Calculating leukemia progression

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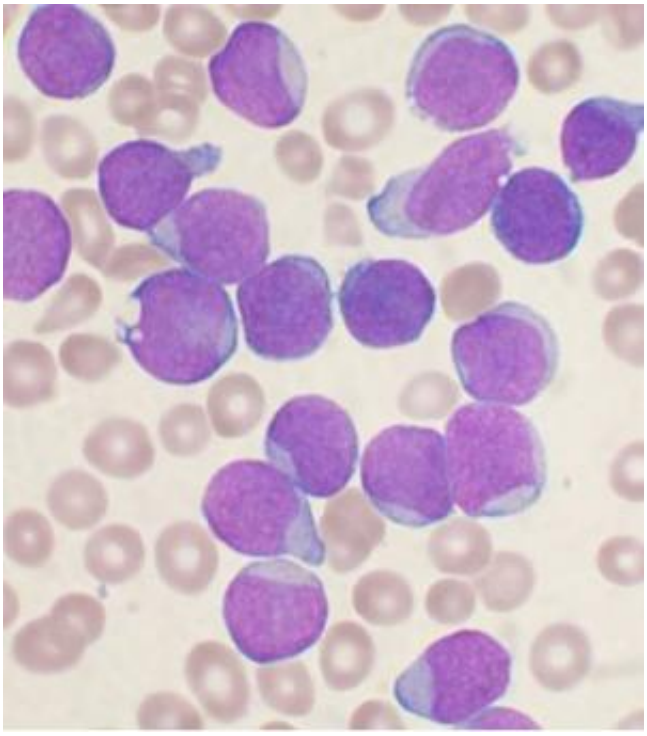

A Wright's stained bone marrow aspirate smear from a patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

A new computational study published in the *International Journal of Bioinformatics Research and Applications* has shown how mutations that give rise to drug resistance occur in a form of cancer known as acute myeloid leukemia (AML).

Juan Carlos Martinez and S.S. Iyengar of Florida International University and Nelson Lopez-Jimenez and Tao Meng of the University

of Miami, explain how cancer cells undergo genetic mutations as the disease progresses. Unfortunately, for the patient some of these mutations can give rise to new proteins that protect the cancer from the effects of anticancer drugs. A similar effect is seen in bacterial infection when microbes become resistant to antibiotics.

The team was able to use data from a longitudinal study of ALS patients for whom normal and malignant tissue samples had been tested at various points in time before and after disease relapse occurred. The team processed DNA sequence data before and after relapse time so that they could map the regions of the patients' genome where mutations were present and so envisage which changes had given rise to the relapse through the emergence of drug resistance or some other factor. Their statistical analysis was highly predictive of the mutation timeline with a confidence interval of 95%, the team reports.

Longitudinal data tracking genomic mutations for tumors from patients throughout the course of their disease at several points in time – as opposed to single genetic snapshots – represents what the team calls a "golden standard". Indeed, such a longitudinal study with a small number of patients is considered by some researchers to be more useful than a large study sample that offers only snapshot data. The success of this research offers new hope for understanding the development of ALS as well potentially leading to new targets for designer, or personalized, drugs for patients with specific cancer mutations.

"The efforts and techniques used in this paper represent the best methods we know to date in identifying meaningful mutational changes in leukemia," the team says. The work could help oncologists predict patient response to therapy, identify patients at greater risk of relapse or disease progression, spot particular "driver" and "passenger" mutations that lead to relapse or drug resistance. The work could also help focus research on potential druggable targets, the team adds. The bottom line

on this research is that ultimately it could improve survival rates for leukemia patients, the team concludes.

More information: "Predicting DNA mutations during cancer evolution." *International Journal of Bioinformatics Research and Applications* 01/2015; 11(3):200. DOI: 10.1504/IJBRA.2015.069186