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CD52 is expressed on human mast cells and is a potential therapeutic target in Waldenstrom's Macroglobulinemia and mast cell disorders.

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BACKGROUND: Alemtuzumab is a monoclonal antibody used in the treatment of CD52-expressing B-cell malignancies, including Waldenstrom's macroglobulinemia (WM). Recent studies demonstrate high levels of alemtuzumab activity in relapsed/refractory disease. One potential target of alemtuzumab is bone marrow mast cells (BMMCs), which provide growth and survival signaling for WM lymphoplasmacytic cells. **PATIENTS AND METHODS:** We therefore examined BMMCs (FceRI+, CD117+) from WM and other mast cell (MC) disorders for expression of CD52. **RESULTS:** We identified cell surface antigen expression by multicolor flow cytometric analysis and found CD52 expressed on human mast-derived cell line-1 (HMC-1) and LAD2 MC lines, on BMMC from 13 of 15 patients with WM, and on BMMCs from 4 of 4 patients with systemic mastocytosis (SM). None of 4 healthy donors expressed CD52. Reverse-transcriptase polymerase chain reaction analysis confirmed CD52 expression in the HMC-1 and LAD2 MC lines, in BMMCs from 14 of 15 patients with WM, and 3 of 3 patients with SM. CD52 transcripts were also detected in BMMCs from 6 of 6 healthy donors, despite the absence of CD52 cell surface expression. Importantly, we observed high levels of alemtuzumab-mediated, antibody-dependent, cell-mediated cytotoxicity against LAD2 MCs and BMMCs from patients with WM and SM. **CONCLUSION:** These studies demonstrate that CD52 is widely expressed on human MCs and WM bone marrow lymphoplasmacytic cells and provide the preclinical rationale for the use of alemtuzumab in the treatment of WM and possibly other MC-related disorders.