Phagocytic Function of monocytes in chronic lymphocytic leukemia

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Chronic lymphocytic leukemia (CLL) is the most common leukaemia in the US and in Europe, including Georgia. Patients with CLL are susceptible to infectious diseases as a result of both, the disease progression and chemotherapy that indicates deficiency of immune responses to pathogens, including innate immunity, mediated by monocytes. Monocytes are also often recruited by therapeutic antibodies which exert anti-tumour toxicity through Fcγ-receptor (FcγR)-mediated phagocytosis of opsonised leukaemic cells.

The aim of this research was to study an important innate component of immunodeficiency in CLL such as functional and phenotypic changes of peripheral blood monocytes, and establish the ability of bispecific antibody to induce phagocytosis of B-CLL cells. For this we studied the ability of freshly isolated ex vivo or activated by G-CSF and IFNγ cytokines monocytes to absorb opsonized and non-opsonized Staphylococcus aureus particles. We identified the expression profile of Fcγ receptors and Toll-like CD180 receptor on monocytes in correlation with CLL Rai stage and treatment.

Our data demonstrated that monocyte ability to engulf opsonized Staphylococcus aureus was significantly decreased and that the monocytes from B-CLL patients compared to normal age- matched control (Mean Fluorescence Intensity (MFI)= 3030±616 in control group; MFI=1360±230 in CLL patients, p=0.0076) volunteers were unable to efficiently phagocytose the bacterial particles. the monocytes stimulated with IFNγ and G-CSF to engulf S. aureus appeared to be lower than that of unstimulated cells (Mean Fluorescence Intensity (MFI)= 1460±467 in unstimulated cells; MFI=546±119 in stimulated cells, p=0.03).Peripheral blood monocytes of CLL patients were characterized by reduced expression of CD64, CD16 and CD180 that would substantially undermine their ability to contribute to anti- bacterial immune responses. In addition, aberrant expression of CD64 would negatively affect the efficiency of antibody-mediated immunotherapies. In contrast, CD32 is significantly increased on CLL cells. This would indicate augmented activation of CLL cells during cells culture which might further support CLL cell survival and expantion in prolipheration centers in bone marrow and lymph nodes. Our data would help to undentify optimal approaches to the correction of monocytic deficiencies in CLL. This would allow first of all, to decrease bacterial infections pre- and post therapeutic intervention, and to develop novel effective treatments of CLL.

This work was supported by Shota Rustaveli National Science Foundation (SRNSF).