Genetics allows personalized disease predictions for chronic blood cancers

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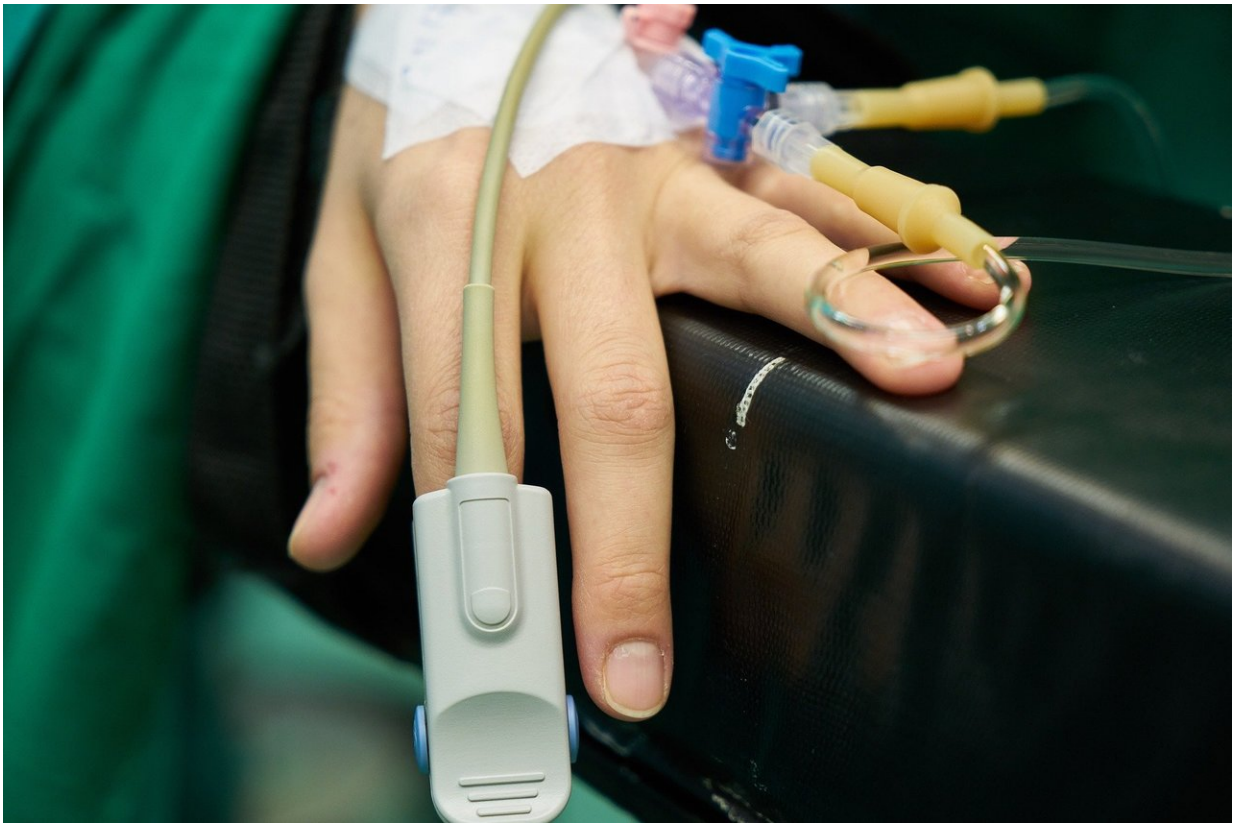

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Scientists have developed a successful method to make truly personalised predictions of future disease outcomes for patients with certain types of chronic blood cancers. The study from the Wellcome

Sanger Institute, the Wellcome-MRC Cambridge Stem Cell Institute, the University of Cambridge, and their collaborators, combined extensive genetic and clinical information to predict the prognosis for patients with myeloproliferative neoplasms. The research also identified eight different genetic subgroups of the disease that link with patterns of clinical disease and patient prognosis.

Published today in the *New England Journal of Medicine*, this work could lead to personalised medicine for patients with these blood cancers . It will help doctors identify those patients who are likely to have a very good future outlook, and which patients may benefit from specific treatments or clinical trials.

Myeloproliferative neoplasms are a group of blood cancers affecting around 30,000 patients in the UK. These cancers are chronic, long term conditions and patients suffer from a risk of blood clots and bleeding. In addition, these cancers can progress to more advanced forms of disease, including acute leukaemia, that have a poor outlook. It is important to patients to know how their disease is likely to progress in the future, but it has not previously been possible to provide personalised predictions for each individual patient.

The current classification system for these blood cancers was created in the 1950s when myeloproliferative neoplasms were divided into three clinical types. However, there are known to be challenges with this classification system. This lack of accurate classification can make it difficult for doctors to decide on the most appropriate treatment for patients and to provide information on future outlook.

To understand the biological factors causing myeloproliferative neoplasms the researchers studied 69 cancer genes from over 2,000 patients with these blood cancers. Using this genetic information, they found there were eight different subtypes of these cancers. These genetic

subtypes were also found to be clinically different from each other, indicating that the researchers had identified real differences between patient groups.

Combining the genetic information for each person with their clinical information, the researchers were then able to develop a method to make personally tailored disease predictions for individual patients suffering from these cancers. They found this personalised method outperformed all current schemes available to make disease predictions and had the additional advantage of giving patient-specific predictions, rather than simply classifying patients into broad risk categories.

Dr. Jyoti Nangalia, a first author on the study from the Wellcome Sanger Institute, said: "Despite some knowledge of the risks of myeloproliferative neoplasms we have been unable to make accurate personal predictions for individual patients. Our new online calculator takes genetic and clinical information available for a patient and makes a prediction of the future outcome of that particular person's disease. In the future this could be used to reassure patients who have a good predicted outcome, and identify patients who are at risk of developing severe disease who could benefit from an alternative treatment approach."

Professor Tony Green, a senior author on the paper from the Wellcome-MRC Cambridge Stem Cell Institute and the University of Cambridge, Department of Haematology, said: "This work represents a step change in our understanding of the myeloproliferative neoplasms. Not only does it reveal a new classification based on causal mechanisms but it also provides for the first time personally-tailored predictions to guide patient management."

The study also revealed that some subgroups shared features with other blood cancers. This work could bring clarity to disease classification of

blood cancers in the future and enable the development and testing of new treatments.

Dr. Peter Campbell, a senior author from the Wellcome Sanger Institute, said: "This research proves the potential of personalised medicine, using genetics. Modern genomics will empower clinicians and support their decisions regarding the best therapies and clinical trials for each patient. We hope our study will be a game changer for patients with these blood cancers by providing better predictions for how their disease may behave in the future, and inform treatment choice."

More information: *New England Journal of Medicine* (2018). DOI: 10.1056/NEJMoa1716614

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