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603.LYMPHOID ONCOGENESIS: BASIC

Chemotherapy-Induced Cellular Senescence Promotes Stemness of B-Cell Non-Hodgkin's Lymphoma Via CCL21/CCR7/NF-Kb Signaling Activation

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A bs tract: Resistance to existing therapies is currently the main reason for treatment failure in refractory/relapsed B-NHL patients, and treatment-induced cellular senescence (TIS) is one of the important mechanisms of tumor drug resistance. In our previous studies, we found that the anti-apoptotic and tumorigenic ability of chemotherapy-induced senescent B-NHL cells was significantly enhanced, and the survival period of tumor-bearing mice was significantly shortened, but the mechanism is still unclear. In this study, we identified the C-C chemokine receptor 7 (CCR7) by single-cell RNA-sequencing, which showed significant differential expression in senescent B-NHL cell population and non-senescent cell population. CCL21/CCR7 dependent B-NHL-TIS initiates downstream transcription of NF-κB, thereby enhancing phenotypic and functional stemness features, including the up-regulation of stemness markers, CD34, CD44, LGR5, CD150, and stronger colony forming ability and cell sphere forming ability. The analysis results of clinical patients showed that the expression of CCR7 in the peripheral blood of B-NHL patients was significantly higher than that of healthy normal people and leukemia patients. The expression of CCR7 in peripheral blood of B-NHL patients before treatment was significantly lower than that of relapsed patients, and The expression in abnormal B lymphocyte population is significantly higher than that in normal T and B lymphocyte population, high expression of CCR7 is associated with recurrence and poor prognosis in B-NHL patients. Targeting CCR7/NF-κB signaling has positive significance in inhibiting the acquisition and maintenance of stemness in aging B-NHL cells and preventing tumor drug resistance and recurrence.

K ey words: Stress-induced senescence; CCR7; CCL21; senescence related stemness; B-cell non-Hodgkin's lymphoma

Disclosures No relevant conflicts of interest to declare.

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