New markers could improve treatment and survival in acute lymphoblastic leukaemia

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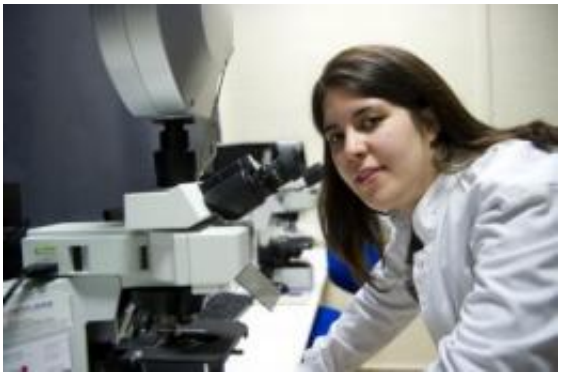

This is ElixabetLópez-López, author of the thesis. Credit: UPV/EHU

Acute lymphoblastic leukaemia, the most common paediatric cancer, has been the subject of study in the PhD thesis of ElixabetLópez.In the work entitled New genetic markers for treatment personalization in paediatric Acute Lymphoblastic Leukaemia, the UPV/EHU biologist has presented new genetic markers that could improve the classification of risk groups and predict treatment toxicity in the patient.That way it would be possible to achieve better personalisation of the treatment.

Over the last few decades survival has increased from 10% to 80%.This improvement has been achieved by using combined therapies and separating the patients into risk groups.For example, stronger treatmentis used in the groups in which a worse response is expected.That way the survival probability in the groups with a poor prognosis is increased,

while chemotherapy toxicity in patients with a better prognosis is reduced.

However, the classification of the risk groups, which today is carried out by means of clinical markers, like the number of lymphocytes or age of the patient, and some genetic markers, is not totally exact.For example, some of the patients initially considered as lower risk do not respond well to the treatment and in the middle of their treatment their therapy is changed to that of greater risk.In these cases, "survival could be improved as the condition would be treated more intensively right from the start," points out López.

On the other hand, children with acute lymphoblastic leukaemia receive very strong doses of chemotherapy, and toxicity problems, which can be very serious, often occur.What is more, "as they are children and the toxicity can leave them with sequelae for the rest of their lives, it is quite important to try and prevent it," says López.Currently, there is no toxicity marker that is used in a standard way.

Quest for new markers

To find new risk markers, the whole genome of tumour cells was combed in the search for deletions and duplications.And the ones that were recurrent and which were exclusive to a risk group were selected, and so were the ones that were found in the patients who were moved from one group to another."We have found a low risk marker which only appears in low risk patients and another that only appears in high risk ones, which could complement the ones that are already being used.And another 5 markers that appear in patients that were changed from low risk to high risk, and in those of high risk.This means that those patients were in fact high risk ones and that they should have been included in that group," explains the author.

On the other hand, the toxicity markers were sought in normal cells to detect variations that are of the individual and not of the tumour.This study has focussed on methotrexate, one of the most important drugs that can cause toxicity.And several possible markers have been found, like some variants of the methotrexate transporter gene and other variants related to microRNAs (short ribonucleic acid molecules which do not give rise to proteins but which carry out a significant regulatory function) that regulate the genes.

López's next aim is to study how the genetic variations found affect gene expression and see exactly why these variations are regulating toxicity or response to treatment. Furthermore, to validate the markers, they are endeavouring to set up some clinical trials."We have found these associations in our population, but a clinical trial would be needed to see whether they really are good markers and whether, in actual fact, survival and toxicity are improved when these markers are used," saysLópez.

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