Targeting the tumor microenvironment in chronic lymphocytic leukemia

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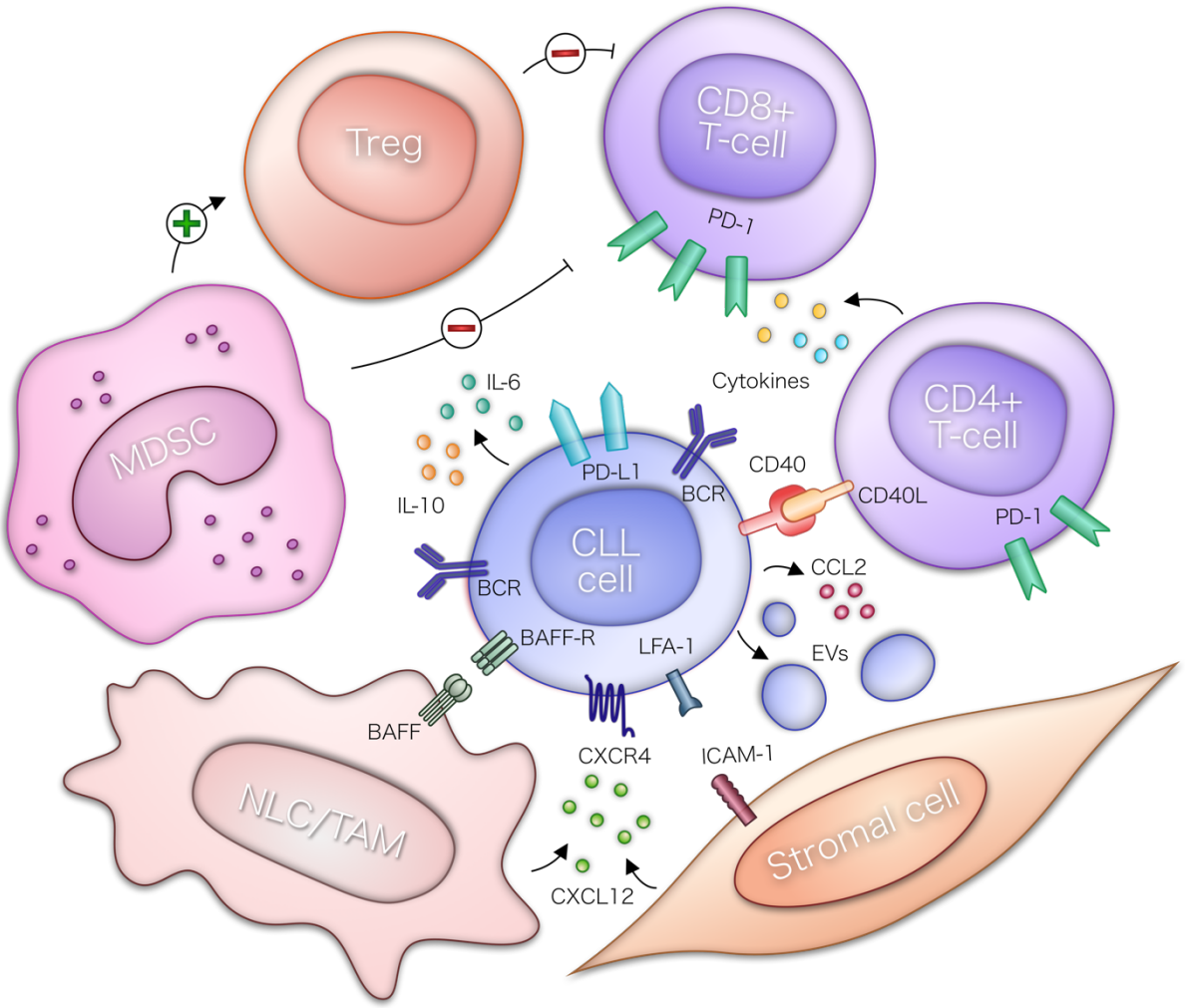
Supplementary figures.

Supplementary figure 1.



Supplementary figure legend.

Supplementary figure 1. Selection of key CLL-TME constituents and interactions. $CD4^+$ T-cells mediate tumor support, for example through cytokine signaling and CD40/CD40L co-stimulation. Chronic activated/exhausted T-cells have increased expression of PD-1. Increased number of T_{Regs} contribute to suppressing T-cell function. CLL cells promote MDSCs, which, in turn, suppress T-cell effector function and promote T_{Reg} differentiation. Bidirectional chemokine signaling between macrophages or stromal cells and CLL cells promote migration of CLL cells into protective niches. Adhesion molecules on CLL cells (LFA-1) bind to stromal cell receptors (ICAM-1). BAFF provided by for example NLCs stimulate BAFF-R on CLL cells, promoting survival and growth. CLL cells recruit and modulate their microenvironment by secretion of for example cytokines, chemokines, and EVs. CLL, chronic lymphocytic leukemia; TME, tumor microenvironment; BCR, B-cell receptor; CD, cluster of differentiation; CD40L, CD40 ligand; PD-1, programmed cell death protein 1; PD-L1, programmed cell death protein-1 ligand ; CCL2, chemokine ligand 2; EVs, extracellular vesicles; LFA-1, lymphocyte function-associated antigen 1; ICAM-1, intercellular adhesion molecule 1; CXCL12, CXC motif chemokine 12; CXCR4, CXC chemokine receptor 4; BAFF, B-cell activating factor; BAFF-R, B-cell activating factor receptor; IL, interleukin; NLCs, nurse like cells; TAMs, tumor associated macrophages; MDSCs, myeloid derived suppressor cells; T_{Reg}, regulatory T-cell.