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GENETICS

The AML mutational landscape

Despite decades of studies on the molecular pathogenesis of acute myeloid leukaemia (AML), the mutations that contribute to the pathogenesis of the disease were still not completely defined, and the relationships of mutations to the epigenetic features of AML were poorly understood. A study by The Cancer Genome Atlas (TCGA) Research Network has now provided a new view of the AML mutational landscape.

Researchers analysed genomes from 200 adults with newly diagnosed AML by whole-genome sequencing (50 patients) or whole-exome sequencing (150 patients) of paired tumour and matched skin samples, which served as controls.

Results showed that AML genomes have fewer mutations than all other common adult epithelial cancers, with an average of 13 mutations per patient. Of these 13 genes, only five were recurrently mutated in AML. Of all the genes in which mutations were found, 23 were found to have a higher-than-expected mutation rate. These included genes already known to be associated with AML, such as *FLT3*, *NPM1* and *DNMT3A*. Most samples had at least one nonsynonymous mutation in one of nine functionally related categories of genes. These categories, which included tumour-suppressor genes, transcription factor fusions and genes involved in epigenetic modifications, are likely to be relevant to AML pathogenesis and indicate that these nonsynonymous mutations are potential driver mutations.

Data from this study will be a useful resource for future work on AML pathogenesis and the molecular classification of AML, and could lead to new treatment options.

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