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# Interleukin-10 gene polymorphism influences the prognosis of T-cell non-Hodgkin lymphomas

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## Summary

Interleukin-10 (IL-10) is one of the cytokines implicated in the pathogenesis of diffuse large B-cell lymphoma (DLBCL) in which it acts as auto/paracrine growth factor for lymphoma growth. T-cell non-Hodgkin lymphoma (NHL) is a heterogeneous disease, the biological basis of which is not fully understood. Some evidence suggests that IL-10 might be associated with the progression of T-cell NHLs and that IL-10 may be involved in a rescue effect, protecting T cells from apoptotic cell death associated with upregulated bcl-2 expression. The current study evaluated the impact of IL-10 gene (*IL10*) polymorphism on the response to chemotherapy and survival in T-cell NHL. *IL10* polymorphisms were determined in 108 patients with T-cell NHL. The response to chemotherapy was not dependent on *IL10* polymorphism, while survival differed significantly according to *IL10* polymorphism. The group with ATA haplotype showed superior overall survival (61·2 ± 5·9% vs. 21·2 ± 11·7%, $P = 0{\cdot}001$) and failure-free survival (35·0 ± 5·7% vs. 13·2 ± 8·7%, $P = 0{\cdot}001$) compared to those without ATA haplotype. The ATA haplotype was identified as a favourable prognostic factor compared to non-ATA haplotype ($P = 0{\cdot}037$, hazard ratio 2·1), together with international prognostic index (IPI) in a multivariate model for overall survival. In conclusion, *IL10* polymorphism may affect the survival of T-cell NHL patients.

**Keywords:** interleukin-10, single nucleotide polymorphism, T-cell non-Hodgkin's lymphoma.

Several cytokines are known to be involved in the pathogenesis of non-Hodgkin Lymphomas (NHLs) including diffuse large B-cell (DLBCL) and T-cell subtype lymphomas (Merz *et al*, 1991). Recent studies suggested that several cytokine gene polymorphisms were associated with susceptibility to NHL, such as tumour necrosis factor gene (*TNF*) (Rothman *et al*, 2006) or interleukin-4 gene (*IL4*) (Lan *et al*, 2006). Interleukin-10 (IL-10) is one of the cytokines implicated in the pathogenesis of DLBCL (Cunningham *et al*, 2003) in which it acts as an auto/paracrine growth factor for lymphoma growth (Voorzanger *et al*, 1996).

The T-cell NHLs are a group of morphologically and clinically distinct lymphoproliferative disorders with various clinical behaviours and clinical outcomes (Rizvi *et al*, 2006). Most studies reported more aggressive clinical courses and worse treatment outcomes in patients with T-cell NHL (5-year survival rate of 20–45%) when compared to corresponding B-cell NHL patients, with exception of cutaneous or anaplastic lymphoma kinase (ALK) positive anaplastic large cell lymphomas (ALCLs) (Armitage *et al*, 1989; Cheng *et al*, 1989; Melnyk *et al*, 1997; Gisselbrecht *et al*, 1998). However, in terms of the prediction of treatment outcomes or long-term survival, use of the International Prognostic Index (IPI) system may provide more accurate prediction on the survival of patients with T-cell NHL than histological diagnosis of subtypes (Savage *et al*, 2004; Escalon *et al*, 2005).

The biological background of the T-cell NHLs has not been extensively investigated compared with DLBCL. As in DLBCL, some evidence suggested that IL-10 might be associated with the progression of T-cell NHLs (Ho *et al*, 1999a,b). For example, increased production of *IL10* mRNA was noted in peripheral T-cell lymphomas (Boulland *et al*, 1998) and in the progression

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of mycosis fungoides (Asadullah *et al*, 1996). In addition, IL-10 was highly expressed in nasal NK/T-cell lymphomas (Shen *et al*, 2001). Gravisaco *et al* (2003) suggested that IL-10 is one of the key regulators of *in vivo* growth of murine T-cell lymphoma cells. In addition, IL-10 was shown to have a rescue effect by protecting T cells from apoptotic cell death associated with upregulated bcl-2 expression (Cohen *et al*, 1997). Furthermore, our group recently reported that the overexpression of bcl-2 may be associated with the progression of T-cell NHLs by interacting with p53-dependent pathway (Jung *et al*, 2006). This implies that IL-10, a potent promoter of bcl-2 expression in haematopoietic cells (Weber-Nordt *et al*, 1996), may be involved in the apoptosis-related resistance mechanism of T-cell NHLs through a bcl-2 mediated pathway (Rassidakis *et al*, 2003).

Besides its action as a growth factor of lymphoma cells, IL-10 is one of the important immunoregulatory cytokines that modulate the balance between T helper cell type 1 (Th1) and type 2 (Th2) immune responses. A recent study revealed a strong correlation of IL-10 promoter gene polymorphism with clinical outcomes in DLBCL patients, and suggested that increased production of IL-10 within the tumour microenvironment might have a protective effect, possibly by increasing T-cell cytotoxicity, inhibiting tumour angiogenesis and antagonising the action of proinflammatory cytokines (Lech-Maranda *et al*, 2004). This finding implies that the role of IL-10 may not be restricted to the growth of lymphoma cells and that it may be involved in the regulation of host immunity. Thus, the regulation of IL-10 production may affect anti-tumour immunity and, ultimately, the survival of NHL patients.

Accordingly, we hypothesised that IL-10 may be associated with the progression and prognosis of T-cell NHLs. We evaluated the impact of IL-10 promoter gene polymorphism on the clinical outcomes of 108 patients with T-cell NHL.

## Patients, materials and methods

### *Study design*

The primary objective of the current study was to determine the relationship of IL-10 promoter gene polymorphisms with treatment outcomes of T-cell NHL patients. The secondary objective was to verify the significance of the IL-10 promoter gene polymorphism in multivariate analysis with other clinical prognostic factors.

### *Patient characteristics and treatment protocol*

From January 1996 to December 2003, 108 patients with a histologically proven diagnosis of T-cell NHL were treated at four hospitals in the Republic of Korea (Kyungpook National University Hospital, Chonnam National University Hwasun Hospital, Dongsan Medical Centre, and Korean Cancer Centre Hospital). This study was approved by the institutional research board in Kyungpook National University Hospital (Daegu, Korea)

Peripheral T-cell lymphoma-unspecified (PTCL-U), extranodal natural killer cell/T-cell (NK/T-cell) lymphoma, ALCL, angioimmunoblastic T-cell lymphoma (AIL), T-cell type lymphoblastic lymphoma and cutaneous T-cell NHL were defined according to the World Health Organization (WHO) criteria (Harris *et al*, 1999). The distribution of subtypes were as follows: PTCL-U in 46 patients (43%), extranodal NK/T-cell lymphoma in 28 patients (26%), ALCL in 25 patients (23%), and AIL in nine patients (8%).

The baseline characteristics of the patients are summarised in Table I. Overall, among 108 patients (median age 53·5 years, male/female 76/32), 64 patients (59%) had stage 3/4 disease and 54 patients (50%) had intermediate to high or high IPI score. In addition, 57 patients (53%) showed serum lactate dehydrogenase (LDH) level over normal limit at presentation, and 71 patients (66%) had more than one site of extranodal involvement with 20 cases of marrow involvement (19%). Combined modality therapy (initial chemotherapy followed by involved field radiation) was given to 26 patients (24%), while chemotherapy alone was used in 82 patients (76%). A median four cycles of chemotherapy was given (range 1–8 cycles). The main reason for fewer than planned cycles of chemotherapy being given was usually treatment failure, especially in the group with advanced stage disease.

Frontline chemotherapy was mainly administered with CHOP (cyclophosphamide, doxorubicin, prednisone, vincristine) regimen in 57 patients (53%), while the remaining 51 patients (47%), were given an intensified chemotherapy regimen: CHOP-E (CHOP regimen plus etoposide 100 mg/$m^2$ on day 1), CHOP-EG (CHOP + etoposide, gemcitabine) (Kim *et al*, 2006), or ProMACE-CytaBOM (bleomycin, cyclophosphamide, cytarabine, doxorubicin, etoposide, leucovorin, methotrexate, prednisone, vincristine) regimen. Patients with stage 1 or 2 disease typically received four courses of chemotherapy followed by involved-field radiotherapy (30–40 Gy), while patients with advanced stage disease received six to eight courses of chemotherapy followed by radiotherapy to bulky sites. Of a total 108 patients, 14 patients were treated with high-dose chemotherapy with autologous stem cell rescue due to progression after response ($n = 4$) or initially high IPI score ($n = 10$). The response to frontline chemotherapy was evaluated after completion of two to three courses of chemotherapy and 1 month after completion of all planed cycles of chemotherapy, then every 4 months.

### *IL-10 genotyping*

Three single-nucleotide polymorphisms in proximal region of IL-10 promoter gene were studied in the current study as previously described (Kim *et al*, 2005). Briefly, blood samples derived from 81 patients were taken after informed consent was given, while paraffin-embedded tissue samples derived from 27 patients, who had provided informed consent for future research, was obtained, were used retrospectively for genomic DNA extraction. Genomic DNA was processed

**Table I.** Patients' characteristics and treatment outcomes according to the *IL10* promoter gene haplotype.

| No of patients (%) | Overall ($n = 108$) | *IL10*promoter gene haplotype | | | *P*-value |
|---|---|---|---|---|---|
| | | ATA/ATA (33, 30·6%) | ATA/ACC (58, 53·7%) | ACC/ACC (17, 15·7%) | |
| Gender (F/M) | 32/76 | 13/20 | 15/43 | 4/13 | NS |
| Age (years), median (range) | 53·5 (16–83) | 48 (18–83) | 53 (16–75) | 56 (17–73) | NS |
| Subtypes | | | | | |
| PTCL-U | 46 (43) | 17 (52) | 24 (41) | 5 (29) | NS |
| Extranodal NK/T | 28 (26) | 8 (24) | 16 (28) | 4 (24) | |
| ALCL | 25 (23) | 6 (18) | 14 (24) | 5 (29) | |
| AIL | 9 (8) | 2 (6) | 4 (7) | 3 (18) | |
| Disease | | | | | |
| Age, ≥60 years | 38 (33) | 12 (36) | 20 (35) | 6 (35) | NS |
| ECOG≥2 | 20 (19) | 4 (12) | 10 (17) | 6 (35) | NS |
| Stage 3,4 | 64 (59) | 19 (58) | 31 (53) | 14 (82) | NS |
| Elevated LDH | 57 (53) | 16 (49) | 29 (50) | 12 (71) | NS |
| Extranodal | 71 (66) | 24 (73) | 33 (57) | 14 (82) | NS |
| BM involvement | 20 (18) | 6 (18) | 9 (16) | 5 (29) | NS |
| IPI | | | | | |
| Score 0–2 | 54 (50) | 18 (55) | 32 (55) | 4 (24) | NS |
| Score 3–5 | 54 (50) | 15 (45) | 26 (45) | 13 (76) | |
| Treatment | | | | | |
| Chemo | 79 (76) | 23 (70) | 42 (73) | 14 (82) | NS |
| Chemo + IFRT | 25 (24) | 10 (30) | 13 (22) | 2 (12) | |
| Cycles of Chemo (range) | 4 (1–8) | 5·5 (1–8) | 4·0 (1–8) | 4·5 (1–8) | NS |
| HDCT/ASCT | 15 (14) | 3 (9) | 11 (19) | 1 (6) | NS |
| Response | | | | | |
| Evaluable | 89 (82) | 27 (82) | 48 (89) | 14 (88) | |
| CR | 46 (52) | 15 (56) | 27 (56) | 4 (27) | NS |
| PR | 20 (22) | 8 (29) | 7 (15) | 5 (37) | |
| SD or PD | 23 (26) | 4 (15) | 14 (29) | 5 (36) | |
| ORR (CR + PR) | 66 (74) | 23 (85) | 34 (71) | 9 (64) | NS |
| Survival | | | | | |
| OS, 2-year | 55·4 ± 5·4% | 59·4 ± 10·2% | 62·1 ± 7·2% | 21·2 ± 11·7% | 0·004 |
| 5-year | 52·8 ± 5·9% | 59·4 ± 10·2% | 57·9 ± 7·8% | 21·2 ± 11·7% | |
| Progression, 2-year | 64·8 ± 5·5% | 69·5 ± 9·7% | 56·9 ± 7·6% | 81·2 ± 11·4% | 0·2 |
| 5-year | 74·0 ± 6·4% | 69·5 ± 9·7% | 70·6 ± 8·3% | 81·2 ± 11·4% | |
| FFS, 2-year | 31·2 ± 5·1% | 29·3 ± 9·4% | 38·3 ± 7·1% | 13·2 ± 8·7% | 0·045 |
| 5-year | 23·4 ± 5·8% | 29·3 ± 9·4% | 26·1 ± 7·6% | 13·2 ± 8·7% | |

IL-10, interleukin-10; PTCL-U, peripheral T-cell lymphoma-unspecified; NK/T, extranodal natural killer/T-cell lymphoma; ALCL, anaplastic large cell lymphoma; AIL, angioimmunoblastic lymphoma; LBL, lymphoblastic lymphoma; CTCL, cutaneous T-cell lymphoma; LDH, lactate dehydrogenase; BM, bone marrow; IPI, International Prognostic Index; IFRT, involved field radiation therapy; HDCT/ASCT, high dose chemotherapy with autologous stem cell transplantation; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, overall response rate; OS, overall survival; FFS, failure-free survival; NS, non-significant.

for the three targets of IL-10 promoter gene polymorphism, which are in the promoter region at −1082 (rs1800896), −819 (rs1800871) and −592 (rs1800872) using polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) techniques as previously described (Kim *et al*, 2005). Selected PCR-amplified DNA samples were sequenced to confirm the genotyping results.

### *Definitions*

Clinical responses to frontline chemotherapy were determined by computed tomography. The responses were scored according to International Working Group criteria (Cheson *et al*, 1999). Overall survival (OS) was measured from the day 1 of the first cycle of frontline chemotherapy until the date of death or last follow-up. Failure-free survival (FFS) was calculated from the day 1 of first cycle of frontline chemotherapy until treatment failure (disease progression, recurrence, or death from any cause).

### *Statistical analysis*

Clinical data were analysed according to information available as of December 2005. The frequency of IL-10 promoter gene

 

genotype and haplotype was calculated using chi-square test. Haplotypes were determined based on a Bayesian algorithm using the Phase program (Stephens *et al*, 2001) (available at http://www.depts.washington.edu/ventures/UW_Technology/Express_Licenses/PHASEv2.php). The haplotype frequencies were estimated with linkage disequilibrium coefficient, D, using the haploview program (Barrett *et al*, 2005) (available at http://www.broad.mit.edu/mpg/haploview). D was expressed as D', giving the value of D as a percentage of the maximum calculated value given the observed allele frequencies. Values of D' ranged between −1 and +1. A/D'/value of 1 denoted complete linkage disequilibrium whereas a value of 0 denoted complete linkage equilibrium.

The clinical characteristics and treatment outcomes were compared using chi-square or Mann–Whitney's *U*-tests according to the genotype or haplotype of the *IL10* promoter gene. Survival estimates were calculated using Kaplan–Meier method for OS and FFS and Anderson's method for the probability of progression. Differences in OS, FFS and the probability of progression were compared using the log-rank test according to (i) the *IL10* promoter gene haplotype; (ii) other clinical prognostic factors including age, performance status, serum LDH level, extranodal involvement, stage or IPI; (iii) the frontline chemotherapy regimen; and (iv) T-cell NHL subtype. For the multivariate survival analyses, Cox proportional hazard models were used to define the prognostic factors for OS, FFS or the probability of progression. A backward conditional procedure was conducted until the *P*-value for the likelihood ratio test was >0·05 with the following variables: the IPI (score 0–2 vs. 3–5), T-cell NHL subtype (ALCL *versus* non-ALCL) and *IL10* promoter gene haplotype (ATA haplotype *versus* non-ATA haplotype). The hazard ratio (HR) and 95% confidence interval (CI) were also estimated. A cut-off *P*-value of 0·05 was adopted for all the statistical analyses. The statistical data were obtained using the Statistical Package for the Social Sciences (SPSS) version 11.5 software (SPSS Inc., Chicago, IL, USA). Multivariate analyses were performed on 104 of 108 patients for whom LDH levels were available.

## Results

### *Genotype and haplotype frequencies of IL-10 promoter gene*

The frequencies of genotypes were as follows: AA allele (100%) for −1082; TT (35·2%), TC (53·3%), and CC (11·4%) for −812; AA (34·4%), AC (54·3%) and CC (11·4%) for −592 loci. The T* and C* allele at −819 loci were found to be strongly linked with the A* and C* allele at −592 loci. The linkage disequilibrium coefficient,/D'/, was 0·92 between genotypes at −819 and −592. The frequencies of each haplotype were as follows: ATA/ATA haplotype in 33 patients (30·6%), ATA/ACC haplotype in 58 patients (53·7%) and ACC/ACC haplotype in 17 patients (15·7%), which was similar to the result of a previous study of the Korean population (Kim *et al*, 2005).

### *Patients characteristics and treatment protocol according to IL-10 promoter gene polymorphism*

The patients' characteristics according to the IL-10 promoter gene haplotype are summarised in Table I. No differences of patients or disease characteristics were observed according to the *IL10* polymorphism.

### *Response to frontline chemotherapy according to IL-10 promoter gene polymorphism*

Out of 89 patients evaluated for the response to frontline chemotherapy, the overall response rate was 74% (66/89 patients) with complete response rate of 52% (46/89 patients), partial response of 23% (20/89 patients), stable disease of 6% (5/89 patients), and progressive disease of 20% (18/89 patients). No difference of response rate was noted between standard *versus* intensified chemotherapy (52% in standard group vs. 49% in intensified group, $P = 0{\cdot}679$).

### *Survival analysis according to IL-10 promoter gene polymorphism*

With a median follow-up duration of 326 d (range 3–2682 d, 750 d among survivors), 58 patients (54%) had relapsed or progressed with 41 deaths (38%). The 2-year OS and FFS rate was 55 ± 5% and 31 ± 5% respectively, while 2-year probability of progression was 65 ± 6%. When comparing OS and FFS according to ATA haplotype of the IL-10 promoter gene, the 2-year OS was significantly better for the ATA haplotype group (61·2 ± 5·9% in ATA haplotype group *versus* 21·2 ± 11·7% in non-ATA haplotype group, $P = 0{\cdot}001$, Fig 1A), as was the 2-year FFS (35·0 ± 5·7% in ATA haplotype group *versus* 13·2 ± 8·7% in non-ATA haplotype group, $P = 0{\cdot}013$, Fig 1B). Even though the probability of progression at 2 years seemed to be in favour of ATA haplotype group, it was not statistically significantly different (61·8 ± 6·1% in ATA haplotype group *versus* 81·2 ± 11·4% in non-ATA haplotype group, $P = 0{\cdot}07$, Fig 1C).

### *Survival according to T-cell NHL subtypes, frontline chemotherapy regimen and other clinical factors in T-cell NHLs*

We also conducted survival analyses to confirm that other previously known prognostic factors, such as IPI, were reproducible in the current cohort. A higher IPI score (as well as its individual components) was associated with an unfavourable prognosis ($P < 0{\cdot}001$).

### *Multivariate analysis*

The results of the multivariate analysis are summarised in Table II. When analysing prognostic factors for OS, the IL-10promoter gene ATA haplotype was found to be an

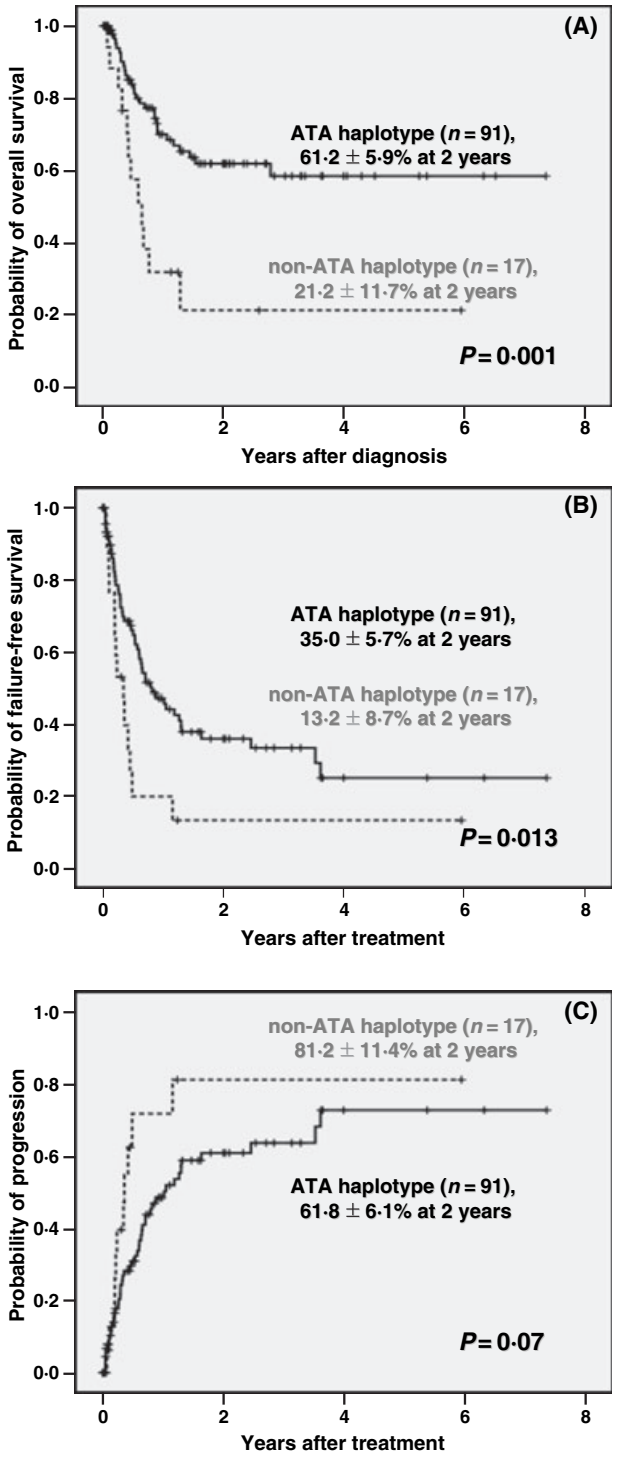


**Fig 1.** Impact of IL-10 promoter gene polymorphism on overall/failure-free survival and probability of progression.

independent prognostic factor compared with non-ATA haplotype; patients without ATA haplotype were found to have an over twofold higher risk of death [$P = 0{\cdot}037$, HR 2·100, 95% CI (1·045–4·218)]. In addition, the group with higher IPI score also showed a higher risk of death.

IL-10 promoter gene haplotype was not identified as an independent prognostic factor in terms of FFS or the probability of progression. Meanwhile, other previously known prognostic factors, such as IPI, influenced FFS or the probability of progression as shown in Table II.

## Discussion

This study demonstrated that the prognosis of patients with T-cell NHL appears to be affected by IL-10 promoter gene polymorphism. Even though a definite association with the response to chemotherapy was not proven, a significant association of IL-10 promoter gene polymorphism with OS or FFS implies that IL-10 may have some impact on the prognosis of T-cell NHL.

The prognostic role of IL-10 has been well addressed in NHL as well as in Hodgkin lymphomas (Sarris *et al*, 1999; Viviani *et al*, 2000; Vassilakopoulos *et al*, 2001; Munro *et al*, 2003; Visco *et al*, 2004). A recent investigation by Lech-Maranda *et al* (2004) demonstrated that IL-10 promoter gene polymorphism is associated with clinical response and prognosis of the patients with DLBCL. However, data is still lacking in patients with T-cell NHL. The potential role of IL-10 in T-cell NHL (Jung *et al*, 2006) has been suggested by several previous investigations (Asadullah *et al*, 1996; Buhl & Sogaard, 1997; Ho *et al*, 1999a,b; Shen *et al*, 2001; Gravisaco *et al*, 2003). Previously, our group has reported that the prognosis of T-cell NHLs may be related to a bcl-2 mediated apoptosis-related resistance mechanism (Jung *et al*, 2006). Another report suggested that IL-10 had a rescue effect on T cells, protecting them from apoptotic cell death associated with upregulation of bcl-2 expression (Cohen *et al*, 1997). Accordingly, IL-10, the promoter of bcl-2 overexpression, could be involved in the mechanism of chemoresistance and prognosis in T-cell NHLs, and should be investigated further in future.

In previous investigations, increased serum IL-10 levels were found to be associated with poor prognosis and shorter survival of patients with NHL and Hodgkin lymphoma (Cortes & Kurzrock, 1997; Khatri & Caligiuri, 1998; Sarris *et al*, 1999; Bohlen *et al*, 2000; Aydin *et al*, 2002; Salgami *et al*, 2002; el-Far *et al*, 2004; Ozdemir *et al*, 2004). Because the ATA haplotype of the IL-10 promoter gene has been associated with low IL-10 inducibility (Lim *et al*, 1998; Crawley *et al*, 1999; Hulkkonen *et al*, 2001; Karjalainen *et al*, 2003; Rady *et al*, 2004). Our data suggest that the group with low IL-10 inducibility (i.e. ATA-haplotype) may have a more favourable prognosis compared to those with non-ATA haplotype although controversy remains which haplotype is the low IL-10 inducibility allele (Roh *et al*, 2002).

The current study showed that the prognosis of T-cell NHL was significantly better for the group with ATA-haplotype ($P = 0{\cdot}001$ for OS, $P = 0{\cdot}013$ for FFS), although any significant difference of response to chemotherapy was not noted according to IL-10 promoter gene polymorphism. The

 

**Table II.** Multivariate analyses of prognostic factors for the overall/failure-free survival and probability of progression.

| Prognostic factors | *P*-value by Log-rank | *P*-value by Cox's | HR | [95% CI] |
|---|---|---|---|---|
| Overall survival | | | | |
| IL-10 promoter gene, non-ATA haplotype | 0·001 | 0·037 | 2·100 | [1·045–4·218] |
| High IPI (score 3–5) | <0·001 | 0·004 | 2·958 | [1·459–6·024] |
| Non-ALCL subtype of T-cell NHLs | 0·444 | NS | – | – |
| Failure free survival | | | | |
| High IPI (score 3–5) | 0·001 | 0·018 | 2·083 | [1·136–3·816] |
| Non-ALCL subtype of T-cell NHLs | 0·107 | NS | – | – |
| IL-10 promoter gene, non-ATA haplotype | 0·013 | NS | – | – |
| Probability of progression | | | | |
| High IPI (score 3–5) | <0·001 | 0·003 | 2·404 | [1·342–4·310] |
| Non-ALCL subtype of T-cell NHLs | 0·142 | NS | – | – |
| IL-10 promoter gene, non-ATA haplotype | 0·065 | NS | – | – |

For the multivariate analyses for OS, FFS and the probability of progression, IPI (score 0–2 vs. 3–5), T-cell NHL subtype (ALCL *versus* non-ALCL) and IL-10 promoter gene haplotype (ATA haplotype versus non-ATA haplotype) were included.
HR, hazard ratio; 95% CI, 95% confidence interval; IPI, International Prognostic Index; ALCL, anaplastic large cell lymphoma; NS, non-significant.

discrepancy of the impact of IL-10 promoter gene polymorphism between on survival and on response or probability of progression, could be explained by the another role of IL-10 in host immunity besides IL-10 dependent bcl-2 mediated chemoresistance or its contribution of lymphoma growth through autocrine/paracrine loops. In lymphoma patients, both lymphoma and bystander reactive cells produced IL-10. Lech-Maranda *et al* (2004) have suggested that IL-10 promoter gene polymorphism may be involved in the host-tumour relationship and that increased IL-10 production within the tumour microenviroment might be tumour protective. In the present study population of T-cell NHL, *IL10* polymorphism may have a similar impact on the survival of patients with T-NHL, although some controversy remains regarding the identity of the IL-10 high inducibility allele in each ethnic population. Accordingly, the constitutional production of IL-10 by host T cells may also contribute to the survival of T-cell NHL patients. However, further studies with larger numbers of patients are necessary to investigate the specific individual subtypes of T-NHL.

Besides IL-10 promoter gene polymorphism, other prognostic factors identified in the current study were relatively consistent with other investigations on the prognostic factors of T-cell NHL (Ansell *et al*, 1997; Gallamini *et al*, 2004; Sonnen *et al*, 2005). These findings support that the characteristics and prognosis of our cohort is relatively reliable and reproducible in the analysis of the prognosis of T-cell NHL.

In conclusion, our findings demonstrated that IL-10 promoter gene polymorphism seems to influence on the clinical outcome of T-cell NHLs, especially in terms of overall survival. Further investigations of other types of gene polymorphism will lead to a better understanding of the biological background of T-cell NHL.

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