

Systems medicine paves the way for improved treatment for leukemia patients

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A multi-disciplinary team of researchers at the Institute for Molecular Medicine Finland, FIMM, and the Helsinki University Central Hospital has developed a novel individualized systems medicine (ISM) strategy which enables selection of potentially effective cancer therapies for individual patients. Furthermore, this strategy helps in understanding and predicting drug resistance and may pave a path for individualized optimization of patient therapies in the clinic for various types of cancers.

Many novel targeted drugs have been introduced to the clinic for [cancer therapy](#), often guided by genomic clues on disease pathogenesis. Clinical treatment of [cancer](#) patients is, however, challenged by the fact that genomics is often not informative in selecting therapies to individual patients. Patients also often develop resistance to therapies that were initially effective. Furthermore, tumor heterogeneity and clonal evolution over time within an individual patient make it difficult to apply cancer genomics as a guide to patient therapy.

ISM combines genomics with comprehensive drug sensitivity testing of patient cells to facilitate optimization of safe and efficacious cancer therapies for individual patients. Furthermore, the ISM strategy aids in understanding and predicting how [drug resistance](#) evolves and how it may be prevented.

Results achieved by applying this strategy to 28 patient samples have been recently published in the *Cancer Discovery* journal.

Most of the patients studied had chemoresistant adult acute myeloid leukemia (AML), a disease characterized by poor prognosis. AML is today largely treated by the same chemotherapeutic agents as applied 30-50 years ago. Here, the researchers measured the response of patients' cells to a panel of 202 cancer drugs covering all approved and many emerging [cancer drugs](#). A list of the most likely effective and ineffective drugs was created for each individual patient and passed on to the treating physician to consider.

Several patients benefited from the therapy selected based on the drug sensitivity testing results. For example, one patient previously unresponsive to three rounds of chemotherapy achieved complete clinical remission with a treatment optimized with the ISM platform.

"We integrate three complementary information sources, drug testing results, genomic profiling of cancer cells and clinical information. Repeated sampling of patients plays a major role in understanding and learning from each success and failure", explains Krister Wennerberg, one of the principal investigators behind this study.

"We are very excited about this ability to provide a truly individualized approach to patient treatment", says hematologist Kimmo Porkka. "In the future, this may pave the way for testing of all types of human cancers".

"It is also important to note that we now tested severely ill patients, completely refractory to current therapies", says Director Olli Kallioniemi from FIMM. "In the future, we hope to impact on therapy of earlier leukemia patients and design effective combinations of treatments".

With the ISM strategy, researchers are now able to generate hypotheses to be tested in clinical trials, both for existing drugs, emerging

compounds and their combinations. In addition, this approach provides a way to prioritize emerging drugs that are likely to have the best success in clinical trials and ultimately reach routine patient care. Therefore, ISM may pave a path for optimizing pharmaceutical drug development pipelines as well as changing the standard of clinical care so that all [patients](#) receive individualized treatment.

More information: Pemovska T, Kontro M, Yadav B, Edgren H, Eldfors S, Sz wajda A, Almusa H, Bespalov MM, Ellonen P, Elonen E, Gjertsen BT, Karjalainen R, Kuleskiy E, Lagström S, Lehto A, Lepistö M, Lundán T, Majumder MM, Lopez Marti JM, Mattila P, Murumägi A, Mustjoki S, Palva A, Parsons A, Pirttinen T, Rämetsä ME, Suvela M, Turunen L, Väström I, Wolf M, Knowles J, Aittokallio T, Heckman CA, Porkka K, Kallioniemi O, Wennerberg K. Individualized Systems Medicine (ISM) strategy to tailor treatments for patients with chemorefractory acute myeloid leukemia. *Cancer Discovery*, December 2013 3:1416-1429.

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