

Distinct chemokine receptor expression profiles in the development and early progression of follicular lymphoma

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Follicular lymphoma (FL) is one of the most frequent non-Hodgkin's lymphoma and represents a heterogeneous disease. Progression of disease within 24 months (POD24) is the most accurate predictor of worse clinical outcome but specific parameters useful for risk stratification before start of therapy are lacking. The role of chemokine receptors (CRs) in the development of various lymphoma entities has been identified as crucial. Thus, we aimed to comprehensively study CR expression profiles in FL.

We investigated 17 well-characterized chemokine receptors (*CCR1-CCR10*, *CXCR1-CXCR5*, *CX3CR1* and *XCR1*) in a cohort of FL patients with POD24 (n=14) and without POD24 (n=57) by RQ-PCR. Non-neoplastic tonsils (n=5) served as non-malignant controls.

The chemokine receptor expression profile of FL substantially differed from that of tonsils, with lower expression of *CCR1*, *CCR6*, *CCR7*, *CXCR1*, *CXCR5*, and *CX3CR1* in this lymphoma entity. Furthermore, an at least 2.5-fold higher expression of *CCR8*, *CXCR1*, *CXCR3* and *CX3CR1* was detected in grade 1-2 FLs compared to grade 3a-b. Interestingly, *CCR3*, *CCR4*, *CCR7*, *CXCR4* and *XCR1* exhibited an at least four fold higher expression in POD24-FLs compared to non-POD24 FLs. Relating the CR expression levels to clinical data of our FL cohort, high levels of *CCR3*, *CCR4* and *CCR10* correlated with poor lymphoma-specific survival. The FL samples can be divided into two distinct clusters, based on their expression profiles. The majority of the records for patients with POD24 were observed in Cluster 2, which was also associated with a reduced overall survival.

Overall, our results indicate that a distinct chemokine expression profile might be implicated in the development and early progression of FL. Thus, several receptors could serve as clinically useful prognostic markers for risk stratification and/or as potential novel therapeutic targets for lymphoma therapy.

Keywords: Follicular lymphoma, Chemokine receptors, POD24

