MedicalXpress

Pharmacoscopy improves therapy for relapsed blood cancer in a first clinical trial

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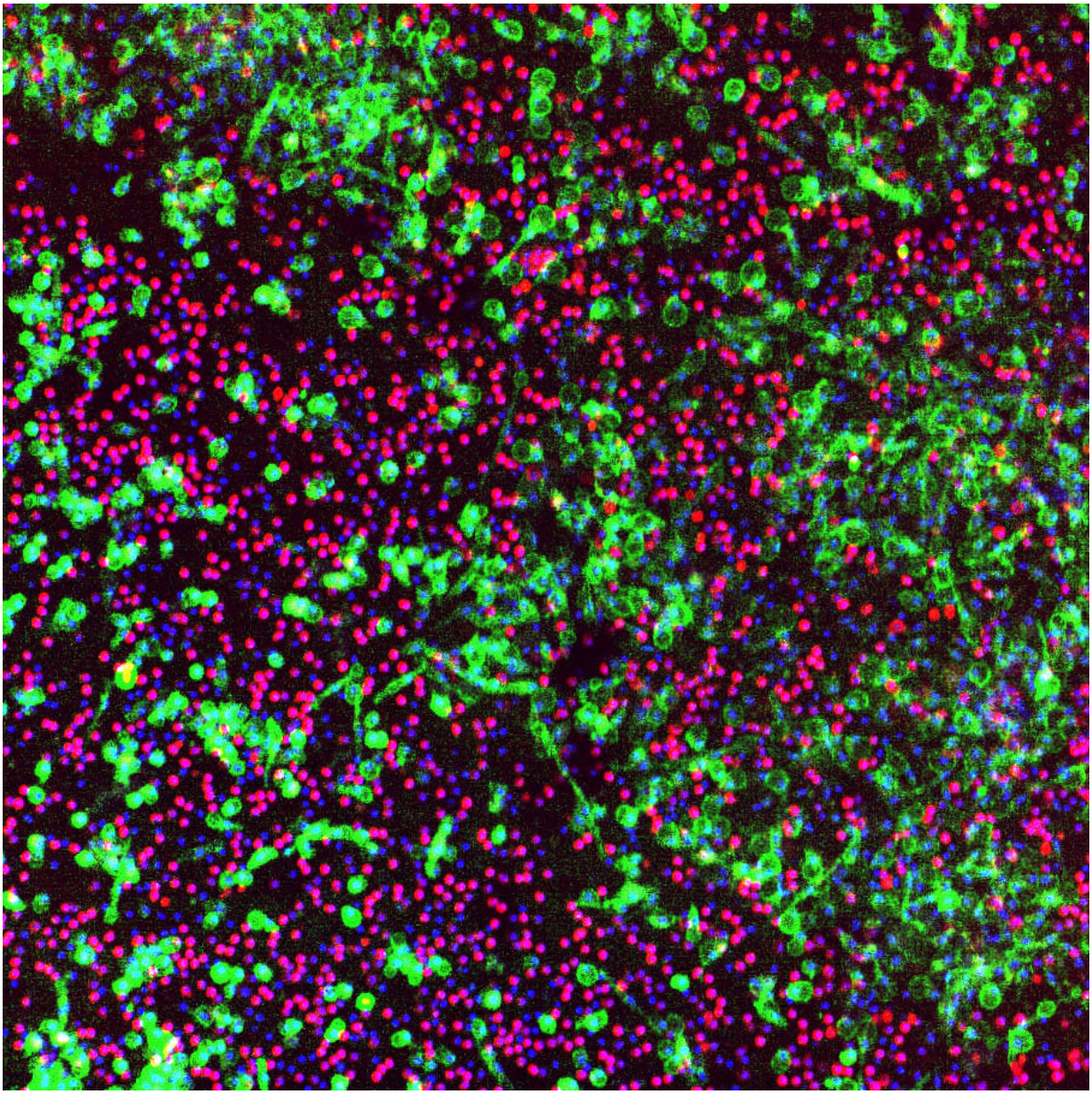


Patient cells imaged by pharmacoscopy. Credit: CeMM/Gregory Vladimer

Researchers at CeMM and the Medical University of Vienna presented a preliminary report in *The Lancet Hematology* on the clinical impact of an integrated ex vivo approach called pharmacoscopy. The procedures measure single-cell drug responses of millions of individual cells to hundreds of possible treatments in small biopsies from cancer patients.

The interim analysis of the first-ever clinical trial with the approach highlights the potential of the method: 88.2 percent of patients receiving pharmacoscopy-guided treatment achieved partial or complete remission, compared to 23.5 percent to their own previous treatment. Further, the median progression-free survival increased four-fold. Retrospectively, pharmacoscopy also predicted the response of AML patients to first-line treatment with 90 percent accuracy. These results show that pharmacoscopy can assist decision-making of the responsible clinicians effectively and thus represent a powerful tool for practical precise and personalized medicine.

Patients suffering from refractory and relapsed blood cancers often have few treatment options and short survival times. At this stage, identifying effective therapies can be challenging for doctors. Even state-of-the-art genetic analyses, due to the high heterogeneity of cancer cells and the impact of mutations on their drug response, do often not suffice to instruct personalized treatments. Pharmacoscopy offers a functional approach: Hundreds of drug options can be quickly pre-tested ex vivo in small liquid biopsy samples collected from individual patients.

The effects of each drug on the individual cells are quantified using high-throughput and high-content automated confocal microscopy. In combination with specially developed analysis methods, machine

learning and other unique algorithms, pharmacoscopy allows quantification of never-before visualized phenotypes. The method was first presented last April in *Nature Chemical Biology*.

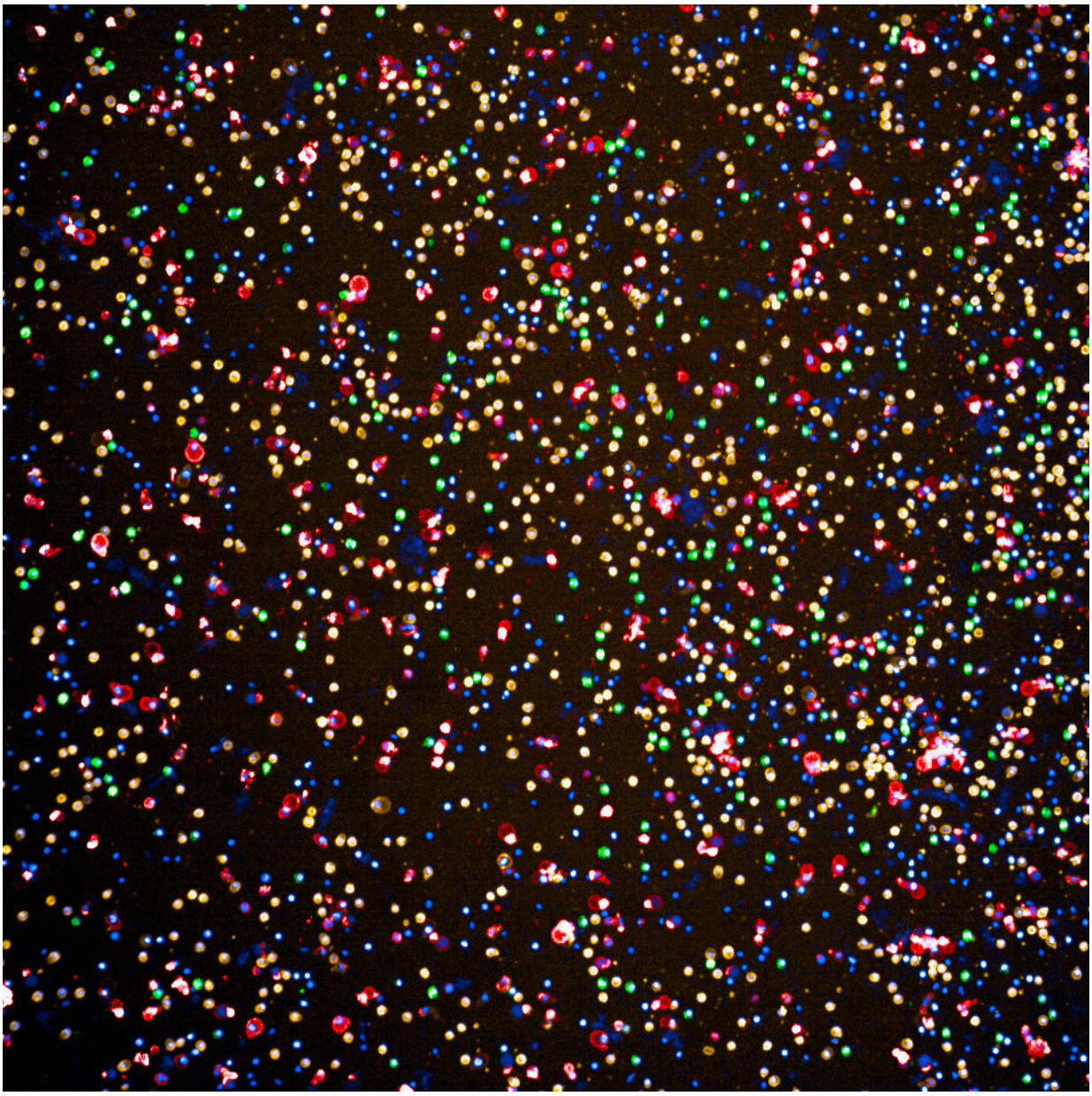
Scientitst at CeMM working with pharmacoscopy. Credit: CeMM/Wolfgang Däuble

The multidisciplinary team is spearheaded by Giulio Superti-Furga, scientific director of CeMM and professor at the Center for Physiology and Pharmacology of the Medical University of Vienna, together with Professor Philip Staber of the Medical University of Vienna.

While the clinical study is still recruiting, interim analysis of the

program showed that 88.2 percent of the patients recruited (15 out of 17) who received pharmacoscopy-monitored personalized therapies achieved partial or complete remission, while only 23.5 percent (four out of 17) responded similarly well to their previous respective treatments.

In addition, the median progression-free survival of patients who were treated in accordance to pharmacoscopy-guided therapy increased from 5.7 weeks to 22.6 weeks compared to their last line of treatment. Further, in a retrospective study organized to determine the ability of the method to stratify responding and non-responding newly diagnosed patients with acute myeloid leukemia (AML), the technique achieved 90 percent accuracy. Before, such accuracy in prediction of treatment outcome was unachievable, with or without genetic assays.



Patient cells imaged by pharmacoscopy. Credit: CeMM/Gregory Vladimer

"Having a robust, fast, and reliable predictive test at our disposal during the patient treatment process, especially at the time of relapse where a new intervention must be selected quickly, will change how medical doctors prioritize drugs to use for late-stage patients," says Philipp

Staber, principal investigator of the clinical trial.

"Evidence that the pharmacoscopy approach is helpful for clinical evaluation of therapy is wonderful. Single-cell functional analysis of primary material gives unprecedented resolution and precision that we are sure to further develop in the future to address yet more diseases," adds Giulio Superti-Furga, whose goal at the beginning of activities of the Research Center for Molecular Medicine ten years ago was to create scientific advancements able to positively impact medical practice.

More information: Berend Snijder et al, Image-based ex-vivo drug screening for patients with aggressive haematological malignancies: interim results from a single-arm, open-label, pilot study, *The Lancet Haematology* (2017). DOI: 10.1016/S2352-3026(17)30208-9

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