NEWS EMBARGOED UNTIL 6PM ON 14TH SEPTEMBER

The study will be published in the September edition of the prestigious journal Cancer Cell, the third most important journal in the field of Oncology.

New therapeutic avenue discovered to fight against leukaemia

Barcelona, 13th September 2010.-A study carried out by researchers from the stem cells and cancer research group of the IMIM (Hospital del Mar Research Institute) has shown that if deactivation of the NFkB protein complex in T cell acute lymphoblastic leukaemia is forced, leukaemia is eliminated. This opens the doors for the development of new drugs for this type of leukaemia.

Up until now, it was known that the Notch and NFkB signalling pathways were activated in T cell acute lymphoblastic leukaemia. Signalling pathways are a group of cell molecules that work together to control one of more cell functions, such as cell multiplication or death. After the first molecule receives an initial signal, it activates the other molecules. This process is repeated until the last molecule is activated and the cell performs its function. Abnormal activation of signalling pathways can lead to cancer.

According to Anna Bigas, coordinator of the IMIM stem cells and cancer research group, "***We have identified new interaction between the Notch and NFkB pathway. This is important because if we stop one of these, the other will no longer have effect. This opens the door to drugs which act as inhibitors of the NFkB pathway or the combination of inhibitors of both pathways at a lower dose, which could make the treatment less toxic and more effective".***

Acute lymphoblastic leukaemia is predominantly a child cancer which manifests itself in the first 10 years of life. It is the most common form of child cancer and groups together a set of neoplasias which are characterised by the proliferation of white blood cells in the blood and bone marrow, which can spread into other organs and tissues. Of the approximately 300 new cancers of this type that are diagnosed in Spain each year, 14% are T cell. Despite the high prevalence, however, 8 out of every 10 cases are treated favourably.

Previous studies have shown that, depending on the expression level of the Notch pathway and depending on the cell context, the Notch membrane receptors contribute to making the cells resistant and avoid their natural death, thus becoming tumour cells. ***"Through this study we have discovered that Notch pathway inhibitors have the ability to block the NFkB pathway, thus preventing the tumour T cells in acute lymphoblastic leukaemia from proliferating"*** states Lluís Espinosa, researcher with the IMIM stem cell and cancer research group.

The experimental part of the study was carried out in the IMIM and in New York University, while the support of the Hospital de Sant Pau and the Hospital del Mar has been a key factor

in confirming, in human leukaemia samples, the discoveries which had been made using cells and mice in the laboratory. This basic experimental research performed on animal models and contrasted both *in vivo* and *in vitro* has enormous clinical relevance as it opens up a new therapeutic strategy for this type of tumour.

Reference Article

"The Notch/Hes1 pathway sustains NF-kB activation through *CYLD* repression in T cell leucemia".
Lluís Espinosa1,*,11, Severine Cathelin2,*, Teresa D'Altri1, Thomas Trimarchi2, Alexander Statnikov3, Jordi Guiu1, Veronica Rodilla1, Julia Inglés-Esteve1, Josep Nomdedeu4, Beatriz Bellosillo5, Carles Besses6, Omar Abdel-Wahab7, Nicole Kucine7,8, Shao-Cong Sun9, Guangchan Song10, Charles C. Mullighan10, Ross L. Levine7, Klaus Rajewsky11, Iannis Aifantis2,&,12 and Anna Bigas1,&. **Cancer Cell**

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