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Analysis of interleukin-10 promoter single nucleotide polymorphisms and risk of non-Hodgkin lymphoma in a Malaysian population

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Abstract
We evaluated the association of two IL10 single nucleotide polymorphisms (SNPs) (rs1800896 and rs1800871) with non-Hodgkin lymphoma (NHL) risk in the three major races of the Malaysian population (Malay, Chinese and Indian; 317 cases and 330 controls). Our initial screening demonstrated that rs1800871 but not rs1800896 was significantly associated with increased NHL risk in Malays (p = 0.007) and Chinese only (p = 0.039). Subsequent combined analysis of the Malay and Chinese revealed significant association of rs1800871 with all (ALL) NHL subtypes (p = 0.001), ALL B-cell subtypes (p = 0.003), diffuse large B-cell lymphoma (DLBCL) subtype (p = 0.002) and ALL T-cell subtypes (p = 0.031). SNP rs1800896 showed increased risk only in follicular lymphoma (FL) (p = 0.0004). We also detected a male-specific association of rs1800871 with increased NHL risk (p = 0.006) in the combined analysis. To our knowledge, this is the first report on the association of IL10 promoter SNPs with NHL susceptibility in the three major races of Malaysia.

Keywords: NHL, genetic susceptibility, SNP, IL10

Introduction
Although the survival rate of non-Hodgkin lymphoma (NHL) has improved substantially, the incidence of the disease has still been increasing steadily worldwide over the last two decades. The prevalence of NHL is highest in North America and Western Europe and lower in Eastern Europe and Asia [1]. In Malaysia, NHL was the sixth most common cancer, with an overall cancer incidence of 4.3% per 100,000, and was more prevalent in males than females, according to the National Cancer Registry 2007 report [2]. The pathogenesis of NHL is still relatively unknown. Currently, immunosuppression remains one of the most well-defined risk factors reported to be associated with the development of NHL. Patients with acquired immunodeficiency syndrome (AIDS), post-organ transplant immune deficiencies and other hereditary abnormalities such as inherited immunodeficiency syndrome have increased risks of developing NHL [3].

Interleukin 10 (IL10), an anti-inflammatory cytokine, is one of the central mediators of the T helper cell Th1/Th2 balance involved in the immune response [4]. The IL10 immunosuppressive effect appears to inhibit cell-mediated immune responses against cancer cells [5]. In lymphoma, IL10 has been reported to act as an auto- or paracrine growth factor for the survival of B-cell lymphoma cells [6–10]. In fact, NHL tumors were reported to produce IL10 and other cytokines to increase cell proliferation [11], while an increased serum IL10 level was associated with poorer outcomes of patients with lymphoma [12–16]. Furthermore, inhibition of IL10 sensitized B-cell NHL cells to apoptosis, whereas IL10 knockout mice developed less age-related malignant B-cell lymphoma [17]. On the other hand, IL10 has also been reported to contain tumor-inhibiting properties by supporting an effective immune attack against malignant cells in vivo, mainly in breast cancer and melanoma [18]. Interestingly, Cervenak et al. reported anti-angiogenic and anti-tumorigenic properties of IL10 in Burkitt lymphoma in vivo [19]. Nonetheless, the literature in general is consistent with IL10 playing a tumor-promoting role in lymphoma. As immunosuppression is thought to be the underlying basis of lymphomagenesis, much interest has focused upon regulation of the IL10 gene.

Single nucleotide polymorphisms (SNPs) are the most abundant DNA sequence variations. These SNPs can alter...