

CD22 as a target for passive immunotherapy

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CD22 is a 135 Kda B cell restricted sialoglycoproteins present in the cytoplasm of virtually all B lineage cells but expressed on the B cell surface only at mature stages of differentiation. In humans the vast majority of IgM+ IgD+ B cells express cell surface CD22 while in lymphoid tissues, CD22 expression is high in follicular mantle and marginal zone B cells and weak in germinal center B cells. In B cell malignancies CD22 expression ranges from 60 to 80% depending on the histological type and on the assays used.

The function of CD22 molecule is uncertain although recent studies have implicated roles for the molecule both as a component of the B cell activation complex and as an adhesion molecule. CD22-deficient mice have reduced number of mature B cells in the BM and circulation; in these mice the B cells have a shorter lifespan and enhanced apoptosis thus indicating a key role of this antigen in B cell development/survival.

After binding with its natural ligand(s) or antibodies, CD22 is rapidly internalized; this provides a potent costimulatory signal in primary B-cell and pro-apoptotic signals in neoplastic B cells.

Preclinically CD22 has shown to be an effective target for immunotherapy of B cell malignancies using either "naked", toxin- and radiolabeled monoclonal antibodies.

Clinical trials in patients with NHL (both indolent and aggressive disease) are now ongoing with a humanized naked ab anti-CD22 (Epratuzumab, Amgen Inc. CA and Immunomedics Inc. NJ) used as single agent or in combination with other monoclonal antibodies (i.e. Rituximab) and/or chemotherapy. Preliminary data from these studies showed these approaches to be safe and effective.