Supplementary Methods

We optimized β2M, MHC class I and MHC class II IHC on a test series of cHLs and evaluated the expression of each on HRS cells. For a subset of cases, we observed β2M, MHC class I, and/or MHC class II expression on the vast majority of HRS membranes at levels equivalent to or greater than that observed on adjacent, non-malignant inflammatory cells (Supplementary Fig. 1, case 1 for β2M and MHC class I, case 2 for MHC class II). For a subset, we detected no β2M, MHC class I, and/or MHC class II expression on the vast majority of HRS cells or cell membranes, despite appropriate internal controls (Supplementary Fig. 1, case 3 for β2M and MHC class I, case 1 for MHC class II). Finally, for a subsets of cases we observed extensive heterogeneity of staining among HRS cells including those with unequivocally positive but reduced membrane staining, relative to adjacent non-malignant cells, and those with a combination of reduced and complete loss of staining in a subset of cells (Supplementary Fig. 1, case 2 for β2M and MHC class I, case 3 for MHC class II).

Given the challenges of quantifying the expression of β2M, MHC class I, and MHC class II on individual HRS cells in stained tissue sections, which are overwhelmingly comprised of non-malignant cells in a densely cellular microenvironment, we devised a 3-tiered scoring system to categorize the predominant patterns of β2M, MHC class I, and MHC class II expression by HRS cells in each case. For cases categorized as *positive*, at least 90% of evaluable HRS cells showed positive membrane staining for the biomarker at levels equivalent to, or greater than that of adjacent non-malignant inflammatory cells. For cases categorized as *negative*, at least 90% of evaluable HRS cells showed no detectable membrane staining for the biomarker relative to non-malignant inflammatory cells. For cases categorized as *decreased*, positive membrane staining of HRS cells was present and unequivocally reduced relative to surrounding cells and/or positive staining was observed in less than 90% of evaluable HRS cells.