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The antiapoptotic protein –
A new independent favorable prognostic factor for childhood acute lymphoblastic leukemia

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The most common malignancy in children is acute lymphoblastic leukemia (ALL). This malignancy occupies a percentage of 25 of all childhood cancers and 75 of all cases of childhood leukemia. One of the most important mechanisms which maintain the balance between life and death is apoptosis. The loss of apoptosis might result in the development of a wide variety of cancers, including ALL. In the last years a complex network of pro or anti – apoptotic proteins, which regulated the apoptosis pathways, have been identified. Livin (MIM no. 605737; baculoviral IAP repeat-containing 7, BIRC7; aliases, ML-IAP or KIAP) is a member of the inhibitor of apoptosis proteins which antagonize both the death receptor and mitochondria - based apoptotic pathways through the inhibition of caspases 3, 7, and 9.

Until this study Livin expression has been regarded as a poor prognostic marker in malignancies. The clinical relevance of Livin expression is still controversial in different types of malignancies. In this study, 222 patients with childhood ALL were analyzed for the expression of Livin using quantitative protein chain reaction to investigate a possible relation between Livin expression and the clinical features at diagnosis and treatment outcomes.

The expression rate of Livin was higher in female patients ($P = 0.042$), patients with an age range of 1 to 9 years ($P = 0.008$), patients with a leukocyte number of less than 50 x 10^3/L ($P = 0.024$), standard-risk patients ($P = 0.006$), patients with t(12;21) ($P = 0.001$), patients with a favorable (leukemic blast < 25%) day 7 bone marrow response ($P = 0.001$). The Livin expression was related to the absence of relapse ($P < 0.001$). Similarly, the relapse-free survival rate (±95% CI) was higher in patients with Livin expression than in patients without Livin expression (97.9% ±4.0% versus 64.9% ±11.8%, $P < 0.001$). Multivariate analysis for relapse-free survival demonstrated that Livin expression was an independent favorable prognostic factor in childhood ALL ($P = 0.049$).

The relation between Livin expression and the clinical features at diagnosis and treatment outcomes in childhood ALL was investigated for the first time in this study. The study conclusion is that the Livin expression is associated not only with the presence of favorable prognostic factors at diagnosis but also with a significantly better relapse-free survival in childhood ALL. A better relapse-free survival appears to be associated with a faster death of leukemic cells in patients with Livin expression in response to apoptotic stimuli provided by chemotherapeutic agents. This study suggests that Livin expression is a novel prognostic marker in childhood ALL and thus needs to be incorporated into the patient stratification and treatment protocols. ❑

Comment on the paper:
Choi J, Hwang YK, Sung KW et al – Expression of Livin, an antiapoptotic protein, is an independent favorable prognostic factor in childhood acute lymphoblastic leukemia. *Blood* 2007; 109:471-477; Seoul, South Korea