# Targeting tumor-resident mast cells for effective anti-melanoma immune responses

**JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**

**ID** 4514967
**Author(s)** Kaesler, Susanne; Wölbing, Florian; Kempf, Wolfgang Eberhard; Skabytska, Yuliya; Köberle, Martin; Volz, Thomas; Sinnberg, Tobias; Amaral, Teresa; Möckel, Sigrid; Yazdi, Amir; Metzler, Gisela; Schaller, Martin; Hartmann, Karin; Weide, Benjamin; Garbe, Claus; Rammensee, Hans-Georg; Röcken, Martin; Biedermann, Tilo
**Author(s) at UniBasel** Hartmann, Karin ;
**Year** 2019
**Title** Targeting tumor-resident mast cells for effective anti-melanoma immune responses
**Journal** JCI insight
**Volume** 4
**Number** 19
**Pages** / **Article-Number** e125057
**Keywords** Chemokines; Immunology; Mast cells; Melanoma; Oncology
**Mesh terms** Animals; Antineoplastic Agents, pharmacology; Biomarkers, Tumor; CTLA-4 Antigen, immunology; Chemokine CXCL10, metabolism; Chemokines; Disease Models, Animal; Humans; Immunotherapy; Mast Cells, pathology; Melanoma, pathology; Mice; Mice, Inbred C57BL; Mice, Knockout; Tumor Microenvironment, drug effects
Immune checkpoint blockade has revolutionized cancer treatment. Patients developing immune mediated adverse events, such as colitis, appear to particularly benefit from immune checkpoint inhibition. Yet, the contributing mechanisms are largely unknown. We identified a systemic LPS signature in melanoma patients with colitis following anti-cytotoxic T lymphocyte-associated antigen 4 (anti-CTLA-4) checkpoint inhibitor treatment and hypothesized that intestinal microbiota-derived LPS contributes to therapeutic efficacy. Because activation of immune cells within the tumor microenvironment is considered most promising to effectively control cancer, we analyzed human and murine melanoma for known sentinels of LPS. We identified mast cells (MCs) accumulating in and around melanomas and showed that effective melanoma immune control was dependent on LPS-activated MCs recruiting tumor-infiltrating effector T cells by secretion of CXCL10. Importantly, CXCL10 was also upregulated in human melanomas with immune regression and in patients with colitis induced by anti-CTLA-4 antibody. Furthermore, we demonstrate that CXCL10 upregulation and an MC signature at the site of melanomas are biomarkers for better patient survival. These findings provide conclusive evidence for a ”Trojan horse treatment strategy” in which the plasticity of cancer-resident immune cells, such as MCs, is used as a target to boost tumor immune defense.
**Publisher** American Society for Clinical Investigation
**ISSN/ISBN** 2379-3708
**URL** http://www.ncbi.nlm.nih.gov/pmc/articles/pmc6795496/
**edoc-URL** https://edoc.unibas.ch/72202/
**Full Text on edoc** No;
**Digital Object Identifier DOI** 10.1172/jci.insight.125057
**PubMed ID** http://www.ncbi.nlm.nih.gov/pubmed/31578309
**ISI-Number** WOS:000488988500001
**Document type (ISI)** Journal Article