Lymphoid malignancies such as lymphoma and leukemia are particularly problematic as the transformation of these cells compromises host defense, and often these tumors evolve mechanisms to evade or escape immune surveillance. Burkitt Lymphoma (BL) is a very aggressive form of non-Hodgkin’s lymphoma and has the fastest doubling time among human tumors [1,2]. BL is primarily found in its endemic form which occurs in tropical climates, such as Papua New Guinea and equatorial Africa, having a > 95% degree of association with Epstein-Barr virus (EBV). A sporadic form of BL occurs elsewhere in the world and has only a 5-15% degree of association with EBV. A third form, HIV-associated BL, is associated with EBV in approximately 40% of cases [3]. In addition to its strong association with EBV, BL incidence in tropical climates very closely follows the distribution of malaria, with areas of endemic malaria having the highest incidence of BL [4]. Despite BL’s strong associations with EBV and malaria, it has yet to be resolved how these factors may contribute, or even if they contribute, to the development of BL. Due to BL’s rapid doubling time, aggressive chemotherapy is required to control its spread and growth [5]. Nearly 100% of BL and 5-8% of diffuse large B-cell lymphoma (DLBCL) harbor a balanced translocation involving c-MYC, which confers an adverse prognosis with chemoresistance and shortened survival. Currently used chemotherapy regimens are quite successful in children and adults, and survival rates exceeding 70% have been reported [6,7]. Unfortunately, these chemotherapy regimens are not as effective in elderly or immunocompromised patients. In addition to inferior responses, these patients are less able to tolerate the aggressive treatment and develop more severe treatment-associated toxicities [1,8,9]. Although the anti-CD20 monoclonal antibody rituximab has been successfully used in conjunction with chemotherapy, the efficacy of its use in immunocompromised patients has been a debated issue [10]. These issues highlight the shortcomings of current BL therapies and make the pursuit of alternative immunotherapies for BL a relevant objective. Immunotherapies which can harness the host’s immune system to target transformed cells, potentially lessening, or even eliminating, dependence on chemotherapy. As in the case of rituximab, immunotherapy may also be used in conjunction with chemotherapy to enhance patient responses. BL’s defect in HLA class I-mediated Ag presentation results from the poor immunogenicity of the EBV Ag, EBNA1. As this is the lone EBV Ag synthesized in BL, no other options are available for HLA class I presentation. The class I defect, however, appears broader and results from expression of a BL-associated molecule, which impairs the presentation of Ag to CD4+ T cells by HLA class I proteins. BLAIM thus represents a potentially novel target to consider for the development of immunotherapy for BL. Successful identification of BLAIM would allow for the development of mAbs which could be used to block the activity of BLAIM and restore class II-mediated Ag presentation. A sustained CD4+ T cell response could then serve to augment development of immunotherapies aimed at generating CD8+ T cell responses. Additionally, BLAIM itself could also be used to generate a more targeted CD8+ T cell response, and to reduce bystander effects in non-malignant cells. A recent study also suggests a defect in BL, which is related to Ag presentation via the alternative or recycling pathway [18]. Alteration of trafficking molecules, such as the GTPase Rab, may affect MHC/peptide recycling.

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and impair immune recognition of B-cell lymphomas [18]. Further characterization of the defects involving these molecules may be important in developing effective immunotherapies for lymphoid malignancies. When considering this evidence, two things become clear. First, it is necessary to pursue the development of improved therapies for BL which demonstrate lower levels of toxicities, especially for patients who are elderly or have compromised immunity. Secondly, further investigation into the numerous defects in Ag processing and presentation displayed by BL could yield novel therapies for BL as well as other lymphoid malignancies.

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