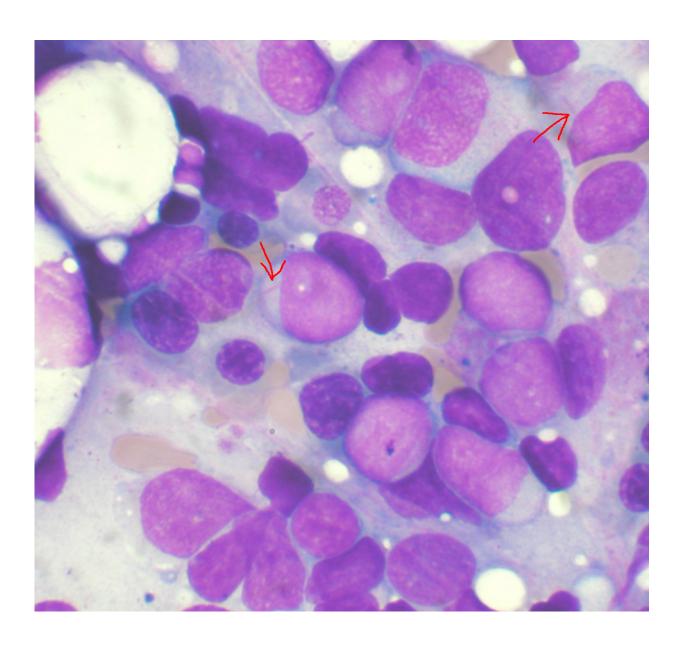


Best treatment option written in cancer's genetic script: AML study finds personalised therapy is possible

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Bone marrow aspirate showing acute myeloid leukemia. Several blasts have Auer rods. Credit: VashiDonsk/Wikipedia/CC BY-SA 3.0

An international collaboration led by clinical researchers at the Wellcome Trust Sanger Institute has shown proof-of-concept that truly personalised therapy will be possible in the future for people with cancer. Details of how a knowledge bank could be used to find the best treatment option for people with acute myeloid leukaemia (AML) are published today in *Nature Genetics*.

AML is an aggressive blood cancer that develops in bone marrow cells. Earlier this year, the team reported there are 11 types of AML, each with distinct genetic features. Now they report how a patient's individual genetic details can be incorporated into predicting the outcome and treatment choice for that patient.

They built a knowledge bank using data from 1,540 patients with AML who participated in clinical trials in Germany and Austria, combining information on genetic features, treatment schedule and outcome for each person. From this, the team developed a tool that shows how the experience captured in the knowledge bank could be used to provide personalised information about the best treatment options for a new patient.

There are two major treatment options for young patients with AML - a stem cell transplant or chemotherapy. Stem cell transplants cure more patients overall but up to one in four people die from complications of the transplant and a further one in four experience long-term side effects. Weighing up the benefits of better cure rates with transplant against the risks of worse early mortality is a harrowing decision for patients and their clinicians. The team showed that these benefits and



risks could be accurately calculated for an individual patient, enabling therapeutic choices to become personalised.

The team estimates that up to one in three patients would be prescribed a different treatment regimen using the tool compared with current practice. In the long term they hope the tool could spare one in ten young AML patients from a transplant while maintaining overall survival rates.

Senior author Dr Peter Campbell of the Wellcome Trust Sanger Institute said: "The knowledge bank approach makes far more detailed and accurate predictions about the likely future course of a patient with AML than what we can make in the clinic at the moment. Current guides use a simple set of rules based on only a few genetic findings. For any given patient, using the new tool we can compare the likely future outcomes under a transplant route versus a standard chemotherapy route - this means that we can make a treatment choice that is personally tailored to the unique features of that particular patient."

The tool is currently available for scientists to use in research but needs further testing before it can be used to prescribe treatments in AML clinics.

Lead author Dr Moritz Gerstung of the European Bioinformatics Institute said: "It has long been recognised that cancer is a complex genetic disease. Our study provides an example of how detailed genetic and clinical information can be rationally incorporated into clinical decisions for individual patients. We tested this philosophy in one type of leukaemia, but the concept could theoretically be applied in other cancers with difficult clinical decisions as well. Our analysis reveals that knowledge banks of up to 10,000 patients would be needed to obtain the precision needed for routine clinical application."

Using large scale genetic studies as a source to predict the best treatment



option for future patients is an idea that Genomics England is trying to build alongside similar programmes around the world, such as the National Institutes of Health Precision Medicine Initiative in the US.

The authors believe this paper is a step towards validation of genetic techniques as a route to personalised medicine.

Co-senior author Dr Hartmut Döhner of University of Ulm said: "Building knowledge banks is not easy. To get accurate treatment predictions you need data from thousands of patients and all tumour types. Furthermore, such knowledge banks will need continuous updating as new therapies become approved and available. As genetic testing enters routine clinical practice, there is an opportunity to learn from patients undergoing care in our health systems. Our paper gives the first real evidence that the approach is worthwhile, how it could be used and what the scale needs to be."

More information: *Nature Genetics*, nature.com/articles/doi:10.1038/ng.3756

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