Analysis of Epidemiological Data by a Probabilistic Model Supports the One Hit Hypothesis for the Transformation from Myelodysplastic Syndrome to Acute Myeloid Leukemia.

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Myelodysplastic syndrome is one of the most common hematological malignancies. About third of MDS patients will progress to Acute Myeloid Leukemia (AML), a condition termed secondary AML, which has a grave prognosis. The onset of clinical intervention, such as bone marrow transplantation, for patients diagnosed with Myelodisplastic Syndrome (MDS) is assumed critical to prevent the deterioration towards a leukemic state as well as to prevent death from bone marrow failure in these patients.

MDS is characterized by significant increase in levels of apoptosis of the hematopoietic progenitors in bone marrow along with increased proliferation of non-maturing blasts. When the percentage of such blasts in the bone marrow rises above twenty to thirty percents, the condition is defined as AML. These observations lead us to speculate that the decrease in apoptotic levels, seen in AML patient, is the sole factor for this transformation.

In this research we analyze a database of more than a thousand AML patients, prospectively followed from the discovery of MDS until death, and propose a simple probabilistic model to account for the MDS-to-AML transformation. Our null hypothesis is that the probability of developing secondary AML is independent of the time elapsing since MDS discovery. By clustering the MDS patients according to severity of MDS disease (clinical prognostic score) we show that each group has its own probability of developing AML.

Our results suggest that patients carrying MDS already for several years are actually at the same risk of the transformation as those just diagnosed. Consequently, unlike the current thoughts, the history of the patient's diagnosis should not be considered in the management decision making. Based on our results, intensive experimental efforts should be carried out to identify the specific gene(s), which are responsible for the transformation from MDS to AML. These can serve as future therapeutic targets for new "rationally-designed" drugs.