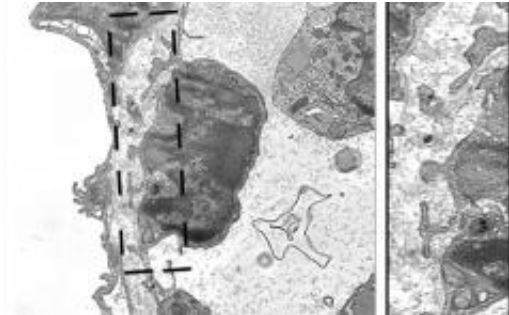


# How tumor cells create their own pathways

July 10 2012

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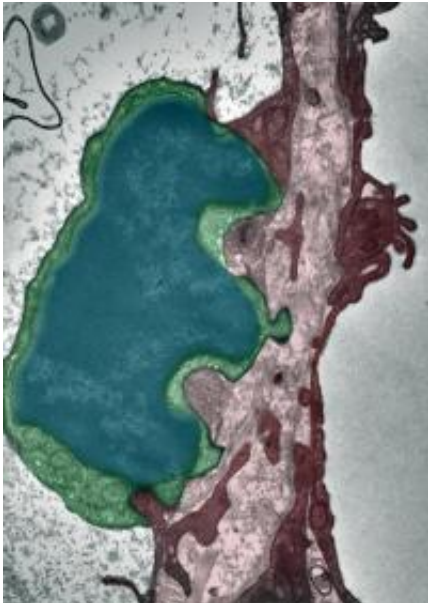


The picture shows a tumor cell that migrates through the wall of a blood vessel into the neighboring tissue. Credit: Marco Prinz/Universitaet Freiburg

Metastasis occurs when tumor cells "migrate" to other organs through the bloodstream. Scientists have now discovered the trick tumor cells use to invade tissue from the blood vessels: They produce signaling proteins to make the arterial walls permeable - thus clearing their pathway to a different organ. The latest findings are published in the current issue of the journal *Cancer Cell*.

How does a tumor cell set up a [signaling pathway](#) in order to metastasize? Scientists at Technische Universität München's (TUM) Klinikum rechts der Isar and Helmholtz Zentrum München have made a significant discovery in this area by studying colon cancer. They have learned that the tumor cells release certain proteins known as chemokines. In the case of metastatic colon [cancer cells](#), the chemokine concerned is CCL2. The CCL2 chemokine docks on to the cells of the

inner blood vessel walls (endothelial cells) and activates the corresponding receptor (CCR2 receptor). This connection makes the endothelial cells permeable – creating a clear path for the tumor cells.

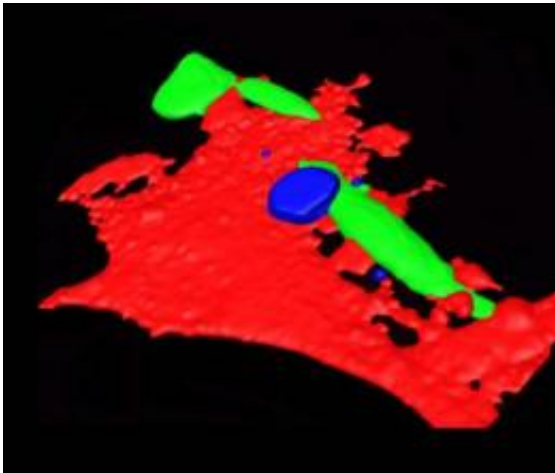


This is an electron microscopy from a tumor cell that is on the way to extravasate through an alveolar endothelium blood capillaries - the tumor cell is depicted in blue green, the endothelial cell in purple red. The protrusion of the tumor cell are seen that form their way through the endothelial cell. Credit: UZH

Professor Mathias Heikenwälder of TUM's Institute of Virology explains that the tumor cells use a clever trick to migrate: "The [tumor cells](#) outwit the endothelial cells by emitting a signal used by healthy cells." To date, research has mainly focused on macrophage cells attracted by the chemokines of the tumors. "By understanding the role of chemokine receptors in relation to endothelial cells we have potentially uncovered a brand new approach to cancer treatment," says Heikenwälder.

"Measuring the number of chemokines could allow us to draw clear

conclusions on the likely spread of a primary tumor to other organs and predict the risk of metastasis in patients," continues Heikenwälder. "Furthermore, the option of blocking the chemokine receptor CCR2 at the endothelial cells gives healthcare professionals a new way of preventing metastases both before and following an operation."



Tumor cells (green) adhere on the endothelium (red) that gets activated and permeable through CCL2-CCR2 signaling. Tumor cell extravasation is facilitated by recruited monocytic cells (blue). Technique: Adaptation of confocal image stacks creating an artificial surface. Credit: UZH

For their research, the scientists used colon cancer tissue and colon cancer cell lines from mice and humans. The next steps will involve studying the findings in greater detail and examining how the new concept can be transferred to other types of cancer.

**More information:** Monika Wolf et al., 2012. Endothelial CCR2 signaling induced by colon carcinoma cells enables extravasation via the JAK2-Stat5 and p38MAPK pathway, *Cancer Cell*, July 2012.

Provided by Technical University Munich

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