Organization Long-Term fellowship* (Heidelberg, Germany) (16 months).
2016: *Terri Brodeur Breast Cancer Foundation fellowship* (New London, Connecticut, USA) (2 years).
2016: *Susan G. Komen post-doctoral fellowship (Dallas, Texas, USA) (3 years).*

C. Contribution to Science

Signaling crosstalk between tumor and stroma cells is a key process of carcinoma development. In solid tumors, the neoplastic cells are immersed in a complex microenvironment including multiple cell types

embedded in an extracellular matrix (ECM). Among the multiple cell types that contribute to the ECM architecture, I focused on Carcinoma Associated Fibroblasts (during my PhD) and neutrophils (during my post-doctoral training) which are responsible for ECM remodeling and tumor progression. In this context, my contributions to the research into crosstalk between cancer cells and microenvironment are the following:

1. Activation and maintenance of pro-invasive fibroblasts during carcinogenesis.

Unveiling the molecular mechanisms that govern fibroblast activation in cancer takes on increasing interest for the discovery of potential targets allowing perfection of therapies counteracting tumor cell dissemination and metastasis, which are the main causes of the patients' demise. During my Ph.D training, I developed new *in vitro* models to study the role of the tumor microenvironment in the early step of metastasis, i.e., local invasion of the tumor cells. Using this three-dimensional cellular culture and mouse model of breast carcinoma I demonstrated the role of the pro-inflammatory cytokine LIF and the JAK1/STAT3 signaling pathway during the activation and the epigenetic maintenance of pro-invasive fibroblasts. This work has resulted in several publications :

Sanz-Moreno, V., C. Gaggioli, M. Yeo, J. Albrengues, F. Wallberg, A. Viros, S. Hooper, R. Mitter, C. C. Feral, M. Cook, J. Larkin, R. Marais, G. Meneguzzi, E. Sahai and C. J. Marshall (2011). "ROCK and JAK1 signaling cooperate to control actomyosin contractility in tumor cells and stroma." **Cancer Cell 20**(2): 229-245.

Albrengues, J., G. Meneguzzi and C. Gaggioli (2013). "Analysis of collective invasion of carcinoma cells in a 3D organotypic model." **Methods Mol Biol** 961: 243-252.

Albrengues, J., I. Bourget, C. Pons, V. Butet, P. Hofman, S. Tartare-Deckert, C. C. Feral, G. Meneguzzi and C. Gaggioli (2014). "LIF mediates proinvasive activation of stromal fibroblasts in cancer." **Cell Rep** 7(5): 1664-1678.

Albrengues J, Bourget I, Maiel M, Philippe C, Benamar S, Croce O, Sanz-Moreno V, Cristofari G, Meneguzzi G and Gaggioli C (2015). "Epigenetic switch drives the conversion of fibroblasts into pro-invasive cancer-associated fibroblasts." ***Nat. Commun*** 6: 10204

2. Neutrophils Extracellular Traps produced during inflammation awaken dormant cancer cells in mice.

We found that sustained experimental lung inflammation—induced by either tobacco smoke exposure or nasal instillation of lipopolysaccharide (LPS)—converted dormant cancer cells to aggressive lung metastases in mice. Both types of sustained inflammation also caused the formation of Neutrophil Extracellular Traps. Inhibiting NET formation or digesting the NETs' DNA scaffold prevented conversion of single disseminated cancer cells to growing metastases in mouse models of breast and prostate cancer. The NET-DNA bound to the extracellular matrix (ECM) protein laminin, bringing two NET-associated proteases, NE and MMP9, to their substrate. This in turn facilitated a sequential cleavage of laminin, first by NE and then by MMP9. The NET-mediated proteolytic remodeling of laminin revealed an epitope that triggered proliferation of dormant cancer cells through integrin activation and FAK/ERK/MLCK/YAP signaling. We generated a blocking antibody against NET-remodeled laminin, and this antibody prevented or reduced tobacco smoke exposure- or LPS-induced inflammation from awakening dormant cancer cells in mice.

Albrengues, J., M. A. Shields, D. Ng, C. G. Park, A. Ambrico, M. E. Poindexter, P. Upadhyay, D. L. Uyeminami, A. Pommier, V. Kuttner, E. Bruzas, L. Maiorino, C. Bautista, E. M. Carmona, P. A. Gimotty, D. T. Fearon, K. Chang, S. K. Lyons, K. E. Pinkerton, L. C. Trotman, M. S. Goldberg, J. T. Yeh and M. Egeblad (2018). "Neutrophil extracellular traps produced during inflammation awaken dormant cancer cells in mice." **Science** 361(6409).

Pommier, A., N. Anaparthy, N. Memos, Z. L. Kelley, A. Gouronnec, R. Yan, C. Auffray, J. Albrengues, M. Egeblad, C. A. Iacobuzio-Donahue, S. K. Lyons and D. T. Fearon (2018). Unresolved endoplasmic reticulum stress engenders immune-resistant, latent pancreatic cancer metastases. **Science** 360(6394).

Complete list of published work:

https://www.ncbi.nlm.nih.gov/pubmed/?term=jean+albrengues