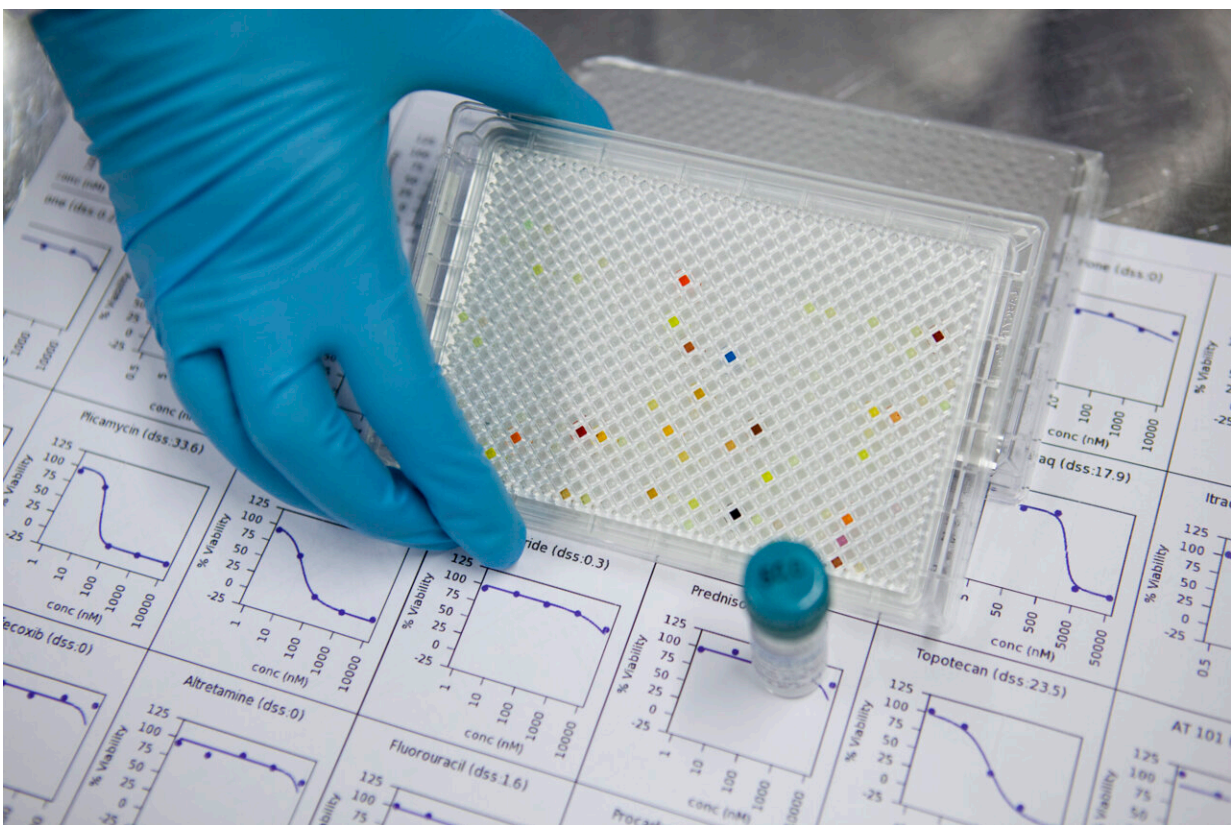


Functional precision medicine using drug sensitivity testing enables tailoring of therapy for leukemia patients

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A plate containing different cancer drugs and a graphical drug sensitivity testing result output. Credit: FIMM, University of Helsinki / Kai Lindqvist

A functional precision medicine study conducted in Finland

demonstrates that treatment selection based on results from drug sensitivity testing of patients' cells can be clinically useful in patients with aggressive hematological cancers.

Clinicians, researchers and technology experts from the Institute for Molecular Medicine Finland FIMM at the University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center have over the last 10 years developed and tested a functional precision medicine approach to assign therapies to individual cancer patients. Their latest results have just been published in *Cancer Discovery*.

The group has focused on patients with hematological cancers, particularly [acute myeloid leukemia](#) (AML), since standard therapies for the advanced forms of these malignancies have a limited effect and the outcome is invariably poor.

More than 500 compounds tested on patient cells

The study presents a novel functional and molecular tumor board (FMTB) strategy, in which drug testing data are integrated with the patients' clinical, genomic and molecular profiling data, and potential treatment recommendations are assigned and discussed in real time to identify the right treatment to the right patients at the right time.

The researchers tested the effects of more than 500 candidate drugs on the patient cells from 186 patients with relapsed adult acute myeloid leukemia (AML), a disease characterized by poor prognosis. Tested compounds included more than 180 approved cancer drugs and many emerging or investigational cancer drugs.

"Our approach combines deep molecular profiling with comprehensive drug sensitivity testing of patient cells to advance the therapy decision-making system for the leukemia patients," said the first author of the

study, Dr. Disha Malani, who completed her Ph.D. studies at FIMM, University of Helsinki while working on the project.

Results demonstrate clear clinical benefit

Based on the profiling results, the group was able to identify potentially actionable drugs for almost all (98%) the studied AML patients. This is a remarkable advancement as compared to the classical approach of using genomics, where informative results are not obtained for most patients. In 37 cases, the patients were actually treated with the recommended drugs and the outcome of the therapy was quantified in an observational clinical case study.

The outcome was excellent in this late-stage refractory AML with no other treatment options available. An overall response rate was 59%. In addition, five patients were successfully bridged to curative hematopoietic stem cell transplantation therapy, and many of these patients are now in long-term remission.

The study demonstrates that individual tailoring of therapy based on functional testing of patient cells in laboratory conditions is both predictive of patients' response in real life, but also feasible, rapid, cost-effective and clinically implementable.

"Compared to genomics-based precision medicine, drug testing provides informative and actionable results in a substantially higher fraction of patients" said Professor Kimmo Porkka from the Helsinki University Hospital Comprehensive Cancer Center and a co-leader of the study.

"We also developed a new method of communicating results to the clinic, via a multidisciplinary functional and molecular tumor board, something that we believe can in the future grow to become a system that learns from past cases to provide increasingly better

recommendations for patient treatment".

The drug testing assay takes only three days and thus provides clinically relevant data faster than genomics profiling, which is crucial in a medical emergency, such as acute leukemia.

"This is clearly advantageous for patients for whom standard therapy alternatives have been exhausted and there is an unmet need for alternative therapy options".

Novel drug response biomarkers identified

To understand the molecular factors driving the individual drug efficacies, the researchers also combined the molecular profiling data across all studied patients and compared these with drug responses to each of the 500 drugs. This approach identified several novel [drug](#) response biomarkers, such as overexpression of the IL15 gene that was functionally and mechanistically associated with resistance to FLT3-inhibitor treatments, an important form of targeted leukemia [therapy](#).

"With the clinical introduction of functional precision medicine, we expect faster and broader implementation of precision medicine across different [cancer](#) types," said Professor Olli Kallioniemi who co-led the study.

"We still need further work in standardizing the methods, getting access to more drugs for patient treatment and data from randomized clinical trials, something that we wish to achieve in collaboration with the global research community, hospitals and the pharma industry. The iCAN Digital Cancer Precision Medicine Flagship research project is focusing on realizing this goal."

More information: Disha Malani et al, Implementing a functional precision medicine tumor board for acute myeloid leukemia, *Cancer Discovery* (2021). [DOI: 10.1158/2159-8290.CD-21-0410](https://doi.org/10.1158/2159-8290.CD-21-0410)

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