ANALYSIS OF CHEMOKINE EXPRESSION PROFILE OF NORMAL AND TUMOR TISSUE FOR EFFECTIVE ADOPTIVE CELL THERAPY

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Background Adoptive cell therapy (ACT) is transfer of ex vivo expanded immune cells to treat cancers. In solid tumors, ACT is less effective because injected immune cells need to infiltrate to the tissue. To improve the ACT, engineering of chemokine receptors on immune cells has been developed. Since tumors secrete different chemokines, it is important to analyze frequently secreted chemokines and modulate their corresponding receptors. We analyzed and compared the chemokine expression in the normal and tumor tissues and proposed useful chemokine receptors for ACT.

Methods RNA sequencing data for tumor and normal tissues were obtained from the TCGA (n=9,807, pan-cancer) and GTEx (n=7,862, normal tissues from whole body). To identify chemokines expressed more in tumor tissues than normal tissues, we compared chemokine expression between TCGA and GTEx data. To identify chemokine receptors which are already expressed in activated T cells, we analyzed gene expression of expanded tumor-infiltrating lymphocytes (TILs) from 14 breast cancer patients.

Results Twenty-nine chemokines were expressed more than twice in tumors than normal tissues in pan-cancer analysis. Total 16 chemokine receptors are matched with these 29 chemokines. We checked expression of corresponding chemokines of 16 chemokine receptors. According to average expression in the normal and tumor tissues, 9 chemokine receptors that covered more than 80% of pan-cancer cases were considered to be useful for engineering of ACT. In RNA sequencing data of the TILs, 3 out of 9 chemokine receptors were highly expressed. About 98.1% of pan-cancer cases showed high expression of chemokines corresponding to these 6 chemokine receptors.

Conclusions Six chemokine receptors (CCR3, CCR4, CCR8, CXCR5, CXCR6, and XCR1) could be useful to modulate for ACT by enhancing cell trafficking.

Ethics Approval This study was approved by the Institutional Review Board of Asan Medical Center, approval number IRB#2015-0438.