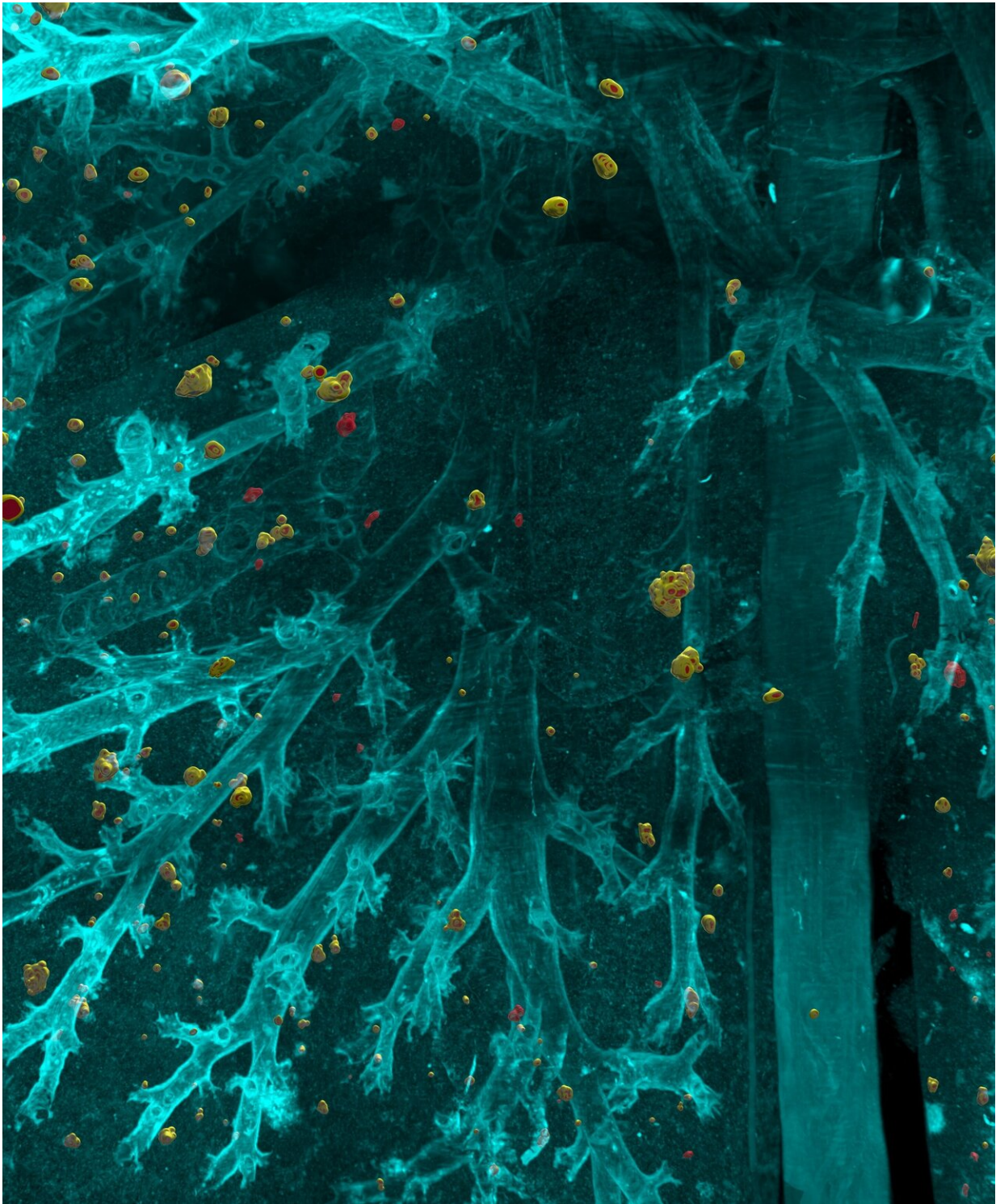


New algorithm detects even the smallest cancer metastases across the entire mouse body

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DeepMACT makes use of artificial intelligence to find even the smallest metastases in the entire mouse body. The picture shows single disseminated cells spreading through the lung. Credit: ©Helmholtz Zentrum München

Cancer is one of the leading causes of death worldwide. More than 90 percent of cancer patients die of distal metastases rather than as a direct result of the primary tumor. Cancer metastases usually develop from single disseminated cancer cells, which evade the body's immune surveillance system. Up to now, comprehensive detection of these cells within the entire body has not been possible, owing to the limited resolution of imaging techniques such as bioluminescence and MRI. This has resulted in a relative lack of knowledge of the specific dissemination mechanisms of diverse cancer types, which is a prerequisite for effective therapy. It has also hampered efforts to assess the efficacy of new drug candidates for tumor therapy.

Transcending human detection capabilities with deep learning

In order to develop new techniques to overcome these hurdles, the team led by Dr. Ali Ertürk, Director of the Institute for Tissue Engineering and Regenerative Medicine at Helmholtz Zentrum München, had previously developed vDISCO—a method of tissue clearing and fixation which transforms mouse bodies into a transparent state allowing the imaging of single cells. Using laser-scanning microscopes, the researchers were able to detect the smallest metastases down to individual [cancer cells](#) in cleared the tissue of the mouse bodies.

However, manually analyzing such high-resolution imaging data would be a very time-consuming process. Given the limited reliability and processing speed of currently available algorithms for this kind of data analysis, the teams have developed a novel [deep-learning](#) based algorithm called DeepMACT. The researchers have now been able to detect and analyze cancer metastases and map the distribution of

therapeutic antibodies in vDISCO preparations automatically. The DeepMACT algorithm matched the performance of human experts in detecting the metastases—but did so more than 300 times faster. "With a few clicks only, DeepMACT can do the manual detection work of months in less than an hour. We are now able to conduct high-throughput metastasis analysis down to single disseminated tumor cells as a daily routine", says Oliver Schoppe, co-first-author of the study and Ph.D. student in the group of Prof. Dr. Bjoern Menze at TranslaTUM, the Center for Translational Cancer Research at TUM.

Detecting cells, gathering data, learning about cancer

Using DeepMACT, the researchers have gained new insights into the unique metastatic profiles of different tumor models. Characterization of the dissemination patterns of diverse cancer types could enable tailored drug targeting for different metastatic cancers. By analyzing the progression of breast-cancer metastases in mice, DeepMACT has uncovered a substantial increase in small metastases throughout the mouse body over time. "None of these features could be detected by conventional bioluminescence imaging before. DeepMACT is the first method to enable the quantitative analysis of metastatic process at a full-body scale", adds Dr. Chenchen Pan, a postdoctoral fellow at Helmholtz Zentrum München and also joint first author of the study. "Our method also allows us to analyze the targeting of tumor antibody therapies in more detail."

How effective are current cancer therapies?

With DeepMACT, the researchers now have a tool with which to assess the targeting of clinical cancer therapies that employ tumor-specific monoclonal antibodies. As a representative example, they have used DeepMACT to quantify the efficacy of a therapeutic antibody named 6A10, which had been shown to reduce tumor growth. The results

demonstrated that 6A10 can miss up to 23 percent of the metastases in the bodies of affected mice. This underlines the importance of the analysis of targeting efficacy at the level of single metastases for the development of novel tumor drugs. The method can potentially also track the distribution of small-molecule drugs when they are conjugated to fluorescent dyes.

On the way to stop the metastatic process

Taken together, these results show that DeepMACT not only provides a powerful method for the comprehensive analysis of cancer metastases, but also provides a sensitive tool for therapeutic drug assessment in pre-clinical studies. "The battle against cancer has been underway for decades and there is still a long way to go before we can finally defeat the disease. In order to develop more effective cancer therapies, it is critical to understand the metastatic mechanisms in diverse [cancer](#) types and to develop tumor-specific drugs that are capable to stop the metastatic process," explains Ertürk.

DeepMACT is publicly available and can be easily adopted in other laboratories focusing on diverse tumor models and treatment options. "Today, the success rate of clinical trials in oncology is around 5 percent. We believe that the DeepMACT technology can substantially improve the drug development process in preclinical research. Thus, could help finding much more powerful drug candidates for clinical trials and hopefully help to save many lives".

The study is published in *Cell*.

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