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摘要:

目的: 构建以IL-3为靶向、力达霉素 (lidamycin, LDM) 为弹头的融合蛋白IL-3-LDM, 观察其对多种CD123 + 白血病细胞的靶向杀伤作用。方法: 原核表达IL-3-LDP (interleukin 3-lidamycin) 融合蛋白, 组装活性烯二炔 (active enediyne, AE) 发色团得到IL-3-LDM。流式细胞术检测不同白血病细胞系 (KG1-a、TF-1、M07e、HL-60、K562、Raji) 表面CD123分子的表达, 并检测融合蛋白IL-3-LDM与各白血病细胞的结合能力; CCK-8检测IL-3-LDM融合蛋白对不同CD123阳性率的白血病细胞的杀伤能力。结果: 组装活性发色团得到的IL-3-LDM蛋白纯度可达90%以上。急性髓系白血病 (acute myeloid leukemia, AML) KG-1a细胞表面CD123阳性率最高 (88.9%), 其次为M07e和TF-1细胞 (>75%), 再次为HL-60细胞 (7.8%), 而K562、Raji细胞CD123表达呈阴性。体外IL-3-LDM融合蛋白对CD123 + 白血病细胞 (KG-1a、M07e、TF-1和HL-60细胞) 的结合能力和杀伤效率与细胞表面CD123的阳性率成正比, 对于CD123表达率最高的KG-1a细胞, LDM的杀伤强度是多柔比星 (adriamycin, ADR) 的1 415.8倍, 而IL-3-LDM的杀伤强度又是LDM的9.6倍。结论: IL-3-LDM融合蛋白可以有效携带细胞毒药物LDM并高效靶向杀伤CD123 + 白血病细胞。

关键词: [IL-3](#) [力达霉素](#) [融合蛋白](#) [CD123](#) [白血病](#) [肿瘤干细胞](#)

Targeting cytotoxicity effect of IL-3-lidamycin fusion protein on CD123 + leukemia cells [Download Fulltext](#)

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Abstract:

Objective: To construct a fusion protein IL-3-lidamycin (IL-3-LDM) with an IL-3 guide and a LDM warhead, and to investigate its targeting cytotoxicity on CD123 + leukemia cells in vivo. Methods: IL-3-LDP (interleukin 3-lidamycin) fusion protein was obtained in a prokaryotic system, and further assembled with active enediyne (AE) to get IL-3-LDM. The expression of CD123 in six leukemia cell lines (KG1-a, TF-1, M07e, HL-60, K562, Raji) was detected by flow cytometry and the binding ability of IL-3-LDM with different leukemia cell lines was examined. The cytotoxicity of IL-3-LDM fusion protein on leukemia cells with different CD123 expression levels was detected by CCK-8. Results: The purity of recombinant protein IL-3-LDM was more than 90% after assembling with AE. The results showed that the CD123 expression ratio was 88.9% on AML (acute myeloid leukemia) KG-1a cells, >75% on M07e and TF-1 cells, 7.8% on HL-60 cells, and negative on K562 and Raji cells. The expression ratio of CD123 on leukemia cells (KG-1a, M07e, TF-1 and HL-60) was positively related to its binding ability and sensitivity to IL-3-LDM in vitro. The cytotoxicity of LDM on KG-1a cells which expressed the highest level of CD123 was 1 415.8 fold stronger than that of adriamycin (ADR), and the cytotoxicity of IL-3-LDM was 9.6 fold than that of LDM. Conclusion: IL-3-LDM fusion protein can effectively target cytotoxic drug LDM to kill CD123 + leukemia cells.

Keywords: [IL-3](#) [lidamycin](#) [fusion protein](#) [CD123](#) [leukemia](#) [cancer stem cell](#)