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Prognostic Significance of Lewis x Related Antigen Expression in Stage I Non-small Cell Lung Cancer

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LEWIS x (Lex), sialyl Lewis x (SLex) and Lewis y (Ley) are type II chain carbohydrate antigens which often accumulate in various cancer tissues [1], and the expression of these antigens has been reported to correlate with prognosis [2–5]. They are synthesised at the cell membrane from a common basic structure, i.e., i antigen, with fucose and sialic acid conjugated by the catalysis of fucosyl and sialyltransferase. Because these synthetic pathways are thought to occur in a stepwise manner, Lex, SLex and Ley may be co-expressed even in a single tumour cell. Thus, in cases with the expression of two or more antigens, it may not be enough to study only a single antigen, but rather it may be necessary to study the co-expression of multiple antigens to estimate their prognostic significance. We, therefore, examined the immunohistochemical expression of these antigens in relation to the prognosis for patients with stage I non-small cell lung cancer (NSCLC).

132 consecutive patients with stage I non-small cell lung cancer, who underwent a curative tumour resection between 1975 and 1991, were included in this study. The surgical protocols were the same for all the patients, and none had received any adjuvant therapy. A streptavidin–biotinyl peroxidase complex method using antibodies against Lex (FH4, kindly provided by Dr Nakasaki, Second Department of Surgery, Tokai Medical School, Japan), SLex (FH6, provided by Otsuka Pharmaceutical, Tokushima, Japan) and Ley (BM1, Japan Immunoresearch Lab., Takasaki, Japan) was performed on formaldehyde-fixed tissues as previously reported [2]. The Lex staining was defined as positive if 5% or more of the cells had membranous staining. The SLex and Ley staining was defined as positive if 30% or more of the cells had membranous staining.

Of the 132 patients, 34 (26%) had blood-borne metastasis. 57 patients (43%) had tumours expressing at least two antigens. The 132 patients were divided into those with no antigen expression (group 0) (n = 31), only one antigen expressed (group 1) (n = 44), both Lex and Ley or SLex and Ley antigens expressed (group 2) (n = 36), and all three antigens expressed (group 3) (n = 21). Patients in groups 2 and 3 had a significantly shorter survival than those in groups 0 and 1. However, there was no significant difference in survival between the patients in groups 0 and 1, nor in groups 2 and 3 (Figure 1).

These results suggest that survival of patients whose tumours express at least two of these antigens is significantly shorter than that of patients whose tumours express only one of these antigens. Therefore, distant metastasis may occur through some co-operative function between the Lex and Ley, and the SLex and Ley antigens. SLex has been reported to be a ligand for the cell adhesion molecule called E-selectin [6, 7]. Lex also has been reported to interact with E-selectin, although with a lower affinity than SLex [6, 8]. Alternatively, cell–cell adhesion through the Ley-to-Ley interaction is repellent, and Ley expression has been reported to correlate with cell motility [9, 10]. Thus, it can be postulated that Lex and SLex play some role in defining the adhesion of cancer cells to the vascular beds, and Ley in defining the invasive potential, namely, the likelihood of blood vessel invasion or transmigration of the tumour from the site of vascular arrest to the extracellular matrix.

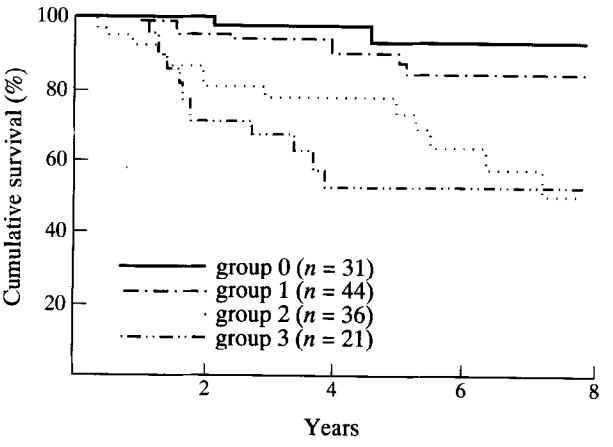

Figure 1. The relationship between survival and Lewis antigen expression of non-small cell lung cancer. Group 0, tumours not expressing Lex, SLex and Ley antigens; group 1, tumours expressing only one antigen; group 2, tumours expressing both Lex and Ley, or SLex and Ley antigens; group 3, tumours expressing all three antigens. $P < 0.01$, group 3 versus group 0 and 1; group 2 versus group 0; $P < 0.02$, group 2 versus group 1; non significant: group 0 versus group 1, group 2 versus group 3.

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