

SPANISH SCIENTISTS DEVELOP A MOLECULAR RISK SCORE FOR OUTCOME PREDICTION IN ADVANCED CLASSICAL HODGKIN'S LYMPHOMA

Madrid, August 26th, 2010 – Researchers from the Spanish National Cancer Research Centre (CNIO) in collaboration with the Spanish Hodgkin Lymphoma Study Group have published a study today in the leading journal *Blood* entitled: “A molecular risk score based on four functional pathways for outcome prediction in advanced classical Hodgkin lymphoma.”

The purpose of this work was to develop a quantitative RT-PCR-based assay for patients with advanced classical Hodgkin's lymphoma, integrating a limited number of genes expressed by the tumour and its microenvironment, applicable to routine formalin-fixed, paraffin-embedded samples. This is the first potentially diagnostic assay for the study of Hodgkin's lymphoma that primarily focuses on a clinical problem; the identification at diagnosis of advanced cHL patients with a high probability of failure (roughly 30% of them will eventually relapse). The approach used in this study has allowed us to establish a multigenic predictive model capable of stratifying at the moment of diagnosis those advanced cHL patients that could benefit from alternative therapeutic approaches.

The main results of this work are as follows:

1. An RT-PCR-based study using routine formalin-fixed, paraffin-embedded samples from a carefully selected, homogeneous set of patients with clear-cut favourable or unfavourable treatment response - coupled with advanced statistical methods to compare the two groups of patients - allowed the identification of genes whose expression is associated with outcome. These genes were grouped into four signatures showing relevant information from both malignant cells (cell cycle, apoptosis) and their microenvironment (macrophage cell populations and IRF4 implicated in the immune response and extracellular matrix) - both of which are important in determining the clinical behaviour of the tumour. Finally, these signatures were used to develop a molecular risk score (MRS) to predict failure.
2. The relationship between the derived MRS continuous probability function and clinical outcome (failure-free survival) was successfully validated in both estimation and validation datasets used in the study.
3. An additional step included clinical variables from the International Prognostic Score (IPS) - which is traditionally used to determine patient outcome such as Stage IV - in a final integrative model that could stratify advanced cHL according to the risk of treatment failure.

The results imply that both the tumour and its microenvironment components are important biological factors associated with a treatment response and an outcome in Hodgkin lymphoma patients. Most importantly, and from a practical point of view, we have developed a molecular risk algorithm which can be used to calculate individual risk scores in advanced cHL patients.

The results have been published in a leading journal, *Blood*, selected by the Special Libraries Association as one of the top 100 most influential research journals of biology and medicine over the past 100 years

For the full article, please see:

<http://bloodjournal.hematologylibrary.org/cgi/reprint/116/8/e12>

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