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Researchers discover new genetic errors that could cause one of the most deadly leukaemias

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Acute dendritic leukaemia is a rare type of leukaemia, but one with the worst prognosis—the average patient survival rate is just 12-14 months—that is difficult to treat. Juan Cruz Cigudosa's team, from the Spanish National Cancer Research Centre's (CNIO) Molecular Cytogenetics Group, has for the first time sequenced the exome –the coding, or protein-generating, regions of the genome— of dendritic cell leukaemia.

The analyses, published in *Leukemia*, the world's leading journal in onco-haematology, uncover new genetic pathways that could revolutionise treatment guidelines for these patients.

'Epigenetic' genes are altered in most cases

For the first time in human leukaemias, scientists have described mutations in four genes (IKZF3, HOXB9, UBE2G2 and ZEB2) that have important cellular functions, such as gene regulation and cellular differentiation.

"In addition to these genes, we have found that more than half of the cases harbour mutations in epigenetic genes at diagnosis —those genes that introduce chemical modifications in the DNA— something that had never been observed in this type of leukaemia", says Cigudosa. "Therapies directed against these epigenetic genes already exist, so these

patients could also benefit from them".

In summary, the genetic profile of acute dendritic cell leukaemia, currently treated as a lymphoid leukaemia, is similar to that of myeloid leukaemia. "These results suggests a change in the treatment guidelines for these patients, who were completely misplaced", says Juliane Menezes, the first author of the study.

According to Cigudosa, "this study is a clear example of the role of genomics in translational research being carried out by Spanish scientists, in general, and more specifically at CNIO".

To carry out this work, the authors analysed the exome of three patients diagnosed with dendritic cell leukaemia and validated the results using a panel of 38 genes and 25 additional patients (known as a targeted resequencing strategy), coming from 9 Spanish hospitals.

More information: Exome sequencing reveals novel and recurrent mutations with clinical impact in blastic plasmacytoid dendritic cell neoplasm. Menezes J, Acquadro F, Wiseman M, Gómez-López G, Salgado RN, Talavera-Casañas JG, Buño I, Cervera JV, Montes-Moreno S, Hernández-Rivas JM, Ayala R, Calasanz MJ, Larrayoz MJ, Florensa L, Gonzalez-Vicent M, Pisano DG, Piris MA, Alvarez S, Cigudosa JC. *Leukemia* (2013). DOI: 10.1038/leu.2013.283

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