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Jagged-1 secreted by stromal cells mediated the different response of HSCs and HPCs to leukemic conditionYizhuo Zhang¹, Chen Tian¹, Lina Wang², Chong Chen², Bing Xia¹, Qing Zhang¹, Tian Yuan¹, Yong Yu¹ and Guoguang Zheng²¹Tianjin Medical University, China²Peking Union Medical College, China

Leukemia is the competition failure between normal and abnormal hematopoiesis. Our previous work found that in Notch1-induced murine T-ALL, normal HSCs were preserved in part because of increased mitotic quiescence of HSCs and resulted exhaustion of HPCs proliferation. The differential expression of Hes1 between HSCs and HPCs resulted in the distinct responses of these cells to the leukemic condition. But the mechanism of how leukemic environment affect the expression of Hes1 in normal HSC is still unknown. To elucidate the mechanism, upstream factors of Hes1 especially the cell surface receptor is detected. Also, the ligand and its origin cells are determined. The results find that Notch1 signaling pathway in normal HSCs is activated while it's silenced in normal HPCs. The adjacent cells around HSCs are stromal cells which secrete Jagged-1. Depletion of Jagged-1 will disrupt the balance between self-renew and proliferation of HSCs leading to their exhaustion. Our study will provide new ideas for the pathogenesis of leukemia, and provide a theoretical basis for the treatment of leukemia.

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