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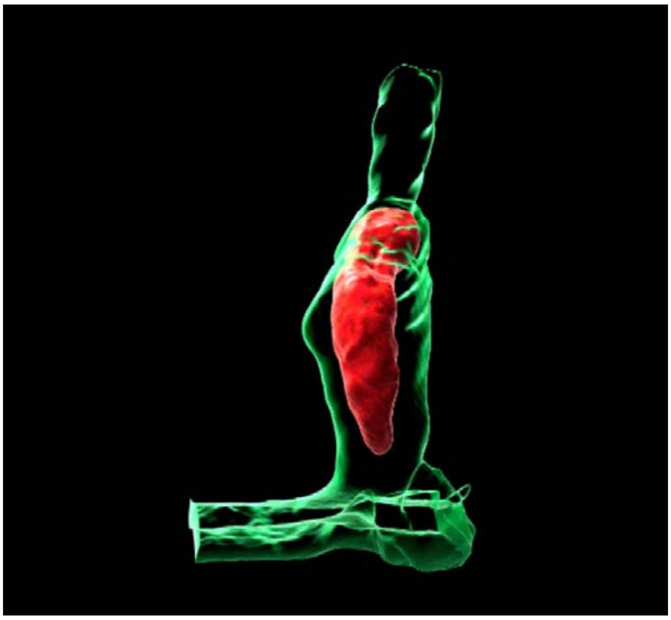
A mechanical view on metastasis and the role of tumor cell viscosity



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A tumor cell lodged in an intersomitic vessel of a zebrafish embryo.

Millions of people worldwide are diagnosed with cancer every year. In advanced tumor diseases, cancer cells detach from the original tumor and settle in other parts of the body to form metastases. On their way, they have to be distributed via the body's own transport system, such as blood or the lymphatic vascular system, and overcome numerous mechanical hurdles. A multidisciplinary research team has investigated how the mechanical properties of tumor cells circulating through blood vessels influence their metastatic pathways. The results, recently published in *Nature Materials*, provide important building blocks for understanding metastasis.

Tumor cells leaving the original tissue and settling in distant organs of the body is referred to as metastasis of the primary tumor. Since in most cases it is not the primary tumor but metastases that cause cancer-related deaths, a fundamental understanding of how tumor cells overcome the body's own barriers is crucial for successful cancer treatment.

To form metastases, tumor cells must detach from the primary tumor, enter the bloodstream, travel through the circulatory system, become lodged in small blood vessels, exit them (extravasation), and finally colonize a new tissue. Although it is known that mechanical properties influence the success of metastasis, the fundamental mechanisms behind this are still unclear.

A collaborative research team of biology and metastasis experts and physicist involving the Max-Planck-Zentrum für Physik und Medizin (MPZPM) and the Centre de Recherche en Biomédecine de Strasbourg (INSERM/Unistra, CRBS) has analyzed the physical constraints that tumor cells face on their way to metastasis, and investigated how their mechanical behaviour affects their progression through the metastatic process. The scientists, led by Prof. Jacky G. Goetz (INSERM/Unistra, CRBS), Prof. Jochen Guck (Max Planck Institute for the Science of Light, MPL/MPZPM) and Dr. Salvatore Girardo (MPZPM), consider circulating tumor cells as objects with a certain size and deformability. These are exposed to forces as they move through the circulatory system and invade surrounding tissues.

The team focuses on the ability of cells to respond to these forces elastically or viscously. Cells are viscoelastic, which means they are both squishy and springy. When you push on them slowly, they behave like a liquid and gradually flow or deform (viscous behaviour). When you push on them quickly, they behave like a spring and snap back to their original shape once the force is removed (elastic behaviour).

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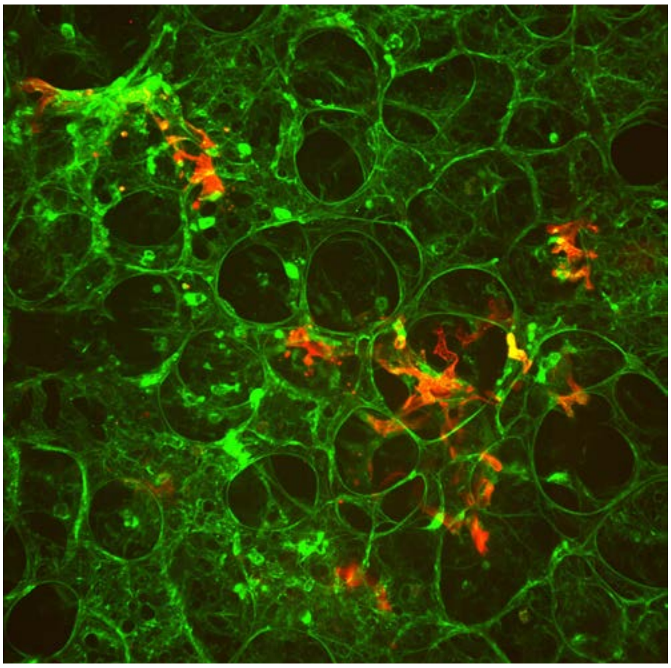
The scientists combine biological models with tailored biophysical tools to probe cellular behavior. For the first time, this combination enabled them to study directly how elastic and viscous behaviors influence tumor cell circulation, arrest, and exit from blood vessels during metastasis. They developed two kinds of biophysical tools: hydrogel beads, that mimic the elastic behavior of cells, and engineered cells modified to exhibit specific viscoelastic profiles.



Tumor cell in the maze of the lung vasculature of a mouse.

The combination of these systems with *in vivo* imaging in two animal models (zebrafish and mouse) enables the team to track their behaviour in the circulatory system.

The researchers demonstrate that viscosity, rather than elasticity, determines whether circulating objects enter small vessels, where they come to a standstill, and how they extravasate, invading the surrounding tissues. Furthermore, they show that viscosity is required for efficient extravasation through endothelial remodeling. At the same time, they find that mechanical properties which support extravasation do not necessarily support later metastatic growth.

"Our work identifies cell viscosity as a key mechanical parameter that controls multiple steps of the metastatic process within blood vessels," says Girardo, head of the Core Facility Lab-on-a-Chip at MPZPM. "We demonstrate that the mechanical traits that help tumor cells leave the bloodstream can conflict with traits that support their later growth at distant sites. This indicates that mechanical adaptation may be necessary during metastasis," adds Goetz, who developed the study design together with Jochen Guck†, former director at MPL and head of the division "Cell Physics".

Understanding and potentially controlling parameters such as cell viscosity could offer new ways to address cancer through mechanics. "This work is deeply rooted in Guck's vision," say Girardo and Goetz. "He firmly believed in approaching medical challenges from a new physical perspective and in combining this with biological understanding to achieve a more comprehensive view of disease. This way of thinking continues to inspire us, as it opens the door to truly novel diagnostic and therapeutic approaches."

Method

The work integrates biophysical methods developed in the division of Jochen Guck (MPL, MPZPM) and D. Müller (ETH Zurich, Department of Biosystems Science and Engineering in Basel) as well as in the lab of Jacky Goetz (INSERM/University of Strasbourg), in addition to cell-like microgel particles developed in MPZPM's Core Facility Lab-on-a-Chip under the direction of Dr. Salvatore Girardo as part of the EU project FLAMIN-GO. *In vivo* imaging in two animal models (zebrafish and mouse) developed by Jacky Goetz (INSERM/University of Strasbourg) was combined with metastasis assays.

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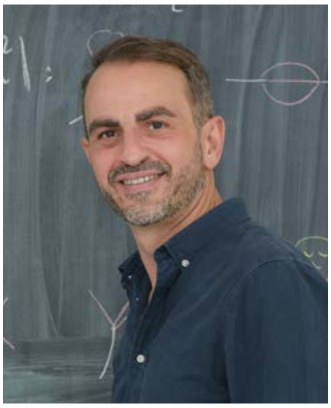

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Cell viscosity influences haematogenous dissemination and metastatic extravasation of tumour cells. *Nat. Mater.* (2026). https://doi.org/10.1038/s41563-025-02462-w

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*The **Max-Planck-Zentrum für Physik und Medizin** is conceived as a joint effort between the Max-Planck-Institute for the Science of Light (MPL), the Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) and the Universitätsklinikum Erlangen (UKER). The new scientific center aims to apply advanced methods from experimental physics and mathematics to basic biomedical research with an emphasis on the intercellular microenvironment. Learn more at mpzpm.mpg.de.*