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An automated pipeline for metastasis detection

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New therapeutic strategies are needed for metastasis, which remains the main cause of death in patients with cancer. Mouse models have been invaluable to improve our understanding of the metastatic process, but limitations in small-animal imaging technologies, such as insufficient resolution, have hampered the development of new therapies. A study published in *Cell* describes a new pipeline for systemic analysis of micrometastases at the full body scale and with a resolution down to individual cells, which might foster the development of anti-metastatic therapies.

The pipeline called DeepMACT (deep learning-enabled metastasis analysis in cleared tissue) was developed to circumvent major limitations in metastasis imaging, such as the difficulty of detecting small fluorescent micrometastases in mice because of tissue-endogenous fluorescence. Human MDA-MB-231 mammary carcinoma cells expressing a fluorescent protein were transplanted in the mammary fat pad of NSG mice and tumors were allowed to grow and metastasize for 6–10 weeks. To enhance the fluorescence in cancer cells, the team of investigators led by Ali Ertük from the ITERM and LMU in Munich used vDISCO, a whole-body immunolabeling method developed in their lab to boost the signal of fluorescent proteins in mice rendered transparent by a clearing method. They showed that several micrometastases, which were not visible by traditional bioluminescence, could be detected in the same mouse by epifluorescence imaging after vDISCO was applied.

The investigators used light-sheet microscopy to image the entire transparent mouse and applied a deep-learning approach to detect and quantify metastases in the 3D images stacks. They determined that the detection performance of DeepMACT came very close to the level of a human annotator, but with a processing speed >60 times faster.

The pipeline also reliably detected micrometastases down to the size of individual cells in a variety of tumor models, including immunodeficient or immunocompetent mice, syngeneic tumors and xenotransplants. The investigators also used DeepMACT to assess the biodistribution and targeting efficiency of a fluorescently labeled therapeutic monoclonal antibody in the breast carcinoma mouse model. "It represents the first method that allows quantitative analysis of the efficiency of antibody-based drug targeting at the full body scale, with a resolution down to the level of individual micrometastases," explain the investigators in their report. An online version of the DeepMACT algorithm is hosted by the Code Ocean initiative and can be executed via any web browser.

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