BORSIG GROUP

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SUMMARY & MISSION STATEMENT

The capacity of tumor cells to metastasize into distant organs is dependent on the adopted tumor microenvironment consisting of altered stroma and infiltrating leukocytes. The aim of our research is to elucidate the cellular and molecular mechanisms leading to formation of a tumor microenvironment that promotes metastasis; and to inhibit metastasis by targeting identified pathways.

OVERVIEW

The main focus of our studies is the tumor microenvironment in tissue-specific metastasis. We analyze the contribution of altered glycosylation, typical for carcinomas, to tissue-specific metastatic spread. We previously showed that cell-cell mediated interactions among metastatic tumor cells; platelets; leukocytes and a locally activated endothelium induce chemokine expression and thereby promote metastasis. The selectin-mediated recruitment monocytic cells have been linked to increased chemokine concentration at metastatic sites. Importantly, local endothelial activation associated with E-selectin expression and increased chemokine production was shown to be essential for an efficient migration of tumor cells through the endothelial cells. The chemokine-driven recruitment of monocytes has been identified as a critical factor for pulmonary metastasis. Therefore, we test the possibility to inhibit blood-borne metastasis by targeting of the identified chemokines. Inflammation is a determining factor of various cancers, including colorectal cancer. We study the effect of microbiota on inflammation and colon tumorigenesis.

SELECTED CANCER RELATED PUBLICATIONS

Gut microbiota modulate T cell trafficking into human colorectal cancer. Cremonesi E., Glaus Garzon J.F., Governa V., Mele V., Amicarella F., Padovan E., Muraro M.G., Trella E., Oertli D., Däster S., Weixler B., Bolli M., Rosso R., Spagnoli G.C., Khanna N., Egli A., Zajac P., Borsig L., Iezzi G. **Gut**. 2018 Feb 6. doi: 10.1136/gutjnl-2016-313498.

Transcription factor c-Myb inhibits breast cancer lung metastasis by suppression of tumor cell seeding. Knopfova L., Biglieri E., Volodko N., Masarik M., Hermanova M., Glaus Garzon J., Ducka M., Kucirkova T., Soucek K., Šmarda J., Benes P., Borsig L. **Oncogene**. 2018 Feb 22;37(8):1020-1030.

Monocyte Induction of E-Selectin-Mediated Endothelial Activation Releases VE-Cadherin Junctions to Promote Tumor Cell Extravasation in the Metastasis Cascade. Häuselmann I, Roblek M, Protsyuk D, Huck V, Knopfova L, Grässle S, Bauer AT, Schneider SW, Borsig L. **Cancer Res.** 2016 Sep 15;76(18):5302-12.

Metastatic growth progression caused by PSGL-1-mediated recruitment of monocytes to metastatic sites. Hoos A., Protsyuk D., Borsig L. **Cancer Res.** 2014 Feb 1;74(3):695-704.

Endothelial CCR2 signaling induced by colon carcinoma cells licenses extravasation via the JAK2-Stat5 and p38MAPK pathway. Wolf M.J., Hoos A., Bauer J., Boettcher S., Knust M., Weber A., Simonavicius N., Moch H., Manz M., Stürzl M., Croner R.S., Konrad A., Schneider C., Aguzzi A., van Loo G., Pasparakis M., Prinz M., Heikenwälder M.*, Borsig L.* **Cancer Cell.** 2012 Jul 10;22(1):91-105.

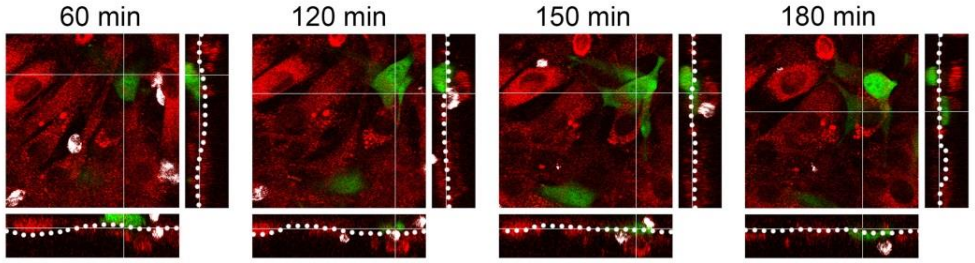

Figure legend: Tumor cell migration through the endothelial cells is mediated by inflammatory monocytes and dependent on endothelial activation. Live imaging of MC-38GFP (green) trans-endothelial (red) migration assisted by monocytes (white) captured at different time points. Dotted line indicates the endothelial monolayer. Bar = 30 µm. (from Häuselmann I. *et al* 2016 Cancer Res 76:5302).